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

FORM 20-F

(Mark One)

☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

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

For the fiscal year ended December 31, 2016

OR

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

For the transition period from _____ to _____

OR

☐ **SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Date of event requiring this shell company report _____
Commission file number 001-37569

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

N/A
(Translation of Registrant's name into English)

Ireland
(Jurisdiction of incorporation or organization)
900 Northbrook Drive
Suite 200
Trevose, PA 19053
+1 610-254-9200
(Address of principal executive offices)
Stephen Long, Chief Legal Officer
Strongbridge Biopharma plc
900 Northbrook Drive
Suite 200
Trevose, PA 19053
+1 610-254-9200
(Name, telephone, email and/or facsimile number and address of Company contact person)

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)

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None
(Title of Class)

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the Annual Report:

35,335,026 ordinary shares were issued and outstanding as of March 10, 2017.

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

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. ☐ Yes ☐☒ No

Note—checking the box above will not relieve any registrant required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 from their obligations under those sections.

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). ☐☒ Yes ☐ No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act. (Check one):

Large Accelerated Filer ☐ Accelerated Filer ☐ Non-Accelerated Filer ☐☒

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP L ☒ International Financial Reporting Standards as issued by the International Accounting Standards Board ☐ Other ☐

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow. ☐ Item 17 ☐ Item 18

If this is an Annual Report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). ☐ Yes ☐☒ No

Strongbridge Biopharma plc
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Introduction

As used herein, "Strongbridge Biopharma", the "Company", "we", "our" and "us" refer to Strongbridge Biopharma plc and its consolidated subsidiaries, unless the context requires otherwise.

The consolidated financial statements and other financial data contained in this Annual Report on Form 20-F are presented in United States dollars ("$") and are prepared in accordance with generally accepted accounting principles in the United States (U.S. GAAP).

Solely for convenience, the trademarks and trade names in this Annual Report on Form 20-F 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 on Form 20-F are the property of their respective owners.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 20-F contains forward-looking statements that involve substantial risks and uncertainties. The forward-looking statements are contained principally in the sections of this Annual Report on Form 20-F titled "Risk Factors," "Information on the Company," and "Operating and Financial Review and Prospects." All statements, other than statements of historical facts, contained in this Annual Report on Form 20-F, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, 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. Other factors that may cause our actual results or developments to differ materially from the expectations contained in the forward-looking statements include, but are not limited to:

- our ability to successfully commercialize Keveyis;
- the timing, progress and results of clinical and preclinical trials for our product candidates, including statements regarding the timing of initiation and completion of these trials, enrollment of patients, dosing of subjects and the period during which the results of these trials will become available;
- our estimates regarding future revenue, expenses, capital requirements and needs for additional financing;
- our ability to become profitable;
- our ability to effectively manage our anticipated growth;
- our ability to secure additional financing when needed on acceptable terms;
- the implementation of our business model, as well as strategic plans for our business, product candidates and technology;
- our strategy to in-license, acquire and develop new product candidates and our ability to execute that strategy;
- potential product liability claims and our ability to obtain adequate insurance;
- potential development and commercial synergies from having multiple product candidates for related indications;
- potential benefits of the clinical development and commercial experience of our management team;
- our ability to attract or retain key employees, advisors or consultants;
- our ability to successfully commercialize our product candidates;

- our commercialization, marketing and manufacturing capabilities and strategy;
- our ability to rely on orphan drug designation for market exclusivity;
- our ability to effectively market any product candidates that receive regulatory approval with a small, focused sales force;
- the timing, scope or likelihood of regulatory filings and approvals for our product candidates;
- our ability to develop and maintain relationships with manufacturers, clinical research organizations and other important contractors and consultants;
- our ability to advance our product candidates through various stages of development, especially through pivotal safety and efficacy trials;
- our expectation regarding the safety and efficacy of our product candidates;
- the potential clinical utility and benefits of our product candidates;
- developments and projections relating to our competitors or our industry;
- the impact of government laws and regulations in the United States and foreign countries;
- our estimates regarding the potential market opportunity for our products and product candidates;
- our ability to expand, protect and enforce our intellectual property rights;
- our ability to defend against assertions or claims by third parties that we infringe on their intellectual property rights;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act; and
- our status as a foreign private issuer under the Securities Exchange Act of 1934, as amended (the "Exchange Act").

We have included important factors in this Annual Report on Form 20-F, particularly the risks discussed in the section of this Annual Report on Form 20-F titled "Risk Factors," that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. You should not place undue reliance on our forward-looking statements because actual results could differ materially from our intentions, plans, expectations, anticipations, projections, estimations, predictions, outlook, assumptions and beliefs about the future. Moreover, our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 20-F as well as the documents that we reference herein and have filed as exhibits to this Annual Report on Form 20-F. The forward-looking statements contained in this Annual Report on Form 20-F are made as of the date of this Annual Report on Form 20-F, and we do not assume any obligation to update any forward-looking statements, except as required by applicable law.

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

A. **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, 2016, 2015, 2014 and 2013 and the balance sheet data as of December 31, 2016, 2015 and 2014 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 on Form 20-F and the section in this filing titled "Operating and Financial Review and Prospects." 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,			
	2016	2015	2014	2013
	(in thousands, except share and per share data)			
Consolidated Statement of Operations Data:				
Operating expenses:				
Research and development	$ 20,023	$ 20,135	$ 5,844	$ 2,534
General and administrative	14,875	22,719	4,588	2,658
Impairment of intangible assets	15,828	—	—	—
Total operating expenses	50,726	42,854	10,432	5,192
Operating loss	(50,726)	(42,854)	(10,432)	(5,192)
Other income (expense), net:				
Foreign exchange loss	(69)	(124)	(204)	(570)
Unrealized gain on fair value of warrants	638	—	—	—
Interest Expense	(20)	—	—	—
Other (expense) income, net	(1,180)	(1,105)	486	282
Total other (expense) income, net	(631)	(1,229)	282	(288)
Loss before income taxes	(51,357)	(44,083)	(10,150)	(5,480)
Income tax benefit	2,638	450	480	93
Net loss	(48,719)	(43,633)	(9,670)	(5,387)
Net loss attributable to non-controlling interest	122	53	—	—
Net loss attributable to Strongbridge Biopharma	$ (48,597)	$ (43,580)	$ (9,670)	$ (5,387)
Net loss attributable to ordinary shareholders:				
Basic	$ (48,597)	$ (43,580)	$ (9,670)	$ (5,387)
Diluted	$ (49,236)	$ (43,580)	$ (9,670)	$ (5,387)
Net loss per share attributable to ordinary shareholders:				
Basic	$ (2.26)	$ (2.62)	$ (1.20)	$ (0.88)
Diluted	$ (2.27)	$ (2.62)	$ (1.20)	$ (0.88)
Weighted-average shares used in computing net loss per share attributable to ordinary shareholders:				
Basic	21,550,353	16,606,669	8,043,175	6,017,895
Diluted	21,655,564	16,606,669	8,043,175	6,017,895

	December 31,		
	2016	2015	2014
	(in thousands)		
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$ 66,837	$ 51,623	$ 15,632
Total assets	137,531	97,330	23,698
Total liabilities	70,559	6,403	4,868
Total shareholders' equity	66,972	90,927	18,821

B. CAPITALIZATION AND INDEBTEDNESS

Not applicable.

C. REASONS FOR THE OFFER AND USE OF PROCEEDS

Not applicable.

D. 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 on Form 20-F, 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 Limited Operating History

We have a limited operating history on which to assess our business, have incurred significant losses over the last several years, and anticipate that we will continue to incur losses until we successfully commercialize Keveyis and one or more of our product candidates.

Until we acquired the U.S. marketing rights to Keveyis®, in December 2016, we were a development-stage biopharmaceutical company with a limited operating history. We have not yet demonstrated an ability to successfully complete a large-scale, pivotal clinical trial, obtain regulatory approval or manufacture and commercialize a product candidate. Consequently, we have no meaningful commercial operations upon which to evaluate our business and predictions about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

Since inception, we have incurred significant operating losses. Our net loss was $48.6 million and $43.6 million for the years ended December 31, 2016 and 2015, respectively. As of December 31, 2016 we had an accumulated deficit of $129.4 million. We have devoted substantially all of our financial resources to identifying, in-licensing, acquiring and developing our product candidates, including conducting clinical trials as well as providing general and administrative support for these operations.

To date, we have financed our operations primarily through private placements of equity securities and the proceeds from our initial public offering of ordinary shares in the United States in October 2015. The amount of our future net losses will depend, in part, on whether we successfully commercialize Keveyis and the rate of our future expenditures as well as our ability to obtain funding through strategic collaborations or grants. To become and remain profitable, we must successfully commercialize Keveyis and develop and eventually commercialize one or more of our product candidates with significant market potential.

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. It may be several years, if ever, before we receive regulatory approval and have a product candidate other than Keveyis approved for commercialization. Our future revenue from Keveyis and from any other product candidates approved for commercialization will depend upon the size of the markets in which our product candidates are marketed, or in which they may receive approval, and our ability to achieve market acceptance and adequate market share for our product candidates in those markets.

We expect to continue to incur significant expenses and increasing operating losses until we successfully commercialize Keveyis and one or more of our product candidates. We anticipate that our expenses will increase substantially if and as we:

- establish a sales, marketing and distribution infrastructure to commercialize Keveyis and any other products for which we may obtain regulatory approval;
- 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 planned future 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.

Further, the net losses we incur 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.

We have never generated any revenue from product sales and may never be profitable.

We have only one product approved for commercialization, and two product candidates in development, and have never generated any revenue from product sales. We will not generate revenue from product sales unless and until we launch Keveyis or successfully complete the development of, obtain regulatory approval for and commercialize one or more of our product candidates. Our ability to generate future revenue from product sales and become profitable depends heavily on our success in many areas, including, but not limited to:

- integrating Keveyis and any other products or product candidates that we in-license or acquire, as well as completing research, formulation and process development, and preclinical or clinical development, as applicable, of those product candidates, including successfully completing clinical trials of those product candidates;

- obtaining regulatory approval of our product candidates;
- incurring additional costs as we advance our product candidates;
- developing a sustainable and scalable manufacturing process for our product candidates, if approved;
- maintaining supply and manufacturing relationships with third parties that can conduct the manufacturing process development and provide adequate, in amount and quality, products to support clinical development and the market demand for our product candidates, if approved;
- obtaining market acceptance of Keveyis and our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- identifying, assessing, in-licensing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Given the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses could increase beyond expectations if we are required by the FDA or the EMA, or any comparable foreign regulatory agency, to perform nonclinical and preclinical studies or clinical trials in addition to those that we currently anticipate.

We anticipate incurring significant costs associated with commercializing Keveyis and any other product candidates that are approved. Further, our revenue will be dependent, in part, upon the size of the markets in the territories for which we have received regulatory approval, the accepted price for the product, 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 sales of our product candidates. If we are not able to generate sufficient revenue from the sale of any approved products, we may never become profitable. 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 any of the foregoing 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 expect that we will need substantial 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 formerly called COR-003) and veldoreotide (formerly called COR-005). 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 obtain regulatory approval for, and to commercialize, our product candidates.

As of December 31, 2016, we had cash and cash equivalents of $66.8 million. We currently believe that our existing cash and cash equivalents, excluding any additional borrowings under the credit facility, is sufficient to fund planned operations into 2019. However, this estimate is based on assumptions that may prove to be incorrect, our operating plans may change as a result of many factors that may currently be unknown to us, and we may need to seek

additional funds sooner than planned. Our future funding requirements will depend on many factors, including, but not limited to:

- the amount of revenue that we receive from sales of Keveyis;
- the cost and timing of establishing 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;
- whether we borrow any additional amounts under our $40 million credit facility;
- 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 candidates, if 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, equity offerings, debt financings, grants, and license and development agreements in connection with any collaborations. Although we have borrowed only $20 million available under our $40 million credit facility, the remainder may be borrowed only if certain product revenue and clinical data milestones are achieved. 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 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 commercialize Keveyis and advance the clinical and preclinical development of our product candidates, we expect to experience significant 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.

In order to increase adoption and sales of Keveyis and other product candidates we may commercialize, we will need to continue developing our commercial organization as well as recruit and retain qualified sales representatives.

Part of our strategy is to continue to build a biopharmaceutical company to successfully execute the commercialization of our products. We may not be able to successfully commercialize our products in the United States or in any other territories where we have commercial rights. We do not have any experience commercializing products on our own. In order to commercialize any approved products, we must continue to build our sales, marketing, distribution, managerial and other non-technical capabilities. Although we intend to establish an initial sales force consisting of approximately twelve orphan disease sales representatives, we currently have limited resources compared to some of our competitors, and the continued development of our own commercial organization to market our products and any additional products we may acquire will be expensive and time-consuming. We also cannot be certain that we will be able to continue to successfully develop this capability.

If we are unable to effectively train and equip our sales force, our ability to successfully commercialize our products will be harmed.

As we recently acquired U.S. marketing rights to Keveyis and hired our sales force, the members of our sales force will have limited experience promoting Keveyis. As a result, we will be required to expend significant time and resources to train our sales force to be effective in their sales efforts for Keveyis. For example, we must train our sales force to ensure that a consistent and appropriate message about Keveyis is being delivered to our potential customers. Our sales representatives may also experience challenges promoting Keveyis when we call on physicians and their office staff. 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 about the benefits of our products and their proper administration and label indication, as well as our patient access programs, our efforts to

successfully commercialize our products could be put in jeopardy, which could have a material adverse effect on our financial condition, share price and operations.

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;
- for product candidates we seek to in-license or acquire, we may not be able to agree to acceptable terms with the licensor or owner of those product candidates;
- 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. We have had limited experience integrating other businesses or product candidates, or in-licensing or acquiring other product candidates. The recent acquisition of the U.S. marketing rights of Keveyis and our June 2015 acquisition of veldoreotide are still being integrated into our business. The integration process following these or any future transactions 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.

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. 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 or Dr. Cohen, 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.

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

Our computer systems, as well as those of our clinical research organizations, or 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 Business

We depend entirely on the success of Keveyis and two product candidates, which are still in clinical development. If we do not obtain regulatory approval for and successfully commercialize one or more of our product candidates or we experience significant delays in doing so, we may never become profitable.

We currently have one product approved for sale and two product candidates in development. We have invested, and continue to expect to invest, a significant portion of our efforts and financial resources in the development of our two product candidates, which are still in clinical development. Our ability to generate product revenues will depend heavily on our successful commercialization of Keveyis and our eventual commercialization, if approved, of one or more of our product candidates currently in development. We are not permitted to market or promote any product candidate before we receive regulatory approval from the FDA, EMA or any comparable foreign regulatory agency, and we may never receive such regulatory approval for our product candidates currently in development. The success of Recorlev and veldoreotide will depend on several additional factors, including, but not limited to, the following:

- successfully completing clinical trials that demonstrate the efficacy and safety of our product candidates;
- successfully completing formulation and process development activities;
- acceptance of our product candidates by patients and the medical community;
- a continued acceptable safety profile following approval;
- obtaining and maintaining healthcare coverage and adequate reimbursement; and
- competing effectively with other therapies, including with respect to the sales and marketing of our product candidates, if approved.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and changes in the competitive landscape. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully complete clinical trials or eventually commercialize our product candidates, if approved.

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 products 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. For example, the results generated to date in preclinical studies or clinical trials for our product candidates do not ensure that later preclinical studies or clinical trials will demonstrate similar results. Further, we have limited clinical data for each of our product candidates and have not completed Phase 3 clinical trials for any of our product candidates. 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.

Companies in the biopharmaceutical industry may suffer setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier clinical trials. For example, levoketoconazole was previously studied for the treatment of type 2 diabetes. In December 2005, prior to the initiation of the first clinical trial by DiObex, our licensee, the FDA placed a clinical hold relating to a safety concern for use of a dosage above 600 mg/day. DiObex modified the clinical trial protocol to limit the highest dose to 600 mg/day, and the clinical hold was lifted by the FDA in February 2006. Furthermore, levoketoconazole did not demonstrate a reduction in blood glucose levels in a small Phase 2 clinical trial in patients with type 2 diabetes mellitus, the original indication for which it was being developed. 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 institutional review boards, 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.

Positive or timely results from preclinical or early stage clinical trials do not ensure positive or timely results in late stage clinical trials or regulatory approval by the FDA, EMA or any comparable foreign regulatory agency. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Preclinical and clinical data are often susceptible to varying interpretations and analyses. 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. The FDA, EMA and any comparable foreign regulatory agency 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.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous 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 late stage clinical product candidates, results may differ in general on the basis of the larger number of clinical trial sites and additional countries involved in Phase 3 clinical trials. 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 June 2015, we acquired veldoreotide and were not involved in and had no control over the preclinical and clinical development of this product candidate prior to such acquisition. As a result, 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. These factors could result in increased costs and delays in the development of veldoreotide, which could hurt our ability to generate future revenues from this product candidate.

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

Our future success is dependent upon our ability to successfully develop, obtain regulatory approval for and then successfully commercialize one or more of our product candidates. Although 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. We cannot be certain that any of our product candidates will be successful in clinical trials or receive regulatory approval. 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 new drug application, or 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.

Any of our current or future product candidates could take a significantly longer time to gain regulatory approval than expected 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.

Several elements of the SONICS Phase 3 clinical trial design for Recorlev 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. In communication we had with the FDA, they 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 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. 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 intend to seek formal advice and guidance from the FDA and the EMA prior to advancing veldoreotide into further studies and pivotal clinical trials. If the feedback we receive is different from what we currently anticipate, this could delay the development and regulatory approval process for this product candidate.

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 numerous and varying regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing and controls, clinical trials, commercial sales, pricing and distribution of our product candidates. 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 will result in our being unable to market and sell such products. If we fail to obtain approval in any jurisdiction, the geographic market for our product

candidates could be limited. Similarly, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

If we or others identify previously unknown, serious side effects of Keveyis, we may be required to perform lengthy additional clinical trials, change the labeling of Keveyis or withdraw it from the market.

If we or others identify previously unknown, serious side effects of Keveyis:

- regulatory authorities may withdraw their approvals;
- we may be required to conduct additional clinical trials, make changes in labeling, implement changes to or obtain re-approvals of facilities that manufacture Keveyis;
- we may experience a significant drop in the sales of Keveyis;
- our reputation in the marketplace may suffer; and
- we may become the target of lawsuits, including class action lawsuits.

Any of these events could harm or prevent sales of Keveyis or could increase the costs and expenses of commercializing and marketing Keveyis.

Physicians may accept Keveyis slowly or may never accept it, 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 primary periodic paralysis. Because primary periodic paralysis 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 primary periodic paralysis, such as acetazolamide;
- 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.

The failure of Keveyis to achieve commercial success could prevent us from generating sufficient revenue 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, if any, we may need to abandon our development of such product candidates.

If our product candidates are 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 showed promise in preclinical or early stage testing have later been found to cause side effects that restricted their use and prevented further development of the compound for larger indications.

For example, 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. In addition, headache and gastrointestinal effects such as nausea and diarrhea were 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 one or more of our product candidates receives regulatory approval, and we or others later identify undesirable side effects caused by such product(s), 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 prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, financial condition, and results of operations.

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.

We may become exposed to costly and damaging liability claims, either in connection with the sale of Keveyis or other 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. Our first commercial product is Keveyis. The current and future use of product candidates by us in clinical trials, and the sale of Keveyis and 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. Any claims against us, regardless of their merit, could be difficult and costly to defend, and could compromise the market acceptance of Keveyis, our product candidates 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. If Keveyis or any of our product candidates were to cause adverse side effects during clinical trials or after approval of the product candidate, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use Keveyis or our product candidates.

We have limited product liability insurance that offers coverage we believe to be appropriate for a company marketing a single pharmaceutical product and developing others. 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 Keveyis or our product candidates, 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 could exceed our total assets.

We have never commercialized a product candidate and we may lack the necessary expertise, personnel and resources to successfully commercialize any of our products that receive regulatory approval on our own or together with suitable partners.

We have never commercialized a product candidate. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, in-licensing or acquiring our product candidates, identifying potential product candidates and undertaking preclinical studies and clinical trials of our product candidates. We currently have a very limited sales force and marketing and distribution capabilities. To achieve commercial success of Keveyis and any product candidates that are approved, we will have to develop our own sales, marketing and supply capabilities or outsource these activities to a third party.

Factors that may affect our ability to commercialize Keveyis and our product candidates on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, obtaining access to or persuading adequate numbers of physicians to prescribe our product candidates and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization requires significant investment, is time consuming and could delay the launch of our product candidates. We may not be able to build an effective sales and marketing organization in the United States, the European Union or other key global markets. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of Keveyis and our product candidates, we may not generate revenues from them.

We operate in a highly competitive and rapidly changing industry, which may result in our 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 new drug 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.

Keveyis is an oral carbonic anhydrase inhibitor, that was approved in the United States to treat hyperkalemic, hypokalemic and related variants of primary periodic paralysis (PPP). Acetazolamide, another 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.

We are currently aware of various companies that are marketing existing drugs that may compete with Recorlev such as Corcept Therapeutics and Novartis. The treatment of endogenous Cushing's syndrome patients who fail or are ineligible for surgery in the United States and Europe are: Korlym (mifepristone) marketed by Corcept Therapeutics in the United States; Signifor (pasireotide) marketed by Novartis in the United States and European Union; and ketoconazole, metyrapone and mitotane marketed by HRA in the European Union. Novartis has submitted an NDA/MAA for Signifor (pasireotide) LAR in Cushing's disease. Additionally, LCI-699 (osilodrostat) is currently in Phase 3 clinical development by Novartis in Cushing's disease patients. Corcept is developing CORT125134, a second-generation glucorticoid receptor modulator; currently in Phase 2. HRA Pharma is developing metyrapone for the US market; currently in Phase 2. Millendo is developing ATR-101, a selective acyl-CoA:cholesterol acyltransferase 1 (ACAT) inhibitor, currently in Phase 2. In addition, Ketoconazole is the most commonly prescribed drug therapy for the treatment of endogenous Cushing's syndrome, even though it is not approved for this use in the United States. Regulatory approval of ketoconazole in the United States for the treatment of endogenous Cushing's syndrome could significantly increase competition for Recorlev due to their similar mechanisms of action.

We are currently aware of various companies that are marketing existing drugs that may compete with veldoreotide such as Novartis, Ipsen and Pfizer. In addition, a number of acromegaly therapies are 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 U.S. 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. Four additional therapies are in Phase 2 clinical development for acromegaly: octreotide long-acting depot (CAM-2029) developed by Novartis and Camurus; ITF-2984 developed by Italfarmaco; BIM-23B065 developed by Ipsen; and ATL-1103 developed by Antisense Therapeutics.

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 product candidates or our technology 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, 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, or 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. Although Recorlev is being developed as a new chemical entity, or NCE, we intend to rely on orphan drug exclusivity rather than NCE exclusivity for nonpatent protection 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 generic or 505(b)(2) applicant that seeks to market its product 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, 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.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage and reimbursement levels and pricing policies.

The successful commercialization of Keveyis and our product candidates, if approved, will depend, in part, on the extent to which coverage and reimbursement for our 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, or 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 Keveyis and/or any product candidate that we commercialize, and, if available, that the reimbursement rates will be adequate. If we are unable to obtain adequate levels of coverage and reimbursement for Keveyis and/or our product candidates, our ability to generate revenue 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 Keveyis or 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, medical necessity or both 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.

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 our product candidates and the future revenues we may expect to receive from these products. 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.

Our products may not gain market acceptance, in which case we may not be able to generate product revenues.

Even if the FDA, EMA or any comparable foreign regulatory agency approves the marketing of any product candidates that we develop, physicians, healthcare providers, patients or the medical community may not accept or use them. Efforts to educate the medical community and third-party payors on the benefits of our products or product candidates may require significant resources and may not be successful. If Keveyis, Recorlev, veldoreotide or any other product candidate that we develop does not achieve an adequate level of acceptance, we may not generate significant product revenues or any profits from operations. The degree of market acceptance of Keveyis, Recorlev, veldoreotide or any other product candidates that are approved for commercial sale will depend on a variety of factors, including, but not limited to:

- whether clinicians and potential patients perceive our 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 of 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 Keveyis, Recorlev, veldoreotide or any other product candidate we may develop is difficult to estimate precisely. Our estimates of the potential market opportunity 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 the assumptions proves to be inaccurate, then the actual market for Keveyis, Recorlev or our other product candidates could be smaller than our estimates of the potential market opportunity. If the actual market for Keveyis, Recorlev or our other product candidates is smaller than we expect, or if the products fail to achieve an adequate level of acceptance by physicians, health care payors and patients, our product revenue 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 our products or product candidates, we may be unable to achieve a sufficient market share to make our products profitable.

The Orphan Drug designation for Keveyis and our 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 Keveyis and/or our other product candidates.

Although Keveyis and our 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 products at a lower price, in which case our business could be harmed.

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. However, 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.

Laboratoire HRA Pharma (HRA) received Orphan Drug designation in the United States and the EU for the use of mifepristone to treat a subtype of Cushing's syndrome. HRA began and terminated a Phase 2 clinical trial in Europe and the United States for this indication. Exelgyn Laboratories, which operates as a subsidiary of Medi Challenge (Pty) Ltd., received Orphan Drug designation for mifepristone to treat Cushing's syndrome in the EU, but it has stated that it has not yet conducted any clinical trials.

The terms of our credit facility place restrictions on our operating and financial flexibility.

The Loan Agreement with Oxford and Horizon includes affirmative and negative covenants applicable to us and any subsidiaries we create in the future. The affirmative covenants include, among others, covenants requiring us to maintain our legal existence and good standing and governmental approvals necessary for us and our subsidiaries to perform our respective businesses and obligations under the Loan Agreement, deliver certain financial reports to the Lenders, maintain insurance coverage, comply with certain financial covenants, dissolve our subsidiary, BioPancreate Inc., within six months of the effective date of the Loan Agreement, and enter into an intercompany license or other agreement with our subsidiary, Strongbridge U.S. Inc., pursuant to which Strongbridge U.S. Inc. will have the exclusive right to market and sell Keveyis products in the United States. The negative covenants include, among others, restrictions on our transferring collateral, changing our business, management, ownership or business location, engaging in mergers or acquisitions, incurring additional indebtedness, paying dividends or making other distributions, making investments, creating liens, or entering into transactions with affiliates, in each case subject to certain exceptions.

The Loan Agreement also includes events of default, the occurrence and continuation of which could cause interest to be charged at the rate that is otherwise applicable plus 5.0% and would provide Oxford, as collateral agent, with the right to exercise remedies against us and the collateral securing the credit facility, including foreclosure against our properties securing the credit facilities, including our cash. These events of default include, among other things, our failure to pay any amounts due under the Loan Agreement, a breach of covenants under the Loan Agreement, a material adverse change, our insolvency, the occurrence of a default under any agreement with a third party that would result in a payment by us or our subsidiaries of greater than $100,000, and/or one or more judgments against us or our subsidiaries in an amount greater than $100,000 individually or in the aggregate.

Our ability to make scheduled payments on or to refinance our indebtedness depends on our future performance and ability to raise additional sources of cash, which is subject to economic, financial, competitive and other factors beyond our control. If we are unable to generate sufficient cash to service our debt, we may be required to adopt one or more alternatives, such as selling assets, restructuring our debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. If we desire to refinance our indebtedness, our ability to do so will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

Risks Related to Our Reliance on Third Parties

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, or if these third-party manufacturers fail to comply with FDA regulations or otherwise fail to meet our requirements, our business will be harmed.

Taro Pharmaceuticals North America, Inc., Inc. produces all of our requirements of 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.

The facilities used by our vendors to manufacture our product and product candidates must be approved by the FDA. We do not control the manufacturing processes of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements known as current good manufacturing practices (cGMPs). If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict requirements of the FDA or others, they will not be able to maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our products or if it withdraws any such approval, we may need to find alternative manufacturing facilities, which would significantly hamper our ability to develop, obtain regulatory approval for or market our products. In addition, sanctions could be imposed on us, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our product candidates, delays, suspension or withdrawal of approvals, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could harm our business. If our suppliers fail to manufacture Keveyis or our product candidates on a timely basis in the quantities that we require, or fail to maintain manufacturing capabilities that meet FDA standards, we may exhaust our Keveyis inventory and not be able to generate revenue, or clinical development programs may be delayed.

We and our collaborators and contract manufacturers are subject to significant regulation with respect to manufacturing of Keveyis and our product candidates. 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 therapeutics 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.

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 Good Manufacturing Practices, or cGMP, current Good Clinical Practices, or cGCP, and Good Laboratory Practice, or 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.

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.

Risks Related to Our Intellectual Property

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

In addition to the exclusivity provided for Keveyis and our product candidates with regulatory orphan drug status, we rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies 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 with respect to our proprietary technology and product candidates.

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 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, or 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, or 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 Keveyis and our product candidates, if approved, and 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 Keveyis 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.

Although we are not currently involved in any litigation, we may be 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.

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 Government Oversight and Regulation

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 obtain regulatory approval will remain subject to continual 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, adverse event reporting, storage, advertising and marketing restrictions, 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. Because our two Phase 3 clinical trials of Recorlev will collect safety data for approximately 125 patients, we currently expect that we would 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;
- 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 key 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 primary periodic paralysis 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 in Europe. Even though we have obtained orphan drug designation for our key 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. Further, even though we have obtained orphan drug designation for our key product candidates, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. 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.

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, as amended by the Health Care and Education Reconciliation Act, or collectively, PPACA, 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.

In 2017, the U.S. Congress has been assessing new legislation designed to repeal and replace core sections of the PPACA. We expect the U.S. Congress to continue to review and assess this legislation, referred to as the American Health Care Act (AHCA), along with other alternative health care reform proposals throughout 2017. Recent Congressional efforts such as the AHCA proposal adds to the uncertainty of the legislative changes enacted as part of PPACA. These changes will likely take time to unfold, and could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the PPACA. 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. In addition, many companies in our industry have received governmental requests for documents and information relating to drug pricing and patient support programs. If we were to become subject to similar requests, we could incur significant expense and experience reputational harm, 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, the Trump Administration has 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. 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.

Our relationships with customers, consultants and payors will be 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 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 the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or 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 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 sales of Keveyis;
- 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 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 35,335,026 ordinary shares outstanding. We have also filed a Registration Statement on Form S-8, registering all 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.

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, or 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. See Part I, Item 10A "Additional Information-Share Capital." 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 passive foreign investment company, or 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.

We are a foreign private issuer and, as a result, we are not subject to U.S. proxy rules and are subject to Exchange Act reporting obligations that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.

We report under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as a non-U.S. company with foreign private issuer status. Because we qualify as a foreign private issuer under the Exchange Act and although we are subject to Irish laws and regulations with regard to such matters and intend to furnish quarterly financial information to the U.S. Securities and Exchange Commission (the "SEC), we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including: (1) the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations with respect to a security registered under the Exchange Act; (2) the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and (3) the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K upon the occurrence of specified significant events. In addition, foreign private issuers are not required to file their annual report on Form 20-F until four months after the end of each financial year, while U.S. domestic issuers that are accelerated filers are required to file their annual report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers are also exempt from the Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

As a foreign private issuer and as permitted by the listing requirements of NASDAQ, we may rely on certain home country governance practices rather than the corporate governance requirements of NASDAQ.

We are a foreign private issuer. As a result, in accordance with NASDAQ Listing Rule 5615(a)(3), we comply with home country governance requirements and certain exemptions thereunder rather than complying with certain of the corporate governance requirements of NASDAQ.

Irish law does not require that a majority of our board of directors consist of independent directors. Our board of directors therefore may include fewer independent directors than would be required if we were subject to NASDAQ Listing Rule 5605(b)(1). In addition, we are not subject to NASDAQ Listing Rule 5605(b)(2), which requires that independent directors must regularly have scheduled meetings at which only independent directors are present.

Our Articles of Association (hereinafter referred to as our Articles) provide that at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy, but no such proxy shall be voted or acted upon at any subsequent meeting, unless the proxy expressly provides for this. Irish law does not require shareholder approval for the issuance of securities in connection with the establishment of or amendments to equity-based compensation plans for employees. To this extent, our practice varies from the requirements of NASDAQ Listing Rule 5635, which generally requires an issuer to obtain shareholder approval for the issuance of securities in connection with such events.

See Part I, Item 10B "Additional Information-Memorandum and Articles of Association." As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

We may lose our foreign private issuer status, which would then require us to comply with the Exchange Act's domestic reporting regime and cause us to incur significant legal, accounting and other expenses.

We are a foreign private issuer and therefore we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers. Losing our status as a foreign private issuer would require us to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers. In order to maintain our current status as a foreign private issuer, either (1) a majority of our ordinary shares must be either directly or indirectly owned of record by non-residents of the United States or (2)(A) a majority of our executive officers or directors may not be United States citizens or residents, (B) more than 50% of our assets cannot be located in the United States and (C) our business must be administered principally outside the United States. If we lose this status, we would be required to comply with the Exchange Act reporting and other requirements applicable to U.S. domestic issuers, which are more detailed and extensive than the requirements for foreign private issuers. We may also be required to make changes in our corporate governance practices in accordance with various SEC and stock exchange rules. The regulatory and compliance costs to us under U.S. securities laws if we are required to comply with the reporting requirements applicable to a U.S. domestic issuer may be significantly higher than the cost we would incur as a foreign private issuer. As a result, we expect that a loss of foreign private issuer status would increase our legal and financial compliance costs and would make some activities highly time consuming and costly. We also expect that if we were required to comply with the rules and regulations applicable to U.S. domestic issuers, it would make it more difficult and expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These rules and regulations could also make it more difficult for us to attract and retain qualified members of our board of directors.

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, or 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. See Part I, Item 10B "Additional Information-Memorandum and Articles".

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 as long as we continue to be an "emerging growth company," we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including 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 the 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 the 2016 Investors in the 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 United States 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.

We have identified a material weakness in our internal control over financial reporting. If we fail to remediate the identified material weakness, or if we otherwise fail to maintain effective internal control over financial reporting and disclosure controls and procedures, we may not be able to accurately report our financial results, detect or prevent fraud, or file our periodic reports in a timely manner, which may, among other adverse consequences, cause investors to lose confidence in our reported financial information and lead to a decline in our stock price.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. We are required under Section 404(a) of the Sarbanes-Oxley Act to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This assessment includes disclosure of any material weaknesses identified by our management in our internal control over financial reporting.

In connection with the preparation of our consolidated financial statements for the year ended December 31, 2016, we concluded that there was a material weakness in the design and operating effectiveness of our internal control over our valuation of the warrants issued in connection with our December 31, 2016 private placement of ordinary shares. As defined in SEC Regulation S-X, a material weakness is a control deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected on a timely basis. The initial calculation was performed with incorrect inputs, which resulted in an adjustment to our consolidated financial statements included in this Form 20-F. As a consequence of this material weakness, management concluded that our internal control over financial reporting, and consequently our disclosure controls and procedures, were not effective as of December 31, 2016.

ITEM 4. INFORMATION ON THE COMPANY

Corporate Information

Strongbridge Biopharma plc, an Irish public limited company, was established on May 26, 2015 under the name Cortendo plc. On September 4, 2015, Cortendo plc changed its name to Strongbridge Biopharma plc. We also have a wholly owned subsidiary, Cortendo AB, organized under the laws of Sweden. See Part I, Item 10I "Subsidiary Information" a for list of subsidiaries of the Company.

Our principal executive offices are located at 900 Northbrook Drive, Suite 200, Trevose, Pennsylvania, 19053 and our telephone number is +1 610-254-9200. For the purposes of Irish law, our registered office is Arthur Cox Building, Ten Earlsfort Terrace, Dublin 2, Ireland.

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 on Form 20-F.

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 (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. Keveyis, for

which we hold the U.S. marketing rights, has orphan drug exclusivity status in the United States through August 7, 2022.

In addition to this neuromuscular disease product, we have two clinical-stage product candidates for rare endocrine diseases, Recorlev® and veldoreotide. Recorlev (levoketoconazole, and formerly called COR-003) is a cortisol synthesis inhibitor currently being studied for the treatment of endogenous Cushing's syndrome. Veldoreotide (formerly called COR-005) is a next-generation somatostatin analog ("SSA") being investigated for the treatment of acromegaly, with potential additional applications in Cushing's syndrome and neuroendocrine tumors. Both Recorlev and veldoreotide have received orphan designation from the FDA and the European Medicines Agency (EMA).

Given the well-identified and concentrated prescriber base addressing our target markets, we intend to use a small, focused sales force to effectively market Keveyis and other products and product candidates, if approved, in the United States, the European Union and other key global markets. We believe that our ability to execute on this strategy is enhanced by the significant commercial and clinical development experience of key members of our management team.

Since the introduction of our new management team in August 2014, we have been building a rare disease, franchise-based business model focused on expansion through a disciplined in-licensing and acquisition strategy. In pursuit of our growth strategy, we have raised over $140 million in equity and debt financings since December 2014. We will continue to identify and evaluate the acquisition of products and product candidates 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.

Recent Developments

Acquisition of Keveyis Marketing Rights and Supply Agreement with Taro Pharmaceuticals Industries Ltd ("Taro")

In December 2016, we acquired the U.S. marketing rights to Keveyis (dichlorphenamide) from a subsidiary of Taro. Keveyis has received orphan drug exclusivity status in the U.S through August 7, 2022. Under the terms of the Asset Purchase Agreement, dated December 12, 2016, 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 (the "Supply Agreement"). 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 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.

Private Placement

On December 22, 2016, we raised $35 million in aggregate proceeds in a private placement (the "2016 Private Placement"). According to the terms of the Securities Purchase Agreement, dated December 22, 2016, we issued and sold 14,000,000 ordinary shares at a purchase price of $2.50 per ordinary share, as well as warrants to purchase 7,000,000 ordinary shares (the "Investor Warrants") to the investors (the "2016 Investors"). The Investor Warrants are exercisable at a price of $2.50 per share beginning on June 28, 2017 and expire in five years from June 28, 2017. In connection with the 2016 Private Placement, we entered into a registration rights agreement with the 2016 Investors pursuant to which we agreed to file a registration statement for the purpose of registering for resale (i) the ordinary shares purchased by the 2016 Investors in the 2016 Private Placement; (ii) the ordinary shares exercisable upon exercise of the Investor Warrants acquired by the 2016 Investors in the 2016 Private Placement; and (iii) any other ordinary shares held by a 2016 Investor that beneficially owned at least 1,000,000 ordinary shares following the closing of the 2016 Private Placement that qualified as "Registrable Securities" as defined therein (the "Registration Rights Agreement").

Loan Agreement with Oxford Finance LLC and Horizon Technology Finance Corporation

On December 28, 2016, we entered into a loan and security agreement (the "Loan Agreement") with Oxford Finance LLC ("Oxford") and Horizon Technology Finance Corporation ("Horizon") (collectively, the "Lenders"). The Loan Agreement provided for a $40 million credit facility, of which $20 million was borrowed initially. Under the Loan Agreement, we have access to two additional tranches of $10 million each which are available to us subject to the achievement of certain specified milestones. The borrowings pursuant to the Loan Agreement mature after 48 months. The Loan Agreement provides for interest-only payments initially for the first 18 months of the loan followed by an amortization period of 30 months, a final payment fee equal to 8% of the amount borrowed and interest payable at an annual rate equal to the sum of 8.22% plus the greater of 0.53% or the 30-day US LIBOR rate. The credit facility provides that if we satisfy certain milestones and borrow the final $10 million tranche, the interest-only period would be extended by an additional six months and the amortization period would be 24 months. We have granted a security interest in substantially all of our existing assets and assets acquired by us in the future, including intellectual property. The Loan Agreement contains facility and prepayment fees, customary affirmative and negative covenants and events of default.

Upon the execution of the Loan Agreement, we issued warrants to the Lenders to purchase an aggregate of 428,571 ordinary shares at an exercise price equal to $2.45 per share (the "Lender Warrants"). The Lender Warrants are immediately exercisable and expire after ten years. The Lender Warrants issued to the Lenders include a provision requiring us to file a registration statement to provide for the public resale of the ordinary shares to be issued upon exercise of the Lender Warrants.

On March 31, 2017 we entered into an amendment to the Loan Agreement that was made effective as of January 27, 2017 and provided for an extension to the dates by which the Company's Swedish subsidiary was required to enter into security documents granting security interests on certain of its assets in favor of Oxford, as collateral agent for the Lender, and to increase the amount of debt the Company can incur under, and the amount of cash collateral it can provide for purposes of, its corporate credit card program from $100,000 to $250,000. In connection with the amendment, the Company paid $150,000 to the Lenders.

Our Products and Product Candidates

- *Keveyis® (dichlorphenamide), an oral carbonic anhydrase inhibitor and the only therapy approved in the United States to treat hyperkalemic, hypokalemic and related variants of primary periodic paralysis.* PPP is a rare genetic, neuromuscular disorder that can cause extreme muscle weakness and/or paralysis. 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 received orphan drug exclusivity status in the U.S through August 7, 2022. Since May 2016, Taro has been supplying Keveyis on a non-commercial basis to patients through a single specialty pharmacy in the United States. We expect to commercially launch Keveyis in the United States in April 2017.

- *Recorlev™ (levoketoconazole, and formerly called COR-003), a cortisol synthesis inhibitor, 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. We are currently conducting SONICS, a pivotal, multinational Phase 3 clinical trial for Recorlev, and anticipate that the study will be fully enrolled in the second quarter of 2017, with top-line data for the primary efficacy analysis available in the first quarter of 2018. In addition, we plan to initiate LOGICS, a second pivotal 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 ongoing SONICS study in a randomized, double-blind, placebo-controlled study that will enroll approximately 35 patients, of which approximately two-thirds will

have completed the SONICS study. Enrollment in the LOGICS study is anticipated to begin mid-year 2017 and top-line data are expected in the third quarter of 2018.

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 anticipate that the studies supporting U.S. approval will likewise support approvals to market Recorlev elsewhere, including in the European Union.

- *Veldoreotide (formerly called COR-005), a novel somatostatin analogue (SSA), in Phase 2 clinical development for the treatment of acromegaly.* Based on the differentiated activation pattern to veldoreotide by somatostatin receptor subtypes ("SSTRs") and its emerging preclinical and clinical profile, we believe that veldoreotide may offer an improved efficacy and safety profile relative to existing drug therapies for acromegaly. Veldoreotide has been granted orphan drug designation by the FDA and the EMA. We have completed the screening of potential long-acting release ("LAR") technologies for veldoreotide and have selected a lead formulation based upon PLGA microspheres. PLGA is a well-known polymer, which has been widely applied in LAR formulations due to its biocompatibility, biodegradability, and favorable release kinetics. Additional veldoreotide development activities will be sequenced to ensure that the Company's existing cash resources are sufficient to fund planned operations at least through 2018.

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 several complementary therapeutic areas.

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

- ***Focus on rare diseases.*** We are developing treatments for rare diseases, initially PPP, endogenous Cushing's syndrome and acromegaly. 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 and has the potential for accelerated regulatory review. 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 has been granted.

- ***Independently commercialize Keveyis and other products in the United States and the European Union.*** We are preparing to independently commercialize Keveyis in the United States and intend to do likewise with our two rare disease product candidates, if approved, in the United States, the European Union, and, selectively, in other key global markets. Given the well-identified and concentrated prescriber base for Keveyis, and our two product candidates, we believe we can use a small, focused sales force to effectively promote our products. We plan to create an initial sales force of approximately 12 representatives in the United States to market Keveyis, and opportunistically expand the sales force with the growth of Keveyis. We anticipate a sales force of approximately 30 representatives in the United States as well as in the European Union to market our two rare disease product candidates, if approved. We believe that the activities involved in our commercialization of Keveyis will provide synergies to our commercialization of Recorlev if successful. We further believe that veldoreotide, if successful, will benefit from significant

development and commercial synergies with our lead product candidate, Recorlev, because both Cushing's syndrome and acromegaly are typically caused by benign pituitary tumors and are mainly treated by neuroendocrinologists. 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.

- ***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 opportunities of products that are already commercially available or that have human clinical data that we believe suggest a high probability of success for development progression and an attractive potential return on investment. As a result of our management team's experience in sourcing, selecting, in-licensing and acquiring product candidates, we were successful in acquiring the U.S. rights to Keveyis 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. For example, Keveyis serves as the basis of our rare neuromuscular franchise, and our product candidates for the treatment of endogenous Cushing's syndrome and acromegaly, if approved, will serve as the basis for our rare endocrine franchise.

- ***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 Neuromuscular Franchise

In December 2016, we initiated our rare neuromuscular franchise by acquiring the U.S. marketing rights to Keveyis® (dichlorphenamide) from Taro Pharmaceuticals U.S.A., Inc., the U.S. subsidiary of Taro Pharmaceutical Industries Ltd. ("Taro U.S."). 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. 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. Primary periodic paralysis may be localized ("focal") or more widespread ("generalized"), and it often goes underdiagnosed and/or undertreated. Types of periodic paralyses 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 episoses can be induced by low blood levels of potassium, and hyperkalemic, when episodes are associated with elevated levels of blood potassium. Primary periodic paralysis is thought to affect as many as 5,000 to 6,000 individuals in the U.S.

Keveyis is an oral carbonic anhydrase inhibitor, and was approved 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 are thought to decrease the frequency and severity of periodic paralysis attacks is unknown. However, it is believed that their effects are mediated both locally and systemically. It is not known whether their effects are disease-modifying. Keveyis has received orphan drug exclusivity status in the U.S through August 7, 2022.

Following FDA approval in August 2015, Keveyis was marketed by Taro U.S.A., Inc.. In May 2016, Taro announced the cessation of their commercial sales and related promotional activities for Keveyis. Since May 2016, Taro supplied Keveyis to patients on a non-commercial basis through a single specialty pharmacy in the United States. Since our acquisition of the U.S. marketing rights to Keveyis from Taro in December 2016, we have been conducting the activities necessary to prepare for our commercial launch, which is expected in April 2017.

We intend to launch and sell Keveyis using experienced sales representatives. Because a large percentage of the people who suffer from PPP remain undiagnosed or inadequately treated, we intend to develop programs to educate the medical community and patients about this illness. In addition, we plan to establish a field-based force of medical science liaisons. We intend to use a specialty pharmacy model 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 may 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.

Our Rare Endocrine Franchise

We have two product candidates in our rare endocrine franchise. Recorlev is being developed for the treatment of endogenous Cushing's syndrome, and veldoreotide is being developed for the treatment of acromegaly. We believe that these clinical product candidates, if successful, will benefit from significant development and commercial synergies based on the fact that both endogenous Cushing's syndrome and acromegaly are typically caused by benign pituitary tumors and are mainly treated by neuroendocrinologists. We believe that we can address the markets for both of these product candidates by targeting the endocrinologists that are focused on the treatment of rare pituitary disorders.

Recorlev—Phase 3 Product Candidate for the Treatment of Endogenous Cushing's Syndrome

Overview

Our lead product candidate, Recorlev (levoketoconazole, and formerly called COR-003) is a cortisol synthesis inhibitor and is a single enantiomer of ketoconazole that we are developing for the treatment of endogenous Cushing's syndrome, a rare endocrine disorder characterized by excessive production of the stress hormone cortisol. In endogenous Cushing's syndrome, elevated circulating cortisol gives rise to a severe disease with variable clinical signs and symptoms, including weight gain, characteristic changes in fat distribution, diabetes mellitus, hypertension, osteoporosis, muscle loss and depression. The active pharmaceutical ingredient in Recorlev, levoketoconazole (a purified enantiomer

of ketoconazole, and also known as 2S,4R-ketoconazole) is a small molecule and exerts its 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 for twice daily oral administration.

Ketoconazole, used off-label 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 single-enantiomer drug, a pure form of one (2S,4R-ketoconazole) of the two enantiomers (2S,4R-ketoconazole) of ketoconazole. Single-enantiomer drugs may offer safety and efficacy advantages over the racemate because one of the enantiomers in the racemate can have safety issues or be less effective in the treatment of the disorder or disease.

Recorlev, like ketoconazole, is a cortisol synthesis inhibitor that inhibits the cortisol synthesis pathway at several points. In light of the shared mechanism of action with ketoconazole and the data from Phase 2 clinical trials, which were conducted in diabetes patients, we believe Recorlev may have a similar beneficial impact on the reduction of significant comorbidities of endogenous Cushing's syndrome, including those associated with cardiovascular-related mortality risk, such as diabetes, weight gain, hypertension and elevation in cholesterol. In addition, based on preclinical results, we believe that Recorlev may offer an improved safety profile relative to existing approved drug therapies. Therefore, we believe that Recorlev has the potential to become a new standard of care for the chronic drug therapy of endogenous Cushing's syndrome.

Overview of 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 symptoms for both are the same. The more common form is exogenous Cushing's syndrome, which is often found in people taking cortisol-like medications for long periods of time, typically at high dosages or in very potent forms. Cortisol-like medications are often used to treat inflammatory disorders such as asthma and rheumatoid arthritis. Unlike the endogenous variant, exogenous Cushing's syndrome is temporary and most clinical signs and symptoms subside after the patient has finished taking the cortisol-like medication.

Endogenous Cushing's syndrome is a rare endocrine disorder characterized by sustained 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, a major part of the endocrine system. 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 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 and 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. 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, or ectopic ACTH or CRH syndrome. The source of ectopic ACTH/CRH secretion is most often small-cell carcinoma of the lung or bronchial carcinoid tumors, but can also arise with almost any endocrine tumor from many different organs. In a smaller number of cases, approximately 20%, endogenous Cushing's syndrome can be ACTH-independent, resulting from excess secretion of cortisol by unilateral adrenocortical tumors, either benign or malignant, or by non-malignant enlargement of the adrenal glands.

In patients with endogenous Cushing's syndrome, the normal feedback mechanism of the hypothalamic-pituitary-adrenal axis is disrupted as a result of a tumor 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 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 and weakness; 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 up to five 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, representing the majority of patients with endogenous Cushing's syndrome, 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 of drug therapy is to inhibit cortisol biosynthesis through the oral administration of an inhibitor of enzymes of adrenal cortisol synthesis. Ketoconazole is the most widely used drug therapy for endogenous Cushing's syndrome. Although approved in the European Union for this indication, ketoconazole is not approved for this indication in the United States. The percentage of endogenous Cushing's syndrome patients treated with ketoconazole monotherapy who achieve normalized levels of cortisol, assessed by measuring urinary free cortisol ("UFC") has been reported from retrospective, uncontrolled studies, with varying definitions of normalization, to 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, such as reduction in high blood pressure, improvement of diabetes, and normalization of hypokalemia, or low potassium blood levels. However, a significant proportion of patients treated with ketoconazole experience tolerability issues and, in some cases, liver injury (or hepatotoxicity). As a result of the hepatotoxicity risk the FDA has issued a boxed warning to prescribers concerning the use of ketoconazole to treat fungal infections, the only approved indication for ketoconazole in the United States. 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 (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 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 of ketoconazole for the treatment of endogenous Cushing's syndrome, based on the well-established use of ketoconazole in medical practice as well as documentation in scientific literature.

An alternative approach to treatment of Cushing's syndrome is the use of drugs that target pituitary tumors that produce ACTH. This approach is only useful for those patients whose endogenous Cushing's syndrome is caused by a pituitary tumor, or Cushing's disease. Among Cushing's disease patients, the dopamine agonist cabergoline, which is not approved for use in Cushing's disease in the United States, has been shown to achieve normalization of UFC levels in about 30% of patients. The SSA pasireotide, which is marketed as Signifor for the treatment of Cushing's disease in the United States, has shown normalization of UFC levels in 15% of patients at a 600 μg twice-daily dose and in 26% of patients at a 900 μg twice-daily dose. 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, HbA1c increased from 5.8% at baseline to 7.3% at Month 6.

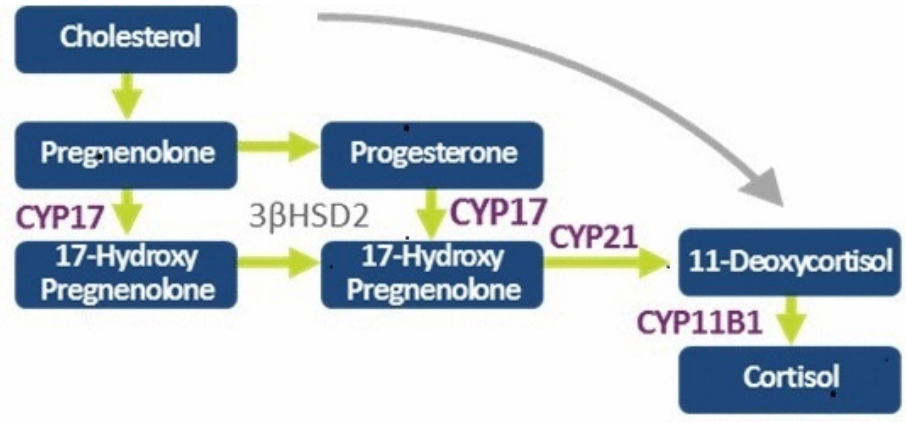
Another alternative, Korlym, or mifepristone, works by inhibiting the action of cortisol at the cortisol-receptor level, but does not lower cortisol levels in the blood, which actually tend to increase during therapy. As a result of this mechanism of action, it is not possible to monitor response by measuring UFC levels, which is the standard way clinicians monitor 24-hour blood cortisol for physicians who treat endogenous Cushing's syndrome. Korlym has been approved in the United States to control hyperglycemia secondary to hypercortisolism in patients with endogenous Cushing's syndrome. Korlym is contra-indicated 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.

We believe that the efficacy 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. Thus, we believe that our potential addressable market for Recorlev would be the estimated one-third of all diagnosed endogenous Cushing's syndrome patients that at any time are eligible for drug therapy, a figure that represents 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, the most commonly used drug therapy for the treatment of endogenous Cushing's syndrome. We believe Recorlev, based on its similar mechanism of action to that of ketoconazole, may reduce UFC and blood pressure, in contrast to Korlym, and may have an anti-hyperglycemic effect, 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:



Our preclinical and pharmacokinetic data suggest that Recorlev might have an efficacy profile at least as favorable as ketoconazole and might also confer less risk of liver injury:

- In *in vitro* studies, Recorlev was found to have higher potency than ketoconazole and its mirror-image enantiomer, 2R,4S-ketoconazole, in inhibiting the key enzymes in cortisol synthesis (CYP11B1, CYP17, and CYP 21). Thus, we believe Recorlev may have the same or higher efficacy compared to ketoconazole at lower dosages, which may in turn reduce typical drug exposure and potentially contribute to improved safety and tolerability.
- The pharmacokinetics of the enantiomers also suggest potentially 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 trial 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 that t 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.
- Compared with racemic ketoconazole, it was observed in *in vitro* studies that Recorlev is less potent than the other enantiomer (its antipode) 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.

Previously, levoketoconazole (then called DIO-902) was studied clinically for the treatment of type 2 diabetes. DiObex, our licensee from 2004 to 2008, initiated five clinical trials to investigate the use of levoketoconazole for type 2 diabetes. In December 2005, prior to the initiation of the first clinical trial by DiObex, the FDA placed a clinical hold on levoketoconazole relating to a safety concern for use of a dosage above 600 mg/day. DiObex modified the clinical trial protocol to limit the highest dose in Phase 2 to 600 mg/day, and the clinical hold was lifted by the FDA in February 2006. In a Phase 2 clinical trial of type 2 diabetes patients, levoketoconazole demonstrated a significant dose response to reducte mean blood concentration levels of C-reactive protein ("CRP"), whereas for ketoconazole, an increase in CRP was observed. CRP tends to increase in the presence of inflammation. Thus, we believe that Recorlev may be associated with a decrease in inflammatory processes compared to ketoconazole. Recorlev, with the same mechanism of action as ketoconazole to reduce blood cortisol, may also have beneficial effects on cardiovascular risk factors including weight loss, reduction in blood sugar, lowering of cholesterol and reduction in blood pressure. Cardiovascular disease is the leading cause of excess mortality in endogenous Cushing's syndrome.

Clinical and Preclinical Development of Recorlev

In the United States, Recorlev is considered a new molecular entity ("NME"). Upon completion of the clinical development program, we intend to file for marketing authorizations in the United States and elsewhere. In the United States, a 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 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 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 Committee for Medical Products for Human Use ("CHMP"), has requested a study of reproductive toxicity that may be completed prior to filing for marketing authorization in Europe, pending further discussions.

We are currently conducting SONICS, a pivotal, multinational Phase 3 clinical trial for Recorlev investigating the safety and efficacy of Recorlev in subjects with endogenous Cushing's syndrome, and anticipate that the study will be fully enrolled in the second quarter of 2017, with top-line data for the primary efficacy analysis available in the first quarter of 2018. In addition, we plan to initiate LOGICS, a second pivotal Phase 3 study of Recorlev for the treatment of endogenous Cushing's syndrome. The LOGICS study will supplement the long-term efficacy and safety data from the ongoing SONICS study in a randomized, double-blind, placebo-controlled study that will enroll approximately 35 patients, of which approximately two-thirds will have completed the SONICS study. Enrollment in the LOGICS study is anticipated to begin mid-year 2017 and top-line data are expected in the third quarter of 2018.

If SONICS can (1) demonstrate consistent and significant clinical benefit by meeting the primary endpoint of the trial, specifically the responder rate measured as normalization of UFC levels and (2) show consistent improvement of objectively quantifiable biomarkers of endogenous Cushing's syndrome comorbidities, such as blood glucose, blood lipids, blood pressure and weight, and improvement of other clinical signs and symptoms of endogenous Cushing's syndrome, we believe this 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, 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 subjects 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 100 unique subjects with this condition will have been treated with Recorlev during SONICS and LOGICS, and some subjects will be treated with a therapeutic dose of Recorlev for as long as 1.5 years at the time of first NDA submission.

In addition to LOGICS, we intend to initiate a long-term open-label extension study with Recorlev to capture even longer-term safety, tolerability and efficacy data from subjects who complete either SONICS or LOGICS and who choose to continue therapy with Recorlev. The open-label extension, preliminarily named OPTICS, is planned to begin enrollment in the second half of 2017 and will continue to accrue data indefinitely, at least until the drug is first marketed. Because our Phase 3 clinical trial will collect safety data from about 100 unique patients with endogenous Cushing's syndrome, 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

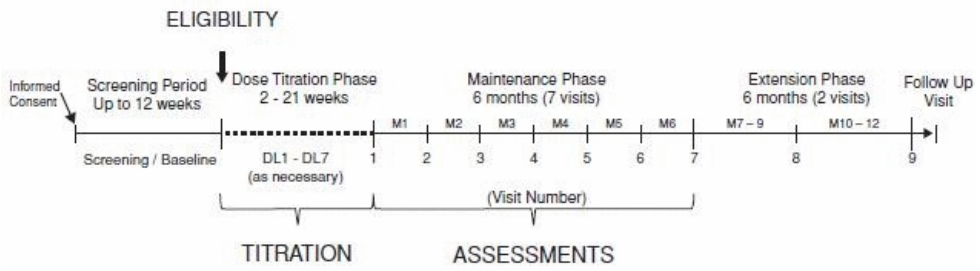
We are conducting SONICS in up to 90 clinical sites in approximately 19 countries, including in the United States, Canada, the European Union and the Middle East. This clinical trial is being conducted pursuant to an IND we filed in April 2013. We enrolled our first patient in the clinical trial in August 2014. Our U.S. IND for Recorlev for the treatment of endogenous Cushing's syndrome took effect in May 2013. We plan to recruit 90 patients and collect safety and efficacy data over a treatment period of at least one year. If we are able to confirm a favorable safety profile of Recorlev in clinical use, we plan to discuss differentiated safety and tolerability labeling from ketoconazole with regulatory authorities.

Following a screening phase, SONICS has three distinct treatment phases. During the dose titration 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, the patient enters the maintenance phase, during which the dose will be fixed and cannot be changed other than for safety reasons, including loss of efficacy At the end of the six month maintenance phase, UFC levels are measured and the responder rate, which is the primary endpoint of the clinical trial, is determined. Patients who have

completed the maintenance 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 subjects with 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 maintenance phase without a dose increase.
- Key secondary endpoints include the number of patients with at least a 50% decrease in UFC levels, as well as changes in blood sugar, blood pressure, cholesterol and weight compared to baseline, and effects on clinical signs and symptoms of endogenous Cushing's syndrome, quality of life measures obtained from the endogenous 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:



If we can (1) demonstrate consistent and significant clinical benefit by meeting the primary endpoint of the trial, specifically the responder rate measured as normalization of UFC levels and (2) show consistent improvement of objectively quantifiable biomarkers of endogenous Cushing's syndrome comorbidities, such as blood glucose, blood lipids, blood pressure and weight, and improvement of other clinical signs and symptoms of endogenous Cushing's syndrome, we believe this would be regarded by regulators as adequate proof of efficacy in this rare disease with a high unmet medical need.

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. In communication we had with the FDA, they 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 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. 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.

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 plan to initiate LOGICS, a second Phase 3 pivotal study. LOGICS will include a concurrent comparison of Recorlev to matching placebo using a randomized, double-blind design that we believe will be both feasible to enroll and ethical to conduct everywhere that SONICS is being conducted. LOGICS will enroll approximately 35 subjects, of which approximately two-thirds will have previously completed the SONICS study. Enrollment in the LOGICS study is anticipated to begin mid-year 2017 and top-line data are expected in the third quarter of 2018. Specifics of the LOGICS design are currently under development.

Clinical Trials in Type 2 Diabetes

Historically, levoketoconazole (then called DIO-902) was studied as a treatment for type 2 diabetes. An IND was filed in 2005 for investigation of the use of levoketoconazole in diabetes. DiObex, our licensee at the time, initiated five clinical trials to investigate the use of levoketoconazole for type 2 diabetes. A total of 159 subjects received at least one dose of levoketoconazole in these clinical trials, including 41 healthy subjects during Phase 1 clinical trials, and 118 patients with type 2 diabetes during Phase 2 clinical trials. Doses of levoketoconazole were administered over the range of 200 mg to 600 mg once a day, or QD, and 400 mg twice a day, or BID, for a single patient for up to 14 days, and 150 mg to 450 mg QD for up to four months.

The pharmacokinetics of levoketoconazole were studied in patients with type 2 diabetes and in normal volunteers in whom the effects of levoketoconazole on the pharmacokinetics of felodipine, a drug used to treat high blood pressure, and atorvastatin (Lipitor), a drug used to lower cholesterol, were evaluated. These drugs were chosen specifically as probes for interaction, because they were intended to be frequently used concomitantly during treatment of type 2 diabetes. In the completed Phase 2a clinical trial, dose dependent reductions from baseline in cholesterol levels contained in lipoproteins, in the form of low-density lipoprotein-cholesterol ("LDL-chol"), and cholesterol incorporated into high-density lipoprotein ("HDL-chol"), as well as total cholesterol were observed, but no differences in measures of glycemic control relative to placebo were detected. A Phase 2b randomized, double-blind, placebo-controlled, study in diabetes (DIO-502) was initiated to test doses of levoketoconazole up to 450 mg daily plus metformin as compared with atorvastatin 10 mg plus metformin in combination or placebo. Additionally, an open-label extension study (DIO-503) was started in parallel. However, in 2008, in light of negative safety reports for other diabetes treatments such as Avandia, DiObex made the decision to voluntarily terminate the development of levoketoconazole for the treatment of diabetes due to the perceived high regulatory and commercial hurdles for its approval and use in type 2 diabetes and considering the emerging efficacy and safety profile of levoketoconazole in type 2 diabetes (as described below). Thereafter, the IND was closed and DiObex terminated the two ongoing Phase 2 clinical trials. DiObex conducted the following five clinical trials with Recorlev in type 2 diabetes pursuant to an IND filed by them in November 2005:

Clinical Trial Number	Clinical Trial Description	Subjects Enrolled	Year and Status	Location	Dose
DIO-501	Phase 1/2a, Trial of Levoketoconazole or Placebo in Patients with Type 2 Diabetes Mellitus	37	2006/2007 Completed. Study report issued.	United States	200-600 mg QD; 400 mg BID
DIO-502	Phase 2b Trial of Levoketoconazole or Placebo in Addition to Metformin and Atorvastatin or Atorvastatin Placebo for Type 2 Diabetes Mellitus	133	2007/2008 Terminated early. Study report issued.	United States, Australia, New Zealand	150-450 mg QD
DIO-503	Phase 2 Open-Label Trial and Pharmacodynamic for 24-Week Study with Levoketoconazole in Combination with Metformin and Atorvastatin in Patients with Type 2 Diabetes Mellitus	13	2007/2008 Terminated early. Study report issued.	United States, Australia, New Zealand	150-450 mg QD
AA34509	Phase 1 Pharmacokinetic Drug Interaction Trial of Levoketoconazole with Felodipine in Healthy Adult Volunteers Under Fasting Conditions	18	2006/2007 Completed. Study report issued.	United States	400 mg QD
AA34510	Phase 1 Pharmacokinetic Drug Interaction Trial of Levoketoconazole and Ketoconazole with Atorvastatin in Healthy Adult Volunteers Under Fasting Conditions	24	2006/2007 Completed. Study report issued.	United States	400 mg QD

Phase 2 Clinical Trials

DIO-501 Clinical Trial

The DIO-501 clinical trial was a double-blind, placebo-controlled, parallel-group clinical trial conducted in patients aged 18 to 70 with a diagnosis of type 2 diabetes. A total of 35 patients were treated: 21 with levoketoconazole

(10 at 200 mg QD, six at 400 mg QD, four at 600 mg QD and one at 400 mg BID); eight with ketoconazole (400 mg QD); and six with placebo. Trial drugs were administered for 14 days.

In this clinical trial, the mean 12-hour plasma cortisol area under the concentration-time curve, or AUC, levels were modestly reduced in the levoketoconazole treatment groups at day 15 compared to baseline, which is consistent with the known mechanism of action of levoketoconazole. However, counter-regulation in diabetic patients with a normal hypothalamic pituitary adrenal axis may have limited the observed cortisol suppression. Similarly, only a small, nonsignificant effect on glycated hemoglobin ("HbA1c"), and fasting glucose levels was observed. Consistent with the known inhibitory effect of ketoconazole on cholesterol synthesis, total cholesterol, LDL-chol, and to a lesser extent HDL-chol levels, but not triglycerides, were significantly decreased in a dose-dependent manner by levoketoconazole. The mean change from baseline in total cholesterol, LDL-chol and HDL-chol at a dose of 400 mg QD was similar to those observed in 400 mg QD ketoconazole and higher in the 600 mg QD levoketoconazole group. Also, for the levoketoconazole treatment groups, there was a statistically significant dose response in the reduction in mean levels of CRP on day 15 compared with baseline, with a p-value of 0.027. In contrast, mean levels of CRP increased in the ketoconazole-treated group and less so in the placebo group. CRP is an indicator of systemic inflammation, including vascular inflammation. The reduction in cholesterol and CRP observed in patients with type 2 diabetes may indicate a potential beneficial effect of levoketoconazole on cardiovascular risk factors. Notably, patients with endogenous Cushing's syndrome tend to have elevated circulating CRP.

Plasma AUC and maximum concentration in blood ("Cmax"), increased in a non-proportional manner over the dose range of 200 mg to 400 mg on days one and 14. Clearance values were similar for the 200 mg and 400 mg doses of levoketoconazole, but significantly decreased at the 600 mg levoketoconazole dose, on days one and 14.

Levoketoconazole was generally well-tolerated. Headache and nausea were the most frequently reported adverse events, some of which were considered drug-related. There were no serious adverse events, and no clinically meaningful changes in hematology, blood chemistry and urinalysis were noted in any treatment group. No treatment-related changes in liver function tests ("LFTs"), were detected.

DIO-502 and DIO-503 Clinical Trials

The DIO-502 clinical trial was a four-month, double-blind, randomized, placebo-controlled, dose-ranging study of levoketoconazole with metformin and atorvastatin that enrolled 133 of a planned 200 patients with type 2 diabetes, consisting of males and females between the ages of 18 and 70. Enrolled subjects were already receiving metformin treatment with a minimum daily dose of 500 mg and had an HbA1c level of 7% to 10%. Additionally, all patients were treated with 10 mg atorvastatin or its placebo to evaluate the effect of levoketoconazole on lipid profiles given cholesterol-lowering drugs. Thus, patients were randomized into eight separate arms in the clinical trial: placebo or levoketoconazole at 150 mg; 300 mg; and 450 mg with either atorvastatin 10 mg or atorvastatin placebo; all received metformin concomitantly.

The DIO-503 clinical trial was an open-label, extension to DIO-502 to evaluate safety, tolerability and pharmacodynamics after 24 weeks of dosing with levoketoconazole in combination with metformin, with and without atorvastatin in subjects with type 2 diabetes.

DiObex terminated these clinical trials prior to their planned completion milestones. At the time of trial termination, a total of 133 patients were enrolled in the DIO-502 and DIO-503 trials, and 129 patients in total had been treated with a study drug, of which 97 patients received at least one dose of levoketoconazole. The investigators subsequently elected to defer efficacy and pharmacokinetics inferences based on incomplete datasets. The frequency of adverse events reported was generally similar across treatment arms. Diarrhea was the most frequently reported adverse event overall with administration of levoketoconazole. No serious adverse events were reported in the terminated studies.

A safety signal of elevated liver enzymes was identified in 10 of the 129 treated patients in the DIO-502 and DIO-503 trials. No case of Hy's law (i.e., an increase of liver transaminases at or above three times the upper level of normal values; increase in total bilirubin at or above two times the upper level of the normal value; no or little sign of cholestasis; and absence of other reasons for liver injury, such as viral hepatitis) was observed. An observation of Hy's Law would have indicated a high risk of potentially serious drug-related hepatotoxicity. Three of the treated patients

were withdrawn from the clinical trials as required in the safety monitoring plan. In these three patients, LFT levels returned to normal after study drug was discontinued. In addition, three other patients had modest elevations in LFT levels. While these levels did not require termination by the trial protocol, the investigators elected to terminate these patients from the clinical trial. LFTs in these patients also returned to normal after the study drug was discontinued. Four additional patients required close monitoring per the protocol, and had resolution of their LFT abnormalities while on the study drug. The first case of elevated liver enzymes occurred in a patient who admitted to excessive alcohol consumption. The remaining cases developed over the following three months. An independent external safety review committee recommended continuation of the studies with no modifications.

Due to the design of these clinical trials, the independent data safety monitoring board for the trials stated that it was impossible to interpret which of the two drugs, levoketoconazole or atorvastatin, was primarily associated with the side effect profile observed (i.e. LFT abnormalities) in these trials. A more detailed analysis of the liver transaminase elevations in this clinical trial by an expert panel showed that there was no correlation between the dose of levoketoconazole and abnormal liver transaminases.

Phase 1 Clinical Trials

AA34509 Clinical Trial

The AA34509 clinical trial was designed primarily to evaluate the effect of levoketoconazole on the pharmacokinetics of concurrently administered felodipine. Healthy volunteers were administered 400 mg of levoketoconazole or placebo QD for eight days. On the fifth day of the trial, subjects received a single 5 mg dose of felodipine. Beginning on day five, pharmacokinetics of levoketoconazole were monitored for 24 hours, and pharmacokinetics of felodipine were monitored for 72 hours. The trial was a cross-over trial involving 18 subjects, 16 of whom completed the trial.

AA34510 Clinical Trial

This clinical trial was designed primarily to evaluate the effect of concomitant administration of levoketoconazole or ketoconazole on the pharmacokinetics of atorvastatin. Healthy volunteers were administered 400 mg of levoketoconazole, 400 mg of ketoconazole or placebo daily for seven days. On day five, all subjects received a single 80 mg dose of atorvastatin. After administration of the racemate, ketoconazole, pharmacokinetics of the two single enantiomers 2R,4S-ketoconazole and 2S,4R-ketoconazole, were evaluated for 24 hours on day five using a chiral bioanalytical method, to distinguish the enantiomers in plasma (blood). Pharmacokinetics of atorvastatin were evaluated for 60 hours starting at the time of administration on day five. The trial was a cross-over trial involving 24 subjects, all of whom completed the clinical trial.

*Key Findings from the Clinical Trials of Recorlev (*levoketoconazole)

Phase 2 Efficacy and Safety Trials in Diabetic Patients:

- AUC and Cmax values were approximately 50% higher with levoketoconazole in comparison with ketoconazole at the same dose of 400 mg. All pharmacokinetic parameters were highly variable, in the sense that they differed within and among subjects.
- Following administration of ketoconazole, plasma levels (AUC or Cmax) of levoketoconazole (2S,4R-ketoconazole) were approximately three times those of the other enantiomer, 2R,4S-ketoconazole. Possible explanations could be reduced absorption of 2R,4S-ketoconazole or decreased uptake and metabolism of levoketoconazole in the liver compared to the other enantiomer.
- Levoketoconazole produced a decrease in some lipid measures, or blood fat, including reduced total cholesterol, LDL-chol and HDL-chol.
- A significant dose-related effect of levoketoconazole for reduction of CRP was observed.

- Trends for reductions in serum cortisol, measured as AUC (0-12 hours), were found after 14 days of treatment with levoketoconazole in diabetic patients.
- In the DIO-501 clinical trial, headache and nausea were the most frequently reported adverse events. No treatment related changes in LFTs were detected. In the DIO-502/503 clinical trials, diarrhea was the most frequently reported adverse event.
- LFTs were elevated in the DIO-502/503 clinical trials in 10 out of the 129 patients treated with either the combination of levoketoconazole and atorvastatin or levoketoconazole alone, in each case co-administered with metformin. The independent data safety monitoring board for the trial stated that it was impossible to interpret which of drugs was primarily associated with the side effect profile observed in the trial.

Phase 1 Drug Interaction Clinical Trials in Normal Volunteers:

- The AUC and the Cmax of felodipine were 10-fold higher when taken with levoketoconazole compared with felodipine alone.
- The AUC of atorvastatin was increased by 50% when administered with levoketoconazole compared with atorvastatin alone.
- A small, but statistically significant decrease of serum cortisol (AUC zero to six hours) was found for levoketoconazole compared with placebo and ketoconazole.
- Headache, nausea, dizziness and back pain were reported as the most frequent adverse events across the two studies.
- In the drug interaction study with atorvastatin, two subjects had elevated LFT values. The subjects had received levoketoconazole plus atorvastatin or ketoconazole plus atorvastatin in the immediately previous study periods in this cross-over study.

Veldoreotide—Phase 2 Product Candidate for the Treatment of Acromegaly

Overview

In June 2015, we acquired veldoreotide (formerly called COR-005, and previously DG3173), a novel SSA that has the potential to provide a new and differentiated treatment option for patients with acromegaly, from Aspireo Pharmaceuticals Ltd. We are developing veldoreotide for the treatment of acromegaly. We acquired veldoreotide as part of our strategy to build our rare endocrine franchise. 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 ("GH") and Insulin-like growth factor 1 ("IGF-1"). The treatment goal is the normalization of GH and IGF-1, which is the main cause of the detrimental clinical signs and symptoms of acromegaly.

Veldoreotide is a novel SSA in Phase 2 clinical development for the treatment of acromegaly patients who have not adequately responded to surgery, or acromegaly patients for whom surgery is not appropriate. 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 SSTRs that are expressed by the tumor. Binding of SSAs to these SSTRs leads to the beneficial inhibition of GH secretion, but can also result in the unwanted inhibition of secretion of other endocrine hormones such as insulin and glucagon in the pancreas and elsewhere. Like other SSAs, veldoreotide is a peptide that we are developing for subcutaneous injection. Based on the differentiated activation pattern of veldoreotide upon binding to SSTR subtypes and preclinical and clinical data, we believe that veldoreotide may offer an improved efficacy and safety profile relative to existing drug therapies for acromegaly. In the five clinical studies completed to date in healthy subjects and patients with acromegaly outside the United States, a beneficial reduction of GH was observed, 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 addition to a dose ranging clinical trial, we anticipate that our clinical program will include at least one multinational pivotal clinical trial for registration, comparing veldoreotide to established treatments or placebo, including

at least six months of controlled treatment to evaluate efficacy and at least one year of observation to evaluate safety. Veldoreotide has been granted orphan drug designation by the FDA and the EMA. We have completed the screening of potential long-acting release (LAR) technologies for veldoreotide and have selected a formulation based upon PLGA microspheres. PLGA is a well-known polymer, which has been widely applied in LAR formulations due to its biocompatibility, biodegradability, and favorable release kinetics. We are in the process of securing intellectual property protection for the lead formulation, which could, if granted by the relevant patent authorities, extend the period of marketing exclusivity for the finished drug product. Additional veldoreotide development activities will be sequenced to ensure that the Company's existing cash resources are sufficient to fund planned operations at least through 2018.

Overview of Acromegaly

Acromegaly is a rare endocrine disorder that most commonly results from a benign tumor of the pituitary gland, or adenoma, leading to excess production of GH and IGF-1, key regulators of growth and metabolism. High levels of GH over-activate GH receptors resulting in excess IGF-1 in patients with acromegaly. A common criterion for the successful treatment of acromegaly is normalization of IGF-1 levels, since reduction of excess IGF-1 correlates closely with relief of clinical symptoms.

The progression of acromegaly is typically slow, and acromegaly often is not clinically diagnosed for 10 years or more. As the disease advances, patients typically exhibit abnormal growth throughout the body. Acromegaly most commonly affects middle-aged patients with the mean age of onset being 40 to 45 years. In adults, the condition results in expansion of the circumference of and increased density of bones and surrounding soft tissues as well as cartilage, causing pain and altered appearance. This altered appearance is most apparent in the head and face, but also impacts the entire body. Patients may experience enlargement of visceral organs and cardiovascular disease. Upper airway obstruction with sleep apnea occurs in approximately 40% to 50% of patients, and is associated with both soft tissue laryngeal airway obstruction and central sleep dysfunction. Patients may also experience metabolic disruptions such as insulin resistance and diabetes, which is estimated to develop in 10% to 15% of patients. In addition, some patients with large tumors experience symptoms caused by the tumor itself, including headaches, vision problems, impotence, low sex drive and changes in the menstrual cycle. These problems, if left untreated, lead to disfigurement, disability, and ultimately premature death.

We estimate the acromegaly drug therapy market in 2014, including octreotide and lanreotide for acromegaly and total pegvisomant, was approximately $990 million worldwide. Based on recent publications, we estimate the diagnosed prevalence of acromegaly to be approximately 24,000 in the United States, and approximately 43,000 in the European Union. Prevalence estimates vary considerably and it is believed that acromegaly is underdiagnosed. Estimates of the mortality rate in patients with acromegaly varies, with published estimates reporting values as high as 2.7 times normal.

Current Treatment Landscape and Limitations on Current Treatment Options

Initial treatment for acromegaly is usually surgery with or without radiation therapy. An estimated 80% of patients are eligible for surgery. The initial surgical cure rate is estimated at approximately 80% to 90% for patients with microadenomas, which are tumors less than 10 mm in diameter, and less than 50% for patients with macroadenomas, which are tumors greater than 10 mm in diameter. Three percent to 10% of patients will experience a recurrence in the years following an initially successful surgery. An estimated 40% to 50% of acromegaly patients will be prescribed drug therapy, including those for whom surgery is infeasible, is contraindicated or has been unsuccessful. The goal of drug therapy is primarily to normalize IGF-1 levels and GH levels. Currently, SSAs are the most commonly used drug therapy for the treatment of patients with acromegaly. Less than one-half of treated patients do not adequately respond to SSAs with full IGF-1 normalization and need alternative or adjunctive drug therapies.

Somatostatin is a naturally occurring cyclic peptide. Somatostatin inhibits the secretion of a broad array of hormones secreted by the pituitary gland, the pancreas and the gastrointestinal tract, or the GI tract, including GH, insulin and glucagon. It also modulates the rate of gastric emptying, the flow of bile from the gallbladder and intestinal blood flow, and inhibits the growth of normal and tumor cells. These functions are mediated primarily by the binding of

somatostatin to a family of five SSTRs. There is considerable overlap between activation of these different receptors and their effects on biological functions. GH secretion is inhibited by activation of some of these receptors.

Pituitary adenomas express various patterns of SSTRs depending on whether they produce primarily GH, ACTH or other pituitary hormones. This excessive production leads to acromegaly, Cushing's disease or other diseases, respectively. SSAs are structurally similar to somatostatins and have a therapeutic effect in pituitary adenomas, since they bind to the SSTRs on these tumors and inhibit secretion of hormones such as GH or ACTH. Currently approved SSAs used to treat acromegaly are: octreotide which is available in two formulations, an immediate-release form that is typically injected three times a day ("TID"), subcutaneously (Sandostatin), and a second that is a long-acting intramuscular depot for monthly injection (Sandostatin LAR); lanreotide (Somatuline), a slow release or autogel formulation for deep subcutaneous injection once a month; and pasireotide available as a long-acting intramuscular depot for monthly injection (Signifor LAR).

There is a significant unmet need in the treatment of acromegaly. Although long-acting SSAs are the most commonly used drugs, they have several limitations, including:

- Variable efficacy: Estimates of responder rate vary significantly by study design, but the proportion of patients who are effectively managed on SSA monotherapies is now believed to be substantially less than 50%.
- Disruption of glucose metabolism: SSAs can inhibit insulin and glucagon secretion, among other hormones, potentially leading to an exacerbation of glucose control issues already experienced by some acromegaly patients. Clinical trials with all approved SSAs for acromegaly showed increased rates of hyperglycemia and hypoglycemia, and pasireotide also showed an increased rate of diabetes.
- Tolerability issues due to gastrointestinal side effects: Up to one-third of patients experience gastrointestinal side effects, which can often be transient, but sometimes may require the adjustment of dosing or choice of drug. Up to 62% of patients have gallbladder complications, such as gallstones or sludge in the gallbladder. Physicians we surveyed estimate that approximately 38% of their SSA patients take medication to prevent gallstones and approximately 20% have had gallbladder surgery in the last five years.
- Convenience: All of the long-acting SSA formulations in the United States require administration by a health care professional, and often necessitate monthly office visits to receive injections.

While long-term monthly administration controls GH hypersecretion in up two-thirds of treated patients, most patients do not respond to SSAs with full IGF-1 normalization and need to move to other drug therapies, which are used as alternatives to or in combination with SSAs. These additional drug therapies also aim to reduce IGF-1. Somavert (pegvisomant) is a human GH receptor antagonist that binds to the GH receptor, but does not activate the mediators leading to IGF-1 production and secretion, thereby acting as a functional GH receptor antagonist, or blocker. The resulting clinical effect is a dose-dependent inhibition of IGF-1. However, because it is administered as a subcutaneous injection on a daily basis, we believe patient acceptance and compliance may be reduced. Dopamine receptor agonists such as cabergoline also inhibit GH secretion by pituitary adenomas expressing the dopamine receptor, which leads to a moderate inhibition of IGF-1. This class of drugs is not approved by the FDA for the treatment of acromegaly.

A number of products are currently in development for the treatment of acromegaly that may potentially compete against veldoreotide. The majority of compounds in development for the treatment of acromegaly are reformulations of octreotide acetate that potentially offer improved convenience to patients and physicians. These compounds are unlikely to address the market's key unmet need for drugs with improved efficacy and safety profile.

Our Solution— Veldoreotide, a Novel Somatostatin Analog

Veldoreotide is a novel multi-receptor targeted SSA in Phase 2 clinical development for the treatment of acromegaly. In contrast to approved SSAs, veldoreotide activates a different subset of SSTRs. Like pasireotide, it activates SSTR2 and SSTR5. However, in contrast to pasireotide, it possesses a similar affinity for SSTR2 than SSTR5.

Veldoreotide is also the only SSA with a high affinity for SSTR4. veldoreotide does not bind to SSTR3 or the opiate receptor at pharmacological concentrations. While the functional consequences of the binding of SSAs to the opiate receptor are not fully understood, it has been suggested as a mechanism contributing to inhibition of insulin secretion by SSAs and may also influence their effect on gastrointestinal motility. *In vitro* data suggest that a higher number of adenomas are a target for GH inhibition by veldoreotide as compared to octreotide, which is referred to as a single receptor targeted SSA that binds and activates predominantly via SSTR2, potentially resulting in an increased responder rate. Preclinical data from animal studies, and clinical data in healthy subjects and patients with acromegaly, showed that insulin secretion was less inhibited, potentially resulting in reduced side effects on blood glucose and an improved safety and tolerability profile. Preclinical data further suggest a reduced effect on gallbladder motility, or flow from the gallbladder.

In four clinical trials with single subcutaneous injections or infusion and in one six-day clinical trial, all of which were conducted with an immediate release formulation of veldoreotide in healthy subjects or patients with acromegaly, veldoreotide was observed to have a tolerability profile comparable to that of octreotide. However, unlike octreotide, subjects treated with veldoreotide were observed to have less or no reduction in peak insulin secretion after a meal. We believe these preliminary clinical findings corroborate the profile of veldoreotide observed in preclinical studies, which suggested inhibition of GH secretion without detrimental effects on post-meal insulin or glucose metabolism. These studies were too short to assess the effect on flow from the gallbladder. 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 its differentiation from existing SSAs. With the potentially superior efficacy, safety and tolerability profile suggested by preclinical studies and early clinical trials, we believe veldoreotide has the potential to become the standard-of-care SSA, with distinct therapeutic advantages relative to currently approved SSAs as treatment of acromegaly.

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 following table summarizes these trials.

Clinical Trial Number	Clinical Trial Descriptions	Subjects Enrolled	Year and Status	Location	Dose
DG3173-II-02	Phase 2 The Effect of Subcutaneous Infusion 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 Veldoreotide and 300 µg 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, Phase 1 Trial to Assess the Pharmacodynamics Effect on Glucose Metabolism of Single Doses Compared to Veldoreotide Octreotide and Placebo in Healthy Male Subjects	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 Subjects	42	2012/2013 Completed. Study report issued.	Switzerland	100-1800 µg TID
DG3173-I-001	Phase 1 Double-Blind Trial to Investigate Safety, Tolerability and Pharmacokinetics of Single Escalating Dosing of Veldoreotide in Healthy Male Subjects	72	2008 Completed. Study report issued.	Germany	10-2000 µg QD

The clinical trials involved 122 healthy subjects in the Phase 1 trials and 28 patients with acromegaly in the Phase 2 clinical trials. No serious adverse events 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 GH 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.

Phase 2 Clinical Trials

DG3173-II-02 Clinical Trial

This clinical trial was an open-label, crossover, active- and placebo-controlled, randomized dose-ranging clinical trial in eight male or female acromegaly patients aged 31 to 54 years that was intended to assess the effect on GH levels of 23-hour constant subcutaneous infusions of different doses of veldoreotide or placebo and three subcutaneous injections of a standard dose of octreotide, administered over the same timeframe. Postprandial insulin and glucose were also assessed over a 4-hour period following a standardized midday meal on the second study day. Pharmacokinetics, safety, and tolerability were also assessed.

Veldoreotide at doses of 920 µg, 2760 µg, and 5520 µg per 23 hours were infused in a random visit sequence at a rate of 0.04 mg, 0.12 mg, and 0.24 mg per hour spaced one week apart. The placebo, saline, was always infused one week prior to veldoreotide, and octreotide at a dose of 300 µg was injected TID one week after the last veldoreotide dose. Patients had not received any specific treatment for acromegaly in the 12 months prior to the clinical trial and had to have blood IGF-1 concentration greater than or equal to 1.2 times the upper limit of normal reference range adjusted for age plus random blood GH greater than or equal to 5 µg/L in the 12 months prior to the clinical trial and increased values at screening.

There was a decrease in $AUC_{11\text{-}23h}$ for serum GH following veldoreotide treatment compared to baseline (placebo). The decrease in $AUC_{11\text{-}23h}$ was greater with octreotide than with placebo and the lower and middle doses of DG3173. The reduction in GH of the 5520 µg dose of veldoreotide closely approached that of octreotide (mean percentage reduction 67% vs. 73%). Six of 8 patients receiving the mid or high dose of veldoreotide achieved at least a 50% reduction in GH $AUC_{11\text{-}23h}$ versus placebo, compared with 7 of 8 achieving the same threshold reduction during octreotide injections.

Prior to eating a standardized meal begun 19 hours after the treatments were started, glucose levels were reduced as compared to pre-dose baseline glucose values among placebo and the two lower veldoreotide treatment groups (median percent reductions of 12%, 8.8%, 4.2%, respectively), whereas they were similar to pre-dose values in the highest veldoreotide group (median increase 3.4%) and had increased in the octreotide group above baseline (median increase 24%). Following the standardized meal, serum glucose increased to a similar extent in placebo and the two lower veldoreotide dose groups (median percent change 27% to 33% above pre-dose baseline), whereas the maximal excursions were somewhat higher in the highest veldoreotide dose group (median 46% above pre-dose) and in the octreotide group (median 63% above pre-dose). Pre-dose insulin values were reduced by all treatments prior to receiving the standardized meal, placebo (median reduction of 25%) less so than the active drugs (median reductions of 49% to 74%), presumably reflecting improved glucose control among active treatments. Insulin excursions following the meal were highly variable and no apparent effect of treatment was readily discernible.

There were no serious adverse events or adverse events leading to withdrawal during the study; all adverse events were mild or moderate in severity. There was no notable effect of veldoreotide dose on overall incidence of adverse events in this small number of patients. Four events in one patient, all following octreotide treatment, were assessed as having a suspected relationship to study treatment, all other events were assessed as having no suspected relationship. The only adverse event reported by more than one patient was headache, reported by four patients receiving veldoreotide. There were no trends or clinically meaningful changes over time in laboratory safety analytes, vital signs or the incidence of abnormal ECGs following veldoreotide or octreotide treatment, overall or in any individual.

DG3173-II-01 Clinical Trial

This clinical trial was an open-label, single-center, single-dose, active-controlled, cross-over clinical trial in 20 male or female acromegaly patients. In a fixed sequence with one week washout between treatments, untreated patients received octreotide 300 µg and then each of four doses of subcutaneous veldoreotide (100 µg, 300 µg, 900 µg, 1800 µg in that sequence).

Patients had not received any specific treatment for acromegaly in the 12 months prior to the trial and had to have blood IGF-1 concentration greater than or equal to 1.2 times the upper limit of normal reference range adjusted for age, plus random blood growth hormone greater than or equal to 5 µg/L in the six months prior to the trial. Mean age was 48 years, 90% were female, and mean body mass index was 29. Thirteen patients had received prior treatment for acromegaly, including nine with prior surgery (three of these with subsequent radiation therapy), and nine with medications.

GH values were obtained at baseline, or prior to treatment, and at intervals over eight hours following each treatment. GH was rapidly suppressed by all treatments, and the effect of veldoreotide was dose-dependent, both in terms of suppression extent and duration of effect. The 1800 µg dose of veldoreotide and octreotide maximally suppressed GH to a similar extent (mean percentage change 60% for each), with a slightly lesser maximal suppression with the 900 µg dose of veldoreotide. This suppression resulted in a similar proportion of patients achieving GH levels less than or equal to 2.5 ng/mL among the two highest doses of veldoreotide and octreotide (37% to 42%). Also, the time to achieve maximal suppression was shorter for the two highest doses of veldoreotide than for octreotide (median two hours for octreotide compared to one hour for the maximally effective veldoreotide dose). However, the duration of GH suppression following single dosing was longer for octreotide than veldoreotide at all doses, resulting in greater suppression by octreotide of GH as measured by AUC 0 to 8 hours (octreotide 60% mean percentage suppression compared to veldoreotide 1800 µg 37% mean percentage suppression). We intend to optimize the formulation of veldoreotide to prolong exposure, which should lead to sustained GH suppression.

Fasting glucose was assessed at screening and at eight hours after each single dose of study drug. Mean glucose concentrations during veldoreotide treatments were similar to the screening values, but were elevated by approximately 2.8 mmol/L after eight hours of treatment with octreotide. At the time of glucose sampling, growth hormone levels were still close to maximally suppressed by octreotide (median 74% below baseline) but had returned to baseline levels in all veldoreotide dose groups except the highest dose group (1800 µg), which was suppressed by a median of 17% below baseline. Glucose values for octreotide were always determined shortly after clinical trial entry. In contrast, glucose values for the higher doses of veldoreotide were drawn several weeks after trial entry. Participation in the clinical trial *per se* would be expected to result in improved glucose control due to observed behavioral changes in trial participants.

There were no serious adverse events. Three out of the 20 patients reported a combined total of three adverse events. One adverse event, a moderately severe headache reported in a 62 year old female as encephalopathy exacerbation, led to early clinical trial discontinuation after the 300 µg dose of veldoreotide follow-up visit. The patient who discontinued early had long-standing acromegaly with a very high IGF-1 at baseline (5.5x upper limit of normal, or ULN) and a history of encephalopathy. The investigator considered the relationship to study drug as unassessable. Pharmacokinetic outcomes for veldoreotide were similar to those from Phase 1 clinical trials.

Phase 1 Clinical Trials

DG3173-I-003 Clinical Trial

This clinical trial was a single-blind, placebo- and active-controlled, single ascending dose, randomized cross-over clinical trial in eight healthy male subjects, aged 18 to 45 years. Octreotide at a dose of 300 µg and veldoreotide at doses of 300 µg, 900 µg and 1800 µg were injected subcutaneously in random order following a mixed meal test, with four- to five-day washouts between administrations.

Relative to placebo, both veldoreotide and octreotide were associated with a delay in the time to peak post-meal insulin. However, the magnitude of peak insulin was similar between placebo and veldoreotide. In contrast, octreotide delayed and suppressed insulin release during the meal, with peak insulin diminished by 81% and AUC by 62% relative to placebo. The differences in all of these measures, including time to peak, magnitude of peak and AUC, between veldoreotide and octreotide were statistically significant with a p-value of less than 0.02 for all parameters. Relative to placebo, all four drug injections were associated with post-meal glucose excursions. The effect of veldoreotide on glucose AUC was dose-related. Glucose was maintained at a high level for a longer time following octreotide relative to veldoreotide. The glucose AUC for octreotide during the test was elevated relative to all doses of veldoreotide.

Peak post-meal glucagon was not influenced appreciably by veldoreotide, whereas a suppression by 50% relative to placebo was observed for octreotide. There was a modest effect of veldoreotide at 900 µg and 1800 µg doses, with up to 28% suppression of glucagon AUC. In contrast, octreotide had a pronounced effect on glucagon AUC, suppressed by 63% relative to placebo.

There were no serious adverse events. Adverse events were mostly mild in severity and did not result in any discontinuations. Injection site redness or itching and gastrointestinal system-related complaints (most commonly diarrhea) were the most commonly reported adverse events for both octreotide and veldoreotide.

DG3173-I-002 Clinical Trial

This clinical trial was a single-blind, placebo- and active-controlled, multiple escalating dose clinical trial in 42 healthy male subjects, aged 18 to 45 years. Veldoreotide was given TID eight hours apart from days two through eight. There were seven clinical trial groups, with six subjects total per group. In the first four clinical trial groups, four subjects received veldoreotide in doses that ranged from 100 µg to 1800 µg TID, one received octreotide 300 µg TID, and one received placebo. In the three remaining clinical trial groups, four subjects received veldoreotide plus octreotide, one received placebo plus placebo and one received octreotide plus placebo.

The effects of veldoreotide with or without added octreotide on GH, insulin and glucose levels were ascertained using a growth hormone-releasing hormone ("GHRH"), test on days one (pretreatment) and three. veldoreotide and octreotide given as monotherapy for four doses both suppressed the GHRH-induced rise in GH, with 900 µg of veldoreotide approximately equivalent to 300 µg of octreotide, with mean AUC reductions compared to pre-drug administrations of 65% and 70%, respectively, whereas the 1800 µg dose of veldoreotide gave somewhat better reduction, with mean AUC reduction of 85%. When the two drugs were used in combination, a maximum suppression of GH response was noted during administration of the veldoreotide 900 µg. The highest dose of veldoreotide 1800 µg was not tested in combination with octreotide. Insulin levels were suppressed following treatment with octreotide by 50% from pre-drug, whereas no such effect was noted during veldoreotide administrations. Blood glucose concentrations were mostly stable following GHRH infusion. Glucose levels were observed to be similar before and after administrations of both veldoreotide and octreotide. There was no clear effect of either drug or saline given alone or in combination with the exception of veldoreotide 300 µg, for which glucose levels tended to be lower after administration, both alone and in combination with octreotide.

Veldoreotide was generally well-tolerated and a maximum tolerated dose was not reached. Adverse events were mostly mild in severity. Injection site redness, itching and gastrointestinal system-related complaints (most commonly diarrhea) were the most commonly reported adverse events and appeared to occur in similar percentages of octreotide- and veldoreotide -treated subjects. There was small to no accumulation of veldoreotide in plasma after repeated doses. Exposure to veldoreotide was dose proportional and linear after the first and last doses. When veldoreotide was given concomitantly with octreotide 300 µg TID, veldoreotide pharmacokinetics were similar to veldoreotide given alone.

DG3173-I-001 Clinical Trial

This clinical trial was a double-blind, placebo controlled, single ascending dose clinical trial in 72 healthy male subjects, age 18 to 45 years. A single subcutaneous dose ranging between 10 µg to 2000 µg of veldoreotide or placebo was administered under fasting conditions. Veldoreotide was generally well-tolerated, and the maximum tolerated dose was not reached.

There were no serious adverse events. There were 21 adverse events reported in 15 subjects of which twenty were regarded as mild in severity and one was moderate (diarrhea, 800 µg dose). The time to maximum drug concentration in blood was generally within one hour. Maximum drug concentration in blood generally increased proportionally with dose. The cumulative urinary excretion of drug was proportional to dose ingested, and fractional excretion was consistently about 4% to 5% of the respective doses administered.

In an exploratory pharmacodynamic analysis, GH plasma concentrations were consistent with the suppression of GH by veldoreotide.

Anticipated Clinical Trials

We expect additional clinical trials of veldoreotide to be designed to establish the optimal dosage range for normalization of IGF-1 in chronic treatment of acromegaly using a proprietary subcutaneous-injection PLGA formulation we recently developed. We expect to conduct a pre-IND meeting with the FDA and a Scientific Advice meeting in Europe prior to advancing veldoreotide into further clinical studies, beginning with Phase 1 safety and proof-of-concept studies in healthy volunteers and patients with acromegaly. In addition to at least one dose-ranging Phase 2 clinical trial, we anticipate that our clinical program will include at least one multinational Phase 3 clinical trial for registration, comparing veldoreotide to other treatments and/or placebo, including at least six months of controlled treatment to evaluate efficacy and at least one year of treatment to evaluate safety. We may also need to assess pharmacokinetics, safety and efficacy in special populations, including patients with liver or kidney disease and perform a thorough-QT study in healthy volunteers.

As a next generation SSA with potential growth-inhibitory effects on other tumor types and neovascularization (and presumably also vasoactive effects), veldoreotide may also have utility in treating other serious rare endocrine and non-endocrine diseases. We plan therefore to explore the utility of veldoreotide in other conditions either in small pilot studies in the respective patient populations and/or in relevant preclinical disease models.

Commercialization Strategy for Keveyis and Our Two Products Candidates in Development

Our existing commercial infrastructure is limited and is focused on Keveyis. We intend to independently commercialize Keveyis in the United States and 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. We plan to initially create a sales force of approximately 12 representatives in the United States to market Keveyis. In building our Keveyis sales force, we have recruited representatives with experience marketing orphan drug designated products.

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 Keveyis current commercial infrastructure when possible. As with Keveyis, 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. Given the relatively concentrated specialty prescriber base, we plan to create a sales force of approximately 30 representatives in the United States as well in the European Union to market our endocrine product candidates, if approved. In building our sales force, we intend to recruit representatives with experience calling on endocrinologists and marketing orphan drug designated products.

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 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 Product Candidates in Development

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 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 data or market exclusivity for our product candidates and methods of treatment, preserve the confidentiality of our 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 data exclusivity and patent term extensions when available, including the relevant exclusivity through orphan drug designation. 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 two are U.S. issued patents, and 17 pending patent applications, of which 6 are U.S. patent applications.

We have one pending United States, one pending Canadian, one pending Brazilian and one pending International (Madrid Protocol) trademark application designating Australia, China, European Community, India, Israel, Japan, Mexico, and Turkey for the mark "Strongbridge Biopharma."

Keveyis

We have acquired U.S. marketing rights to Keveyis. We are not aware of any issued patents or pending patent applications related to Keveyis. Although we intend to rely primarily on orphan exclusivity for Keveyis, we also expect to explore additional life cycle management opportunities.

Recorlev

We own 44 granted 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 Europe, China and Japan. We have three pending U.S. patent applications and one pending PCT application directed to methods of treating a disease or condition associated with elevated cortisol levels or activity with Recorlev. We also have an issued patent in the U.S. directed to reducing C-reactive protein levels and systemic inflammation through administration of a once-daily dose of Recorlev. Additionally, we have three pending US applications and eight pending foreign applications in Canada, Europe and Japan for next-generation product candidates, including new chemical entities. Patents in this portfolio, if and when issued, are expected to expire in 2026, 2027 and 2030 if there are no patent term adjustments or extensions.

Veldoreotide

While we own granted patents related to our product candidate veldoreotide in the United States and other major territories, including Europe and Canada, the terms of these patents may not extend beyond the launch date of this

product candidate. We have also filed a PCT application in 2017 directed to various methods and formulations of veldoreotide. To the extent we are not able to obtain further patent exclusivity as a result of the PCT application or other future patent filings, we intend to rely on orphan and data/marketing exclusivity for veldoreotide.

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 United States, is not subject to patent term adjustments in the same way as U.S. patents.

The term of a patent that covers a 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, or 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 our 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:

- **Keveyis:** Acetazolamide, another 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.

- **Recorlev:** A number of therapies are currently approved and in various stages of development for endogenous Cushing's syndrome. Currently, the marketed therapies for the treatment of endogenous Cushing's syndrome patients who fail or are ineligible for surgery in the United States and Europe are: Korlym (mifepristone) marketed by Corcept Therapeutics in the United States; Signifor (pasireotide) marketed by Novartis in the United States and European Union; and ketoconazole, metyrapone and mitotane marketed by HRA in the European Union. Novartis has submitted a NDA/MAA for Signifor (pasireotide) LAR in Cushing's disease. Additionally, LCI-699 (osilodrostat) is currently in Phase 3 clinical development by Novartis in Cushing's disease patients. Corcept is developing CORT125134, a second-generation glucorticoid receptor modulator; currently in Phase 2. HRA Pharma is developing metyrapone for the US market; currently in Phase 2. Millendo is developing ATR-101, a selective acyl-CoA:cholesterol acyltransferase 1 (ACAT) inhibitor, currently 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. Four additional therapies are in Phase 2 clinical development for acromegaly: octreotide long-acting depot (CAM-2029) developed by Novartis and Camurus; ITF-2984 developed by Italfarmaco; BIM-23B065 developed by Ipsen; and ATL-1103 developed by Antisense Therapeutics.

Discontinued License Agreements

Antisense Therapeutics

In April 2016, we executed an agreement (the "Settlement Agreement") with Antisense Therapeutics ("Antisense") to terminate the exclusive license agreement (the "Antisense License Agreement") that we and Antisense entered into in May 2015. The Antisense License Agreement provided us with development and commercialization rights to Antisense's product candidate, ATL1103, for endocrinology applications (specifically excluding the treatment of any form of cancer and the treatment of any complications of diabetes). Pursuant to the terms of the Settlement Agreement, we have made a one-time payment of approximately $770,000 to Antisense and returned to Antisense, for no consideration, the shares of Antisense owned by us. We also agreed to transfer to Antisense all data, reports, records and materials resulting from our development activities and all ATL1103 drug compound in our possession. The Settlement Agreement provides for the release by each party of all obligations and liabilities under the Antisense License Agreement.

Cornell Center for Technology Enterprise and Commercialization

In October 2016, our wholly owned subsidiary, BioPancreate Inc., provided a notice to Cornell University, through its Cornell Center for Technology Enterprise and Commercialization ("CCTEC"), in accordance with the terms of its agreement with CCTEC entered into in March 2011, of the termination of the agreement. The notice was provided in accordance with our decision to terminate our development program for BP-2002, a gene-modified probiotic in pre-clinical development for the potential treatment of type 1 and 2 diabetes that was the subject of the agreement. Because we had not yet reported our financial results for the three and six months ended June 30, 2016 at the time of providing the notice of termination, we recorded an impairment charge of $5.2 million in June 2016 since the conditions that caused the impairment existed as of June 30, 2016. The impairment charge represented the value of the intangible asset we had previously capitalized related to the license agreement.

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 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 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 check points 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 recently enacted federal Drug Supply Chain Security Act imposes new obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this new federal legislation, manufacturers will be 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, under this new legislation, manufacturers will have 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. Although we currently do not have any products on the market, we may be subject, and once our product candidates are approved and we begin commercialization, will be subject to additional healthcare laws and regulations enforced by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. 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, or collectively, 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 generally took effect in September 2013 and 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 intend to commercialize products that could be reimbursed under federal and other governmental healthcare programs, we plan to develop 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 will be sold in a foreign country, we may be 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 of any future approved products, if and when commercialized, will 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 products, if approved, unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of our products will therefore depend substantially, both domestically and abroad, on the extent to which the costs of our products will be 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.

In 2017, the U.S. Congress has been assessing new legislation designed to repeal and replace core sections of the PPACA. We expect the U.S. Congress to continue to review and assess this legislation, referred to as the American Health Care Act (AHCA), along with other alternative health care reform proposals throughout 2017. Recent Congressional efforts such as the AHCA proposal adds to the uncertainty of the legislative changes enacted as part of PPACA.

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.

Properties and Facilities

We lease 14,743 square feet of office space at 900 Northbrook Drive, Suite 200, Trevose, Pennsylvania 19053 for research and development and administrative activities. We believe that our existing facility is adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms. We also lease 3,173 square feet of office space in Radnor, Pennsylvania, which was subleased in September 2015.

Corporate Information

Strongbridge Biopharma plc, an Irish public limited company, was established on May 26, 2015 under the name Cortendo plc. On September 4, 2015, Cortendo plc changed its name to Strongbridge Biopharma plc. We also have a wholly owned subsidiary, Cortendo AB, organized under the laws of Sweden. See Part I, Item 10I "Subsidiary Information" a for list of subsidiaries of the Company.

Cortendo AB was established in October 1996 under the name Stefan Kronvall Medical AB and registered in Sweden in December 1996 for the purpose of developing medically innovative products for pharmaceutical diagnostics and other health care products. Stefan Kronvall Medical AB changed its name to Cortendo AB in 1997, to Cortendo Invest AB in 2003 and then to Cortendo AB (publ) in 2011.

In order to effect a corporate reorganization, on September 8, 2015 we settled an exchange offer, which we refer to as the Exchange Offer, pursuant to which holders of 99.449% of the outstanding shares of Cortendo AB exchanged their shares for beneficial interests in ordinary shares of Strongbridge Biopharma plc in the form of depositary receipts on a 1-for-1 basis and non-accredited holders of Cortendo AB shares located within the United States, representing 0.133% of the outstanding shares of Cortendo AB, agreed to exchange their shares for cash, which cash settlement occurred on September 14, 2015. Non-accredited U.S. holders of ordinary shares of Cortendo AB received cash in an amount equivalent to the value of one ordinary share of Strongbridge Biopharma plc for each share of Cortendo AB validly exchanged. Pursuant to individual agreements with the holders of options to purchase shares of Cortendo AB, the outstanding options of Cortendo AB were converted to options to purchase an equivalent number of ordinary shares of Strongbridge Biopharma plc. In September 2016, we acquired the non-controlling interest in Cortendo AB, after which Cortendo AB became a wholly owned subsidiary of Strongbridge Biopharma plc.

Following the settlement of the Exchange Offer, Strongbridge Biopharma plc became the parent of Cortendo AB and its subsidiaries. As a result of the settlement of the Exchange Offer, the historical financial statements of Cortendo AB became, for financial reporting purposes, the historical consolidated financial statements of Strongbridge Biopharma plc and its subsidiaries as a continuation of the predecessor. During the period from the settlement date of the Exchange Offer through the acquisition of all the shares of Cortendo AB not tendered in the Exchange Offer, the 0.418% interest in Cortendo AB was accounted for as a non-controlling interest.

Implications of Being an "Emerging Growth Company"

We qualify as an "emerging growth company," as defined in the Jumpstart our Business Startups Act of 2012 or the JOBS Act. An emerging growth company may take advantage of specified reduced reporting and regulatory requirements in contrast to those otherwise applicable generally to public companies. These provisions include:

- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to Section 404 the Sarbanes-Oxley Act of 2002;
- an exemption from the requirement to provide certain executive compensation disclosure;
- an exemption from the requirement to hold a non-binding advisory vote on executive compensation or to seek shareholder approval of any golden parachute payments not previously approved;
- an exemption from any requirements adopted by the Public Oversight Board (PCAOB) requiring mandatory audit firm rotation or a supplement to the auditor's report in which the auditor would be required to provide additional information about the audit and the financial statements of the issuer.

We may take advantage of these reduced reporting and other regulatory requirements for up to five years or such earlier time that we are no longer an emerging growth company. We will remain an "emerging growth company" until the earliest of: (1) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (2) the last day of the fiscal year following the fifth anniversary of the date of the completion of our initial public offering; (3) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; and (4) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. In addition, the JOBS Act provides that an emerging growth company may delay adopting new or revised accounting standards until those standards apply to private companies. We have irrevocably elected not to avail ourselves of this delayed adoption of new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as public companies that are not emerging growth companies. If we choose to take advantage of any of these reduced reporting burdens, the information that we provide shareholders may be different than you might get from other public companies.

Implications of Being a Foreign Private Issuer

As a foreign private issuer under the Exchange Act, we are exempted from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including:

- the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act;
- the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and
- the rules under the Exchange Act requiring the filing with the Securities and Exchange Commission of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K upon the occurrence of specified significant events.

ITEM 4A. UNRESOLVED STAFF COMMENTS

None

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

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 "Selected Consolidated Financial Information" and the financial statements and the related notes thereto included elsewhere in this 2016 Annual Report on Form 20-F. 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 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 on Form 20-F, 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 U.S. Food and Drug Administration ("FDA") for hyperkalemic, hypokalemic, and related variants of primary periodic paralysis. Keveyis, for which we hold the U.S. marketing rights, has orphan drug exclusivity status in the United States through August 7, 2022. In addition to this neuromuscular disease product, we have two clinical-stage product candidates for rare endocrine diseases, Recorlev and levoketoconazole. Recorlev (levoketoconazole, and formerly called COR-003) is a cortisol synthesis inhibitor currently being studied for the treatment of endogenous Cushing's syndrome. Veldoreotide (formerly called COR-005) is a next-generation somatostatin analog (SSA) being investigated for the treatment of acromegaly, with potential additional

applications in Cushing's syndrome and neuroendocrine tumors. Both Recorlev and veldoreotide have received orphan designation from the FDA and the European Medicines Agency ("EMA").

Given the well-identified and concentrated prescriber base addressing our target markets, we intend to use a small, focused sales force to effectively market our products, in the United States, the European Union and other key global markets. We believe that our ability to execute on this strategy is enhanced by the significant commercial and clinical development experience of key members of our management team. We will continue to identify and evaluate the acquisition of products and product candidates 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.

We have never been profitable and have incurred net losses since our inception in 1996. Our operations to date have been focused on identifying, in-licensing, acquiring and developing our product candidates, organizing and staffing our company, business planning and raising capital. We have funded our operations primarily through equity offerings. We incurred a net loss attributable to Strongbridge Biopharma of $48.6 million and $43.6 million for the years ended December 31, 2016 and 2015, respectively. At December 31, 2016, our accumulated deficit was $129.4 million.

See Part 1, Item 4 "Information on the Company – Overview – Recent Developments" for a description of our acquisition of Keveyis from Taro Pharmaceutical Industries Ltd., our Private Placement and our Loan Agreement with Oxford Finance LLC and Horizon Technology Finance Corporation.

Financial Operations Overview

The following discussion sets forth certain components of our statements of operations as well as factors that impact those items.

Revenues

We have not generated any revenue during the periods presented. Our ability to generate product revenue and become profitable depends upon our ability to obtain regulatory approval for and to successfully commercialize our product candidates.

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 agreements with third parties;
- costs of acquiring preclinical study and clinical trial materials, and costs associated with formulation and process development;
- depreciation, maintenance and other facility-related expenses; and
- costs to secure an exclusive license agreement with Antisense Therapeutics.

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, using information and data provided to us by our external research and development vendors and clinical sites.

Through the first half of 2014, we were focused on product candidates that are now outside the scope of our strategic focus, specifically the development of Crespine, an osteoarthritis program, and a next generation cortisol inhibitor, or NGCI, program. By the end of 2014, we changed our strategic focus to rare endocrine diseases and other rare diseases, specifically the development of Recorlev. As a result, we significantly reduced activities to develop the Crespine and NGCI programs. We returned our commercial rights to Crespine to the originator in the first half of 2014. We expect to spend only such amounts as are necessary to maintain our intellectual property on the NGCI program.

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.

General and Administrative Expenses

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, and other consulting services. We expect to incur additional general and administrative costs as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC and those of any national securities exchange on which our securities are traded, additional insurance expenses, investor relations activities and other administrative and professional services.

Interest Expense

Interest expense primarily represents interest payable to Oxford and Horizon, amortization of our debt discount, and issuance costs associated with loan and security agreement.

Unrealized Gain on Fair Value of Warrants

We classified the warrants issued in connection with our December 2016 Private Placement as a liability. 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 and comprehensive loss. The decrease in the fair value of the warrants between the issuance date and December 31, 2016 resulted in a unrealized gain of $0.6 million during the 12 months ended December 31, 2016.

Other Income (Expense), Net

Other income (expense), net, consists of interest income generated from our cash and cash equivalents, gains from the revaluation of foreign currency forward contracts, foreign exchange gains and losses and gains and losses on investments.

Our consolidated financial statements are reported in U.S. dollars, which is also our functional currency. 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 currency gain (loss) in other income (expense) in our consolidated statements of operations.

Historically, our cash and cash equivalents have been held primarily in foreign currencies. However, most of our expenses have been U.S. dollar denominated. To reduce our currency exposure, we used a hedging program from the fourth quarter of 2013 through the second quarter of 2015. The foreign currency forward contracts used in our hedging program were not entered into for speculative purposes and, although we believe they served as effective economic hedges, we did not seek to qualify for hedging accounting. In 2014, our operations continued to shift to the United States, but a large portion of our cash and cash equivalents were still held in foreign currencies. In the first half of 2015, all of our forward contracts expired.

Critical Accounting Policies and Significant Judgments 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 20-F, we believe the following accounting policies to be the most critical to the judgments and estimates used in the preparation of our 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 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 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.

Business Combinations

When acquiring new enterprises over which we obtain control, the acquisition method is applied. Under this method, we identify assets and liabilities of these enterprises and measure them at fair value at the acquisition date. Allowance is made for the tax effect of the adjustments made.

The excess of the consideration transferred, the amount of the non-controlling interest in the acquiree and the acquisition date fair value of previous equity interest in the acquiree over the fair value of the identifiable net assets acquired is recorded as goodwill.

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 or another appropriate method. 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 Pharmaceutical Industries Ltd, we have 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 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 will be amortized as units are sold over an estimated 8 year period.

Purchased identifiable intangible assets with indefinite lives, such as our in-process research and development, 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 has been reduced. To test these assets for impairment, we compare the fair value of the asset to its carrying value. The method we use to estimate the fair value measurements of indefinite-lived intangible assets is based on the income approach. For the impairment analysis for the year ended December 31, 2016, significant unobservable inputs used in the income approach valuation method include discount rates, royalty rates and probabilities of product candidate advancement from one clinical trial phase to the next. The probabilities of product candidate advancement we used were based on standalone statistical analysis on a phase-by-phase basis.

During the first half of 2015, as a result of our acquisition of Aspireo Pharmaceuticals Ltd.'s veldoreotide, our intangible assets increased by $31.3 million.

As of December 31, 2016, there were material events that led to the impairment of our intangible assets. We recorded a $5.2 million impairment relating to our BioPancreate IPR&D and a $10.6 million impairment for our veldoreotide IPR&D for the year ended December 31, 2016.

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, 2016, 2015 and 2014. During the first half of 2015, our goodwill increased by $5.1 million as a result of our acquisition of veldoreotide from Aspireo Pharmaceuticals Ltd. As of December 31, 2016, there were no events or changes in circumstances indicating possible impairment.

Stock-Based Compensation

We account for stock based compensation awards in accordance with 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 account for non employee and liability-classified stock based awards based on the then current fair values at each financial reporting date until the performance is complete for non employee awards, or until the award is settled (exercised) for liability-classified awards. Changes in the amounts attributed to these awards between the reporting dates are included in stock based compensation expense (credit) in our statements of operations. We include liability-classified stock options in non current liabilities in our balance sheets as their settlement (exercise) does not require use of cash, cash equivalents or other current assets.

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 initial public offering (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 common stock, 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 are also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from estimates. We record stock based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from our estimates, the differences are recorded as a cumulative adjustment in the period the estimates were revised. Historical forfeitures have been insignificant.

Income Taxes

We use the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and tax bases of assets and liabilities, and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. We assess the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

We have evaluated the positive and negative evidence bearing upon the realizability of our deferred tax assets. Based on our history of operating losses in Ireland and Sweden, we have concluded that it is more likely than not that the benefit of our deferred tax assets will not be realized. Currently, as a result of intercompany service agreements which provide a source of taxable income going forward, the Strongbridge U.S. Inc. is more likely than not to realize its deferred tax assets. Separately, as a result of writing off its intellectual property, BioPancreate will have a full valuation allowance against its prior separate company federal attributes and all existing state attributes.

Results of Operations

Comparison of the Years Ended December 31, 2016 and 2015

The following table sets forth our results of operations for the years ended December 31, 2016 and 2015.

	Year Ended December 31,		Change
	2016	2015	$
	(in thousands)		
Operating expenses:			
Research and development	$ 20,023	$ 20,135	$ (112)
General and administrative	14,875	22,719	(7,844)
Impairment of intangible assets	15,828	—	15,828
Total operating expenses	50,726	42,854	7,872
Operating loss	(50,726)	(42,854)	(7,872)
Other (expense) income, net	(631)	(1,229)	598
Loss before income taxes	(51,357)	(44,083)	(7,274)
Income tax benefit	2,638	450	2,188
Net loss	(48,719)	(43,633)	(5,086)
Net loss attributable to non-controlling interest	122	53	69
Net loss attributable to Strongbridge	$(48,597)	$(43,580)	$ (5,017)

Research and Development Expenses

The following table summarizes our research and development expenses during the years ended December 31, 2016 and 2015:

	Year Ended December 31,		Change
	2016	2015	$
	(in thousands)		
Product development and supporting activities	$ 16,183	$ 13,537	$ 2,646
Antisense Therapeutics license fee	—	3,899	(3,899)
Compensation and other personnel costs	3,239	1,906	1,333
Stock-based compensation expense	601	793	(192)
Total research and development expenses	$ 20,023	$ 20,135	$ (112)

Research and development expenses were $20.0 million for the year ended December 31, 2016, a $0.1 million decrease compared to the year ended December 31, 2015. The $2.6 million increase in product development and supporting activities was primarily attributed to a $3.0 million increase in expense to the ongoing clinical trials for Recorlev, and a $1.4 million increase due to the initiation of the development activity for veldoreotide, partially offset by reduced development spend due to discontinued programs for COR-004 and BioPancreate. Research and development expenses for the year ended December 31, 2015 included $3.9 million of the $5.0 million in aggregate cash paid to Antisense Therapeutics upon entering into a license agreement in May 2015, with the remaining $1.1 million of cash paid recorded as the initial carrying value of our investment in the equity of Antisense Therapeutics. Compensation and related costs increased by $1.3 million, for the year ended December 31, 2016 as compared to the same period in 2015 due to increased headcount of research and development personnel during the 2016 period. Non-cash stock-based compensation decreased $0.2 million due to the departure of certain research and development personnel.

General and Administrative Expenses

The following table summarizes our general and administrative expenses during the years ended December 31, 2016 and 2015:

	Year Ended December 31,		Change
	2016	2015	$
	(in thousands)		
Outside professional services	$ 5,626	$ 8,054	$ (2,428)
IPO preparation costs	—	4,007	(4,007)
Corporate development and licensing transaction costs	—	3,390	(3,390)
Compensation and other personnel costs	4,888	3,783	1,105
Stock-based compensation expense	4,006	3,147	859
Facility costs	355	338	17
Total general and administrative expenses	$ 14,875	$ 22,719	$ (7,844)

General and administrative expenses were $14.9 million for the year ended December 31, 2016, a decrease of $7.8 million compared to the year ended December 31, 2015. The $2.4 million decrease in outside professional and consulting services was primarily due to decreased legal fees in support of general corporate matters, employee recruiting fees, and consulting fees for general business efforts. General and administrative expenses for the year ended December 31, 2015 also included $4.0 million of legal and accounting fees related to the redomiciliation of the Company from Sweden to Ireland and the indirect activities necessary to prepare the Company's financial records for the U.S. initial public offering completed in October 2015. General and administrative expenses for the year ended December 31, 2015 also included $3.4 million of transaction fees and expenses related to the acquisition of veldoreotide from Aspireo Pharmaceuticals, the license of COR-004 from Antisense Therapeutics, and other business development activities. Compensation and related personnel costs increased by $1.1 million, and non-cash stock-based compensation by $0.9 million, during the year ended December 31, 2016 due to increased headcount of administrative personnel during the 2016 period.

Other Income (Expense), Net

The following table summarizes our other income (expense), net, during the years ended December 31, 2016 and 2015:

	Year Ended December 31,		Change
	2016	2015	$
	(in thousands)		
Foreign exchange (loss)	$ (69)	$ (124)	$ 55
Interest expense	(20)	—	$ (20)
Unrealized gain on fair value of warrants	638	—	$ 638
Loss on termination of license agreement with Antisense Therapeutics	(1,051)	—	$ (1,051)
Other expense, net	(129)	(1,105)	$ 976
Total other (expense) income, net	$ (631)	$ (1,229)	$ 598

Other income (expense), net, increased for the year ended December 31, 2016 as compared to the year ended December 31, 2015. The decrease in other expense, is mostly due to the impairment of our Antisense investment in 2015 of $.5 million as well loss on our Radnor lease of $.2 million, where as in 2016 we returned the license to Antisense and incurred a loss on termination charge of $1.1 million. We also recorded an unrealized gain on the fair value of our warrants.

Income Tax Benefit

We recorded income tax benefit of $2.6 million for the year ended December 31, 2016 and $0.5 million for the year ended December 31, 2015. For the year ended December 31, 2016, the benefit was primarily due to BioPancreate's write off of intellectual property and certain permanent deductions at Strongbridge U.S. Inc.. Additionally, Strongbridge U.S. Inc. is more likely than not to recognize it's deferred tax assets. In December 31, 2015 the benefit was due to the generation of U.S. state and federal net operating loss carry forwards and federal tax credit carry forwards. The income tax benefit for U.S. state and federal net operating loss carry forwards and the federal tax credit carry forwards has been recognized to the extent it is supported by the deferred tax liabilities recorded in connection with the acquisition of BioPancreate.

Net Loss Attributable to Non-Controlling Interest

We recorded a net loss attributable to non-controlling interest of $122,000 for the year ended December 31, 2016. The non-controlling interest results from the 0.418% of Cortendo AB shares not acquired by Strongbridge Biopharma plc pursuant to the exchange offer that expired September 3, 2015. In September 2016, the non-controlling interest was acquired by the Company.

Comparison of the Years Ended December 31, 2015 and 2014

The following table sets forth our results of operations for the years ended December 31, 2015 and 2014.

	Year Ended December 31,		Change
	2015	2014	$
	(in thousands)		
Operating expenses:			
Research and development	$ 20,135	$ 5,844	$ 14,291
General and administrative	22,719	4,588	18,131
Total operating expenses	42,854	10,432	32,422
Operating loss	(42,854)	(10,432)	(32,422)
Other (expense) income, net	(1,229)	282	(1,511)
Loss before income taxes	(44,083)	(10,150)	(33,933)
Income tax benefit	450	480	(30)
Net loss	(43,633)	(9,670)	(33,963)
Net loss attributable to non-controlling interest	53	—	53
Net loss attributable to Strongbridge	$(43,580)	$ (9,670)	$(33,910)

Research and Development Expenses

The following table summarizes our research and development expenses during the years ended December 31, 2015 and 2014:

	Year Ended December 31,		Change
	2015	2014	$
	(in thousands)		
Clinical development and supporting activities	$ 13,537	$ 5,412	$ 8,125
Antisense Therapeutics license fee	3,899	—	3,899
Compensation and other personnel costs	1,906	164	1,742
Stock-based compensation expense	793	268	525
Total research and development expenses	$ 20,135	$ 5,844	$ 14,291

Research and development expenses were $20.1 million for the year ended December 31, 2015, an increase of $14.3 million compared to the year ended December 31, 2014. The $8.2 million increase in clinical development and supporting activities was primarily attributed to a $4.8 million increase in expenses related to the ongoing clinical trials for Recorlev, and a $3.4 million increase due to the initiation of the development activity for Recorlev and veldoreotide. Research and development expenses for the year ended December 31, 2015 included $3.9 million of the $5.0 million in aggregate cash paid to Antisense Therapeutics upon entering into a license agreement in May 2015, with the remaining $1.1 million of cash paid recorded as the initial carrying value of our investment in the equity of Antisense Therapeutics. Compensation and related costs increased by $1.7 million, and non-cash stock-based compensation increased $0.5 million, for the year ended December 31, 2015 as compared to the same period in 2014 due to increased headcount of research and development personnel during the 2015 period.

General and Administrative Expenses

The following table summarizes our general and administrative expenses during the years ended December 31, 2015 and 2014:

	Year Ended December 31,		Change
	2015	2014	$
	(in thousands)		
Outside professional services	$ 8,054	$ 3,335	$ (4,719)
Redomiciliation and IPO preparation costs	4,007	—	(4,007)
Corporate development and licensing transaction costs	3,390	—	(3,390)
Compensation and other personnel costs	3,783	1,165	(2,618)
Stock-based compensation expense	3,147	(17)	(3,164)
Facility costs	338	105	(233)
Total general and administrative expenses	$ 22,719	$ 4,588	$(18,131)

General and administrative expenses were $22.7 million for the year ended December 31, 2015, an increase of $18.1 million compared to the year ended December 31, 2014. The $4.7 million increase in outside professional and consulting services was primarily due to increased legal fees in support of general corporate matters, employee recruiting fees, audit fees, market analysis costs, and consulting fees for business development efforts. General and administrative expenses for the year ended December 31, 2015 also included $4.0 million of legal and accounting fees related to the redomiciliation of the Company from Sweden to Ireland and the indirect activities necessary to prepare the Company's financial records for the U.S. initial public offering completed in October 2015. General and administrative expenses for the year ended December 31, 2015 also included $3.4 million of transaction fees and expenses related to the acquisition of veldoreotide from Aspireo Pharmaceuticals, the license of COR-004 from Antisense Therapeutics, and other business development activities. Compensation and related personnel costs increased by $2.6 million, and non-cash stock-based compensation by $3.2 million, during the year ended December 31, 2015 due to increased headcount of administrative personnel during the 2015 period. Facility costs increased by $0.2 million primarily as a result of entering into a lease for our Trevose, Pennsylvania office space in April 2015.

Other Income (Expense), Net

The following table summarizes our other income (expense), net, during the years ended December 31, 2015 and 2014:

	Year Ended December 31,		Change
	2015	2014	$
	(in thousands)		
Foreign exchange loss	$ (124)	$ (204)	$ (80)
Other income, net	(1,105)	486	1,591
Total other (expense) income, net	$ (1,229)	$ 282	$ 1,511

Other income (expense), net, changed from expense of $0.3 million in 2014 to expense of $1.2 million in 2015. The change was primarily due to the charges related to the wind down of our previous foreign currency hedging program and the write down of our investment in Antisense equity to market value.

Income Tax Benefit

We recorded income tax benefit of $0.5 for the years ended December 31, 2015 and 2014, due to the generation of U.S. state and federal net operating loss carry forwards and federal tax credit carry forwards. The income tax benefit for U.S. state and federal net operating loss carry forwards and the federal tax credit carry forwards has been recognized to the extent it is supported by the deferred tax liabilities recorded in connection with the acquisition of BioPancreate.

Net Loss Attributable to Non-Controlling Interest

We recorded a net loss attributable to non-controlling interest of $53,000 for the year ended December 31, 2015. The non-controlling interest results from the 0.418% of Cortendo AB shares not acquired by Strongbridge Biopharma plc pursuant to the exchange offer that expired September 3, 2015.

Liquidity and Capital Resources

Our operations have been financed primarily by net proceeds from the issuance of ordinary shares and the issuance of debt. Our primary uses of capital have been third-party expenses associated with the planning and conduct of clinical trials, costs of process development services and manufacturing of our product candidates, and compensation-related expenses. We expect our funding requirements for operating activities to increase in 2017 and possibly beyond due to expenses associated with the commercialization of Keveyis, the execution of the Phase 3 SONICS and LOGICS clinical trials for Recorlev, and selling, general and administrative expenses. We also expect our cash needs to increase to fund potential in-licenses, acquisitions or similar transactions as we pursue our strategy. These expenses may be offset only in part by sales of Keveyis. In addition, beginning in June 2018, we will be required to make monthly principal payments to repay amounts borrowed under our credit facility.

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. We believe that our cash resources will be sufficient to allow us to fund planned operations at least into 2019, which is after the expected receipt of data from the Recorlev SONICS and LOGICS Phase 3 clinical trials.

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

- the amount of revenue that we receive from sales of Keveyis; 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;
- whether we borrow any additional amounts under our credit facility;
- 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.

We expect to continue to incur losses. Our ability to achieve and maintain profitability is dependent upon the successful commercialization of Keveyis, the development, regulatory approval and commercialization of our product candidates and achieving a level of revenues 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. 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.

Cash Flows

Comparison for the Years Ended December 31, 2016 and 2015:

	Year Ended December 31	
	2016	**2015**
Net cash (used in) provided by:		
Operating activities	$ (31,714)	$ (37,360)
Investing activities	(3,392)	(4,294)
Financing activities	50,320	77,404
	15,214	35,750
Effect of exchange rate changes on cash and cash equivalents	—	241
Net increase in cash and cash equivalents	$ 15,214	$ 35,991

Operating Activities

Net cash used in operating activities was $31.7 million for the year ended December 31, 2016, compared to $37.4 million for the year ended December 31, 2015. The decrease in net cash used was primarily due to business development activities and fees related to indirect activities necessary to redomicile the Company and to prepare the Company's financial records for the U.S. initial public offering that occurred in 2015.

Investing Activities

The $3.4 million of cash used in 2016 investing activities related to the purchase of Keveyis. The $4.3 million of cash used in 2015 investing activities primarily related to the acquisition of veldoreotide and the license of COR-004 in 2015.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2016 was $50.3 million and consisted of $32.7 million of proceeds from the issuance of ordinary shares and warrants in a private placement financing and $19.3 million proceeds from the issuance of debt and warrants. Net cash provided by financing activities for the year ended December 31, 2015 was $77.4 million, which consisted of proceeds from the issuance of ordinary shares in private placement financings and our IPO in October of 2015.

Contractual Obligations and Other Commitments

The following table summarizes our future minimum commitments at December 31, 2016:

	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	$ 5,003	$ 5,058	$ 11,022	$ 8,025	$ 29,108
Debt Payments	$ —	$ 12,667	$ 7,333	$ —	$ 20,000
Operating leases	$ 311	$ 503	$ —	$ —	$ 814
Total contractual obligations	$ 5,314	$ 18,228	$ 18,355	$ 8,025	$ 49,922

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

We are obligated to make future payments to third parties under in-license agreements, including sublicense fees, royalties and payments that become due and payable upon the achievement of development and commercialization milestones. As the amount and timing of sublicense fees and the achievement 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. See footnote 6 of the consolidated financial statements for a description of our license agreements.

Off-Balance Sheet Arrangements

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

Quantitative and Qualitative Disclosures About Market Risk

At December 31, 2016, we had cash and cash equivalents of $66.8 million, which consisted of 100% of bank deposits in the United States. 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.

Recent Accounting Pronouncements

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

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Executive Officers and Board of Directors

The following table presents information about our officers and directors as of March 1, 2017.

NAME	AGE	POSITION
Executive Officers		
Matthew Pauls	46	Chief Executive Officer and Director
A. Brian Davis	50	Chief Financial Officer
Fredric Cohen, M.D.	52	Chief Medical Officer
Stephen Long	51	Chief Legal Officer
Robert Lutz	48	Chief Business Officer
Non-Employee Directors		
John H. Johnson	59	Director, Chairman of the Board
Richard S. Kollender	47	Director
Garheng Kong, M.D., Ph.D.	41	Director
Jeffrey W. Sherman, M.D., FACP	61	Director
Mårten Steen, M.D., Ph.D.	41	Director
Hilde H. Steineger, Ph.D.	50	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 Mast Therapeutics, Inc., a publicly traded biopharmaceutical company, since October 2015. 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.

Robert Lutz has served as our Chief Business Officer since October 2014. Prior to joining Strongbridge, he worked as a full-time consultant at Medgenics, a publicly traded, early-stage, gene-therapy and rare disease biotech company, from May 2014 to September 2014. Mr. Lutz worked at Shire Pharmaceuticals, a publicly traded specialty biopharmaceutical company, from November 2012 to April 2014, where he most recently served as Vice President and held key leadership positions in the Neurosciences Business unit. Prior to Shire Pharmaceuticals, Mr. Lutz worked in a variety of roles, including Vice President and Senior Associate, for Cinergy Corp., an electric and gas utility company. Mr. Lutz worked as a Senior Analyst at Alan B. Slifka and Co., a hedge fund, after having started his career at Goldman Sachs, where he served as a Financial Analyst in their principal investment area. He holds a B.A. in economics and computer science from Amherst College and an M.B.A. from the Kellogg School of Management.

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. Mr. Johnson currently serves as a member of the board of directors of Cempra Pharmaceuticals, Inc., Histogenics Corporation, Portola Pharmaceuticals, Inc. and Sucampo 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 August 2016, Mr. Kollender has served as Chief Business Officer and Chief Financial Officer of Rapid Micro Biosystems. Since January 2011, Mr. Kollender has served as a Partner and Executive Manager of Quaker Partners Management, LP, a healthcare investment firm, which Mr. Kollender initially joined in 2003 and was promoted to partner in 2005. Mr. Kollender serves as a director of Tarsa Therapeutics. Mr. Kollender previously served as a director of Celator Pharmaceuticals, Inc., Rapic Micro Biosystems, Inc., Insmed, Transave, Inc., Nupathe, Inc., TargetRx, Inc., Precision Therapeutics, Inc., Transport Pharmaceuticals, Inc. and Corridor Pharmaceuticals. 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 a MBA and Health Administration and Policy Degree with honors from the University of Chicago, and has 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 focused on medical products, devices, diagnostics, consumer health and healthcare IT. 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 Cempra, Inc., Histogenics Corporation, 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, M.D., FACP, has served as a member of our board of directors since October 2016. He currently serves as the chief medical officer and Executive Vice President of Research and Development at Horizon Pharma plc. He has 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 senior leadership positions at IDM Pharma Takeda Global Research and Development, Neopharma, Searle/Pharmacia, Bristol-Myers Squibb, and is past president of the Drug Information Association (DIA). Dr. Sherman earned his M.D. from the Rosalind Franklin University of Medicine and Science/The Chicago Medical School. He completed internship and residency programs at Northwestern University Feinberg School of Medicine, where he currently serves as an adjunct assistant professor, and a fellowship program at the University of California San Francisco. He received a B.A. in Biology from Lake Forrest 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, 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. Currently, he serves as a member of the board of directors of Wilson Therapeutics AB, Altimmune Inc. and BioClin Therapeutics Inc. He previously served on the boards of Ultragenyx 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 consultant for the Strategic Innovation Management in the Nutrition & Health Division of BASF. She previously served as the Head of Strategic Innovation Management and 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 ASA. She previously served as a member of the boards of directors of Aifew AS, Algeta ASA, Weifa AS, Invent2 AS, Alertis AS, Clavis Pharma ASA and Biotech Pharmacon ASA. Dr. Steineger holds a Ph.D. in medical biochemistry from University of Oslo.

Board Composition

The Irish Companies Act provides for a minimum of two directors for public limited companies. Our Articles of Association provide for a minimum of two directors and a maximum of 13 directors. Our shareholders may from time to time increase or reduce the maximum number, or increase or reduce the minimum number (subject to the minimum requirements of the Irish Companies Act), of directors by special resolution. Our board of directors determines the number of directors within the range of two to 13. Our board currently consists of seven directors.

Our Articles divide our board of directors into three classes, with members of each class being elected to staggered three-year terms. At each annual general meeting, directors will be elected for a full term of three years to succeed those directors of the relevant class whose terms are expiring. A nominee is elected to the board of directors by a plurality of votes cast. Our Class I directors, consisting of Drs. Steineger and Steen, were elected at our annual general meeting in May 2016 for a term ending in May 2019. Our Class II directors, consisting of Messrs. Johnson and Kollender, and Dr. Sherman, are expected to be nominated for election at our annual general meeting in May 2017 for a term ending in May 2020. Our Class III directors, consisting of Dr. Kong and Mr. Pauls, are expected to be nominated for election at our annual general meeting in May 2018 for a term ending in May 2021.

Holders of our ordinary shares are entitled to one vote for each share at all meetings at which directors are elected.

Our Articles provide for a minimum of two directors. In the event that an election results in only one director being elected, that director shall be elected and shall serve for a three-year term, and the nominee receiving the next greatest number of votes in favor of his or her election shall hold office until his or her successor shall be elected.

Any vacancy on our board of directors, including a vacancy resulting from an increase in the number of directors or from the death, resignation, retirement, disqualification or removal of a director, shall be deemed a casual vacancy. Subject to the terms of any one or more classes or series of preferred shares, any casual vacancy shall only be filled by the decision of a majority of our board of directors then in office, provided that a quorum is present and provided that the appointment does not cause the number of directors to exceed any number fixed by or in accordance with our Articles as the maximum number of directors.

Any director of a class of directors elected to fill a vacancy resulting from an increase in the number of directors of such class shall hold office for the remaining term of that class. Any director elected to fill a vacancy not resulting from an increase in the number of directors shall have the same remaining term as that of his predecessor. A director retiring at a meeting shall retain office until the close or adjournment of the meeting.

Our Articles provide that our shareholders may, by an ordinary resolution, remove a director from office before the expiration of his or her term. Additionally, our Articles provide that a director may be removed with or without cause at the request of not less than 75% of the other directors.

We are a foreign private issuer. As a result, in accordance with the NASDAQ stock exchange listing requirements of The NASDAQ Global Select Market, or NASDAQ, we may rely on home country governance requirements and certain exemptions thereunder rather than relying on the stock exchange corporate governance requirements. For an overview of our corporate governance principles, see “Description of Share Capital and Articles of Association” in the Company’s Registration Statement on Form F-3 filed January 12, 2017 (file number 333-215531) which is incorporated herein by reference.

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.

Committees of the Board of Directors

The standing committees of our board of directors consist of a nomination and governance committee, an audit committee and a compensation committee. Each committee operates under a charter. Copies of each committee’s charter are posted on the Investors section of our website, which is located at www.strongbridgebio.com.

Nomination and Governance Committee

The current members of our nomination and governance committee are Mårten Steen, John H. Johnson and Garheng Kong, with Dr. Steen serving as chairman. Our board of directors has determined that each member of our nomination and governance committee is independent under the applicable listing requirements of NASDAQ.

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.

Compensation Committee

The current members of our compensation committee are John H. Johnson, Garheng Kong and Richard S. Kollender, with Mr. Johnson serving as chairman. Our board of directors has determined that each member of our compensation committee is independent under the applicable listing requirements of NASDAQ.

B. COMPENSATION

Summary Compensation Table

The following table sets forth information concerning cash and non-cash compensation paid for 2016 and 2015 to certain of our executive officers (referred to herein as "our executive officers").

Name and position	Year	Salary ($)	Bonus ($)[1]	Total
Matthew Pauls	2016	$ 468,000	$ 198,900	$ 666,900
Chief Executive Officer	2015	$ 428,653	$ 241,250	$ 669,903
A. Brian Davis (2)	2016	$ 334,750	$ 123,858	$ 458,608
Chief Financial Officer	2015	$ 248,522	$ 145,250	$ 393,772
Fredric Cohen, M.D. (3)	2016	$ 318,747	$ 134,900	$ 453,647
Chief Medical Officer				

(1) The amounts in this column represent the discretionary bonuses paid with respect to 2016 and 2015 performance.

(2) Mr. Davis's employment commenced in March 2015.

(3) Dr. Cohen's employment commenced in August 2015 and he was promoted to Chief Medical Officer in November 2016.

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 an employment agreement with (1) Mr. Pauls effective August 23, 2014, for his service as our President and Chief Executive Officer, (2) Mr. Davis effective March 23, 2015, for his service as our Chief Financial Officer, and (3) Dr. Cohen effective August 5, 2015, for his service as our Chief Medical Officer. Dr. Cohen was originally hired as Vice President, Clinical Research and Development. The term of the employment agreement for Mr. Pauls is through August 23, 2017, the term of the employment agreement with Mr. Davis is through March 23, 2018, and the term of the employment agreement for Dr. Cohen is through August 5, 2017. The employment agreements will automatically renew for one-year terms unless either party gives notice of non-renewal at least 90 days prior to the end of the term. The agreements also provide for annual incentive bonus targets for Messrs. Pauls and Davis, and Dr. Cohen of 50%, 40% and 40%, respectively.

Under their 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 do not match these contributions. Our executive officers are not eligible for retirement benefits other than under our 401(k) plan. The company is not required to, and had not, set a side any amounts relating to pension or retirements.

Outstanding Equity Awards at March 1, 2017

The following table includes certain information with respect to option awards that were outstanding as of March 1, 2017 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 [1]	—	$ 8.06	8/23/2014	8/23/2019
	72,727	— [1]	$10.74	8/23/2014	8/23/2019
	—	81,818 [1]	$13.43	8/23/2014	8/23/2019
	123,176	331,369 [2]	$15.71	5/26/2015	5/26/2025
	56,250	168,750 [3]	$ 3.94	2/26/2016	2/26/2026
	—	375,000 [3]	$ 2.90	2/23/2017	2/23/2027
A. Brian Davis	14,773	39,772 [2]	$15.71	5/26/2015	5/26/2025
	44,455	88,908 [4]	$18.80	7/21/2015	7/21/2020
	16,250	48,750 [3]	$ 3.94	2/26/2016	2/26/2026
	—	180,000 [3]	$ 2.90	2/23/2017	2/23/2027
Fredric Cohen, M.D.	30,682	51,136 [5]	$18.12	8/5/2015	8/5/2025
	7,500	22,500 [3]	$ 3.94	2/26/2016	2/26/2026
	—	40,000 [5]	$ 4.16	6/13/2016	6/13/2016
	—	10,000 [5]	$ 3.95	11/23/2016	11/23/2026
	—	173,000 [3]	$ 2.90	2/23/2017	2/23/2027

(1) These options vest in three equal annual tranches. The first tranche of these options vested on August 23, 2015. The second tranche vests on August 23, 2016. The third tranche vests on August 23, 2017. 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.

(2) 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.

(3) 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.

(4) 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.

(5) These options vest with respect to one-fourth of the shares to vest on the one-year anniversary of the Date of Grant and the remaining three-fourths of shares to vest in 12 equal, 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.

Restricted Stock Units Grants

On February 26, 2016, our board of directors approved grants of restricted stock units, or RSUs, to Messrs. Pauls and Davis, and Dr. Cohen in the amounts of 40,000, 20,000 and 13,000, respectively. On June 13, 2016 and November 23, 2016, our board of directors approved grants of RSUs for Dr. Cohen in the amounts of 5,000 and 4,000,

respectively. These RSUs vest, with respect to 100% of the grants, on the second anniversary following the date of grant, provided that the executive 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," 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.

If any of our other executive officers is terminated due to our election not to renew the term of the employment agreement, subject to the execution of a release of claims, he will be entitled to (1) an amount equal to the sum of 12 months of base salary and the target bonus for Mr. Pauls, or six months of base salary and one-half of the target bonus for our other executive officers, paid in installments over the 12-month period following termination for Mr. Pauls or the six-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) 12 months following the termination date for Mr. Pauls, or six 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 our election not to renew the term of the employment agreement, 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 directors received fees in cash in 2016 and 2015 for their service on the board as summarized below:

Name	Year	Fees earned or paid in cash ($)
John H. Johnson	2016	$ 96,713
	2015	$ 65,050
Richard S. Kollender	2016	$ 57,795
	2015	$ 33,126
Garheng Kong, M.D., Ph.D.	2016	$ 46,685
	2015	$ 12,934
Jeffrey W. Sherman, M.D., FACP[2]	2016	$ —
	2015	$ —
Mårten Steen, M.D., Ph.D.	2016	$ 47,780
	2015	$ 35,833
Hilde H. Steineger, Ph.D.	2016	$ 47,780
	2015	$ 35,833
H. Joseph Reiser[1]	2015	$ 18,749
Espen Tidemann Jørgensen[1]	2015	$ 14,348
Ernest Eichenberg III[1]	2015	$ 10,938
Joseph M. Mahady[1]	2015	$ 22,029
Eigil Stray Spetalen[1]	2015	$ 21,349

(1) Messrs. Reiser, Eichenberg, Jørgensen, Spetalen and Mahady resigned from the board of directors of Cortendo AB in 2015.

(2) Dr. Sherman joined the board of directors in October 2016.

The following table includes certain information with respect to option awards that were outstanding as of March 1, 2017 for our current non-employee directors.

	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
John H. Johnson	18,181	— (1)	$10.74	3/17/2015	3/17/2020
	—	18,181 (1)	$13.43	3/17/2015	3/17/2020
	—	18,181 (1)	$16.11	3/17/2015	3/17/2020
	13,224	— (2)	$17.55	10/16/2015	10/16/2025
	—	40,000 (4)	$ 5.50	5/12/2016	5/12/2026
Richard S. Kollender	9,090	— (1)	$10.74	3/17/2015	3/17/2020
	—	9,090 (1)	$13.43	3/17/2015	3/17/2020
	—	9,090 (1)	$16.11	3/17/2015	3/17/2020
	9,918	— (2)	$17.55	10/16/2015	10/16/2025
		40,000 (4)	$ 5.50	5/12/2016	5/12/2026
Garheng Kong, M.D., Ph.D.	11,110	13,890 (3)	$17.55	10/16/2015	10/16/2025
	9,385	— (2)	$17.55	10/16/2015	10/16/2025
		40,000 (4)	$ 5.50	5/12/2016	5/12/2016
Jeffrey W. Sherman, M.D., FACP	—	60,000 (5)	$ 5.22	10/1/2016	10/1/2026
Mårten Steen, M.D., Ph.D.	11,110	13,890 (3)	$17.55	10/16/2015	10/16/2025
	9,918	— (2)	$17.55	10/16/2015	10/16/2025
	—	40,000 (4)	$ 5.50	5/12/2016	5/12/2016
Hilde H. Steineger, Ph.D.	11,110	13,890 (3)	$17.55	10/16/2015	10/16/2025
	9,918	— (2)	$17.55	10/16/2015	10/16/2025
	—	40,000 (4)	$ 5.50	5/12/2016	5/12/2026

(1) These options vest in three equal annual tranches. The first tranche of these options vested on March 17, 2016. The second tranche vests on March 17, 2017. The third tranche vests on March 17, 2018. These options will fully vest and become exercisable upon a change of control provided that the individual is a member of our board of directors on the date of such change of control.

(2) These options vested on April 30, 2016. These options will fully vest and become exercisable upon a change of control provided that the individual is a member of our board of directors on the date of such change of control.

(3) These stock options vest with respect to one-third of the shares on October 16, 2017. The remaining two-thirds of the stock options vest in equal monthly installments over the 24-month period commencing after October 16, 2017. All of these options will fully vest and become exercisable upon a change of control provided that the individual is a member of our board of directors on the date of such change of control.

(4) These options vest on the earlier of May 12, 2017 or the date of the company's 2017 Annual General Meeting. These options will fully vest and become exercisable upon a change of control provided that the individual is a member of our board of directors on the date of such change of control.

(5) These options vest in three equal annual tranches. The first tranche vest on October 1, 2017; the remaining two tranches vest equally on October 1, 2018 and 2019. All of these options will fully vest and become exercisable upon a change of control provided that the individual is a member of our board of directors on the date of such change of control.

Our board of directors' compensation program provides 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—$15,000
    - Compensation Committee Chair Retainer—$10,000
    - Governance Committee Chair Retainer—$7,500
    - Audit Committee Member (other than Chairman) Retainer—$7,500
    - Compensation Committee Member (other than Chairman) Retainer—$5,000
    - Governance Committee Member (other than Chairman) Retainer—$3,750
- 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

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. A total of 628,155 shares of our common stock have been reserved for issuance pursuant to the Non-Employee Director Plan. The shares of our common stock 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 of our common stock on the last day of the immediately preceding fiscal year. The Share Pool will be reduced on the date of grant, by one share of our common stock for each award under the Non-Employee Director Plan; provided that awards that are valued by reference to shares of our common stock 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 shares of our common stock 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 common stock 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 common stock 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 shares of our common stock 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. Shares of common stock 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 share of our common stock. 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. A total of 3,343,434 shares of our common stock have been reserved for issuance pursuant to the 2015 Plan. The shares of our common stock 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 shares of our common stock on the last day of the immediately preceding fiscal year. A maximum of 1,000,000 shares of our common stock 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 shares that may be issued under the 2015 Plan as incentive stock options is 3,343,434. The Share Pool will be reduced on the date of grant, by one share of our common stock for each award under the 2015 Plan; provided that awards that are valued by reference to shares of our common stock 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 shares of our common stock subject to such awards will again be available for awards under the Share Pool. Notwithstanding the foregoing, the following shares of our common stock 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 common stock 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 common stock 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 common stock 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 shares of our common stock that vest in accordance with terms and conditions established by the compensation committee. The compensation committee will determine the number of shares of 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. Shares of our common stock 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 share of our common stock. 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 1,000,000 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.

D. EMPLOYEES

As of December 31, 2016, we had 24 full-time employees, each of whom is working in the United States. Of these full-time employees, 9 were engaged in research and development and 15 were engaged in general and administrative activities.

E. SHARE OWNERSHIP

The following table sets forth certain information as of March 1, 2017 regarding beneficial ownership of our ordinary shares by all of our current directors and executive officers. The number of ordinary shares beneficially owned by each entity, person, executive officer or director is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any ordinary shares over which the individual has sole or shared voting power or investment power

as well as any ordinary shares that the individual has the right to acquire within 60 days of March 1, 2017 through the exercise of any option or other right. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all ordinary shares held by that person.

Executive Officers and Directors	No. of Shares	% of total Shares
Matthew Pauls	338,465	*
Fredric Cohen, M.D.	38,182	*
A. Brian Davis	123,030	*
Stephen Long	122,536	*
Robert Lutz	98,543	*
John H. Johnson	49,586	*
Richard S. Kollender	28,098	*
Garheng Kong, M.D., Ph.D.	21,885	*
Jeffrey W. Sherman, M.D., F.A.C.P.	0	*
Mårten Steen, M.D., Ph.D.	22,418	*
Hilde H. Steineger, Ph.D.	22,418	*
All Current Executive Officers and Directors as a Group (11 persons)	**865,161**	**2.4%**

* Indicates beneficial ownership of less than 1% of the total outstanding ordinary shares.

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. PRINCIPAL SHAREHOLDERS

The number of ordinary shares beneficially owned by each entity, person, executive officer or director is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any ordinary shares over which the individual has sole or shared voting power or investment power as well as any ordinary shares that the individual has the right to acquire within 60 days of March 1, 2017 through the exercise of any option or other right. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table below have sole voting and investment power with respect to all ordinary shares held by that person.

Ordinary shares that a person has the right to acquire within 60 days of March 1, 2017 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all executive officers and directors as a group. The percentage of beneficial ownership of our ordinary shares prior to the offering is based on an aggregate of 35,335,026 shares outstanding as of March 1, 2017.

The following table presents information relating to the beneficial ownership of our ordinary shares as of March 1, 2017.

Name of Beneficial Owner		No. of Shares	% of total Shares
Caxton Alternative Management LP	(1)	5,394,994	15.3%
Growth Equity Opportunities Fund III, LLC	(2)	4,141,308	11.7%
HealthCap VI, L.P.	(3)	3,236,008	9.2%
Vivo Capital VIII, LLC	(4)	3,000,000	8.5%
Broadfin	(5)	2,894,581	8.2%

(1) Based on the information disclosed in a Schedule 13G filed with the SEC on December 30, 2016 by Caxton Corporation ("Caxton"), CDK Associates, L.L.C. ("CDK") and Bruce Kovner, in which Caxton, the manager of CDK, and Mr. Kovner, the Chairman and sole shareholder of Caxton, each reported shared voting and dispositive power with respect to 5,394,994 ordinary shares and CDK reported shared voting and

dispositive power with respect to 5,102,433 ordinary shares. Caxton and Mr. Kovner disclaim beneficial ownership of the ordinary shares reported except to the extent of their pecuniary interest therein. The address of Caxton and CDK is 731 Alexander Road, Princeton, NJ, 08540. The business address of Mr. Kovner is 1001 North U.S. Highway 1, Jupiter, FL 33477.

(2) 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 dispositve power with respect to 4,141,308 ordinary shares.. 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.

(3) Based on the information disclosed in a Schedule 13G/A filed with the SEC on January 17, 2017 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, 3,236,008 ordinary shares. HealthCap GC is the sole general partner of HealthCap. The address of HealthCap and HealthCap GP is 18, Avenue d'Ouchy, 1006 Lausanne, Switzerland.

(4) Based on the information disclosed in a Schedule 13G filed with the SEC on January 9, 2017 by Vivo Capital VIII, LLC ("Vivo"), in which Vivo reported sole voting and dispositive power with respect to 3,000,000 ordinary shares. According to the Schedule 13G, the ordinary shares are held of record by Vivo Capital Fund VIII, L.P. (2,636,000 ordinary shares) and Vivo Capital Surplus Fund VIII, L.P. (364,000 ordinary shares). Vivo serves as the general partner for each of these entities. The address of Vivo is 505 Hamilton Street, Palo Alto, CA, 94301.

(5) Based on the information disclosed in a Schedule 13G/A filed with the SEC on February 10, 2017 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, 3,494,581 ordinary shares (including 600,000 ordinary shares issuable upon the exercise of warrants). The number reported in the table above for Broadfin Capital does not include the 600,000 ordinary shares issuable upon the exercise of the warrants, as these shares are not exercisable within 60 days of March 1, 2017. Mr. Kotler is the managing member of Broadfin Capital and a director of Broadfin Fund. The address of Broadfin Capital and Mr. Kotler is Broadfin Capital, 300 Park Avenue, 25th floor, New York, N.Y. 10022. The address of Broadfin Fund is 20 Genesis Close, Ansbacher House, Second Floor, PO Box 1344, Grand Cayman KY1-1108, Cayman Islands.

B. RELATED PARTY TRANSACTIONS

On December 22, 2016, we entered into a Share Purchase Agreement to sell $35 million of our shares in a private placement (14,000,000 shares at a subscription price of $2.50 per share). Certain of our existing 5% shareholders that beneficially own more than 5% of our ordinary shares and/or their affiliates purchased ordinary shares in this transaction, including New Enterprise Associates, Broadfin, Eigil Stray Spetalen and HealthCap VI, LP, of which Dr. Steen, one of our directors, is a partner.

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.

C. INTERESTS OF EXPERTS AND COUNSEL

Not applicable.

ITEM 8. FINANCIAL INFORMATION

Financial Statements

Our audited Consolidated Financial Statements are filed as part of this Annual Report pursuant to Item 18-"Financial Statements" and are found immediately following the text of this Annual Report.

No significant change has occurred since the date of our annual financial statements, included in this Annual Report on Form 20-F per Item 8.B.

Legal Proceedings

We are not currently a party to any material legal proceedings.

Dividends

We have not paid cash dividends on our ordinary shares and do not intend to pay cash dividends on our ordinary shares in the foreseeable future.

ITEM 9. THE OFFER AND LISTING

A. Offering and Listing Details

Not applicable.

B. Plan of Distribution

Not applicable.

C. Market

Our shares were quoted on the Norwegian Over-The-Counter Market until October 20, 2015 when trading ceased. On October 15, 2015, a registration statement was declared effective by the U.S. Securities and Exchange Commission and on October 16, 2015 our initial U.S. public offering of 2,500,000 ordinary shares at a price to the public became effective commencing our listing and trading on The NASDAQ Global Select Market under the symbol "SBBP".

The following table sets forth the monthly high and low sale prices of our ordinary shares as quoted on The NASDAQ Global Select Market since our shares began trading on October 16, 2015:

	High	Low
October 16, 2015 through October 31 2015	$14.30	$ 6.90
November 2015	$ 8.80	$ 6.32
December 2015	$ 7.83	$ 5.00
March 2016	$ 6.33	$ 3.80
June 2016	$ 4.83	$ 3.30
September 2016	$ 6.24	$ 4.45
December 2016	$ 3.85	$ 2.05

D. Selling Shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the issue

Not applicable.

ITEM 10. ADDITIONAL INFORMATION

A. Share Capital

Not applicable.

B. Memorandum and articles of association

The information contained under the caption of "Description of Share Capital and Articles of Association" in the Company's Registration Statement on Form F-1 filed October 16, 2015 (file number 333-206654) is incorporated herein by reference.

C. Material Contracts

See Part I, Item 6B "Directors, Senior Management and Employees—Compensation—Employment Agreements" for a description of employment agreements with our executive officers.

See Part I, Item 4 "Information on the Company – Overview – Recent Developments" for a description of our Asset Purchase Agreement and Supply Agreement with Taro Pharmaceutical Industries Ltd.

See Part I, Item 4 "Information on the Company – Overview – Recent Developments" for a description of our Private Placement, Securities Purchase Agreement and Registration Rights Agreement.

See Part I, Item 4 "Information on the Company – Overview – Recent Developments" for a description of our Loan Agreement with Oxford Finance LLC and Horizon Technology Finance Corporation.

On June 30, 2015, we acquired veldoreotide from Aspireo Pharmaceuticals Ltd., an Israeli company. Veldoreotide was formerly called COR-005 by us and DG3173 by Aspireo Pharmaceuticals. Under the terms of the acquisition agreement, we issued to Aspireo Pharmaceuticals 2,062,677 common shares, which had a value of $33.2 million on June 30, 2015. In connection with this acquisition, we made a payment to OCS in the amount of $3.0 million, which represents the repayment of amounts previously granted by OCS to Aspireo Pharmaceuticals, plus interest, that were used in support of research and development conducted by Aspireo Pharmaceuticals for the development of veldoreotide. The approval by OCS of the transfer of the assets relating to veldoreotide by Aspireo to the Company was subject to the repayment of the original grant plus interest.

See Part I, Item 4 "Information on the Company – Discontinued License" for a description of our Settlement Agreement with Antisense Therapeutics.

See Part I, Item 4 "Information on the Company – Discontinued License" for a description of our agreement with the Cornell Center for Technology Enterprise and Commercialization.

D. Exchange Controls

None.

E. Taxation

The following summary contains a description of the material Irish and U.S. federal income tax consequences of the acquisition, ownership and disposition of our ordinary shares, but it does not purport to be a comprehensive description of all the tax considerations that may be relevant. The summary is based upon the tax laws of Ireland and regulations thereunder and on the tax laws of the United States and regulations thereunder as of the date hereof, which are subject to change.

Irish Tax Considerations

Scope of Discussion

The following is a summary of the material Irish tax considerations applicable to certain investors who are the beneficial owners of our ordinary shares. This summary is based on existing Irish tax law and our understanding of the practices of the Irish Revenue Commissioners. Legislative, administrative or judicial changes may modify the tax consequences described in this summary, possibly with retroactive effect. Furthermore, we can provide no assurances that the tax consequences contained in this summary will not be challenged by the Irish Revenue Commissioners or will be sustained by an Irish court if they were to be challenged.

This summary does not constitute tax advice and is intended only as a general guide. This summary is not exhaustive and shareholders should consult their own tax advisers about the Irish tax consequences (and the tax consequences under the laws of other relevant jurisdictions), which may arise as a result of being a shareholder in our company including the acquisition, ownership and disposition of our ordinary shares. Furthermore, this summary applies only to shareholders who will hold our ordinary shares as capital assets and does not apply to all categories of shareholders, such as dealers in securities, trustees, insurance companies, collective investment schemes, pension funds or shareholders who have, or who are deemed to have, acquired their shares by virtue of an office or employment performed or carried on in Ireland.

Irish Tax on Chargeable Gains

Non–Resident Shareholders

Shareholders who are not resident or ordinarily resident in Ireland for Irish tax purposes should not be liable to Irish tax on chargeable gains realized on a disposal of our ordinary shares unless such shares are used, held or acquired for the purpose of a trade or business carried on by such a shareholder in Ireland through a branch or an agency.

A shareholder who is an individual and who is temporarily not resident in Ireland may, under Irish anti-avoidance legislation, still be liable to Irish tax on any chargeable gain realized on a disposal of our ordinary shares during the period in which the individual is a non-resident.

Irish Dividend Withholding Tax

Our company does not anticipate paying dividends for the foreseeable future. However, if in the future we were to pay a dividend or make a distribution to our shareholders, that distribution may be subject to dividend withholding tax, or DWT, at the standard rate of Irish income tax (currently 20%) unless one of the exemptions described below applies.

For DWT and Irish income tax purposes, a dividend includes any distribution made to shareholders, including cash dividends, non-cash dividends and any additional shares taken in lieu of a cash dividend. Where an exemption from DTW does not apply in respect of a distribution made to a particular shareholder, we are responsible for withholding DWT at source in respect of the distributions made and remitting the tax withheld to the Irish Revenue Commissioners.

General Exemptions

Certain shareholders, both individual and corporate, are entitled to an exemption from DWT. In particular, dividends paid to a non-Irish resident shareholder will not be subject to DWT where the shareholder is beneficially entitled to the dividend and is:

- an individual shareholder resident for tax purposes in Ireland and that is resident for tax purposes in a "relevant territory" and the individual is neither resident nor ordinarily resident in Ireland;
- a corporate shareholder that is not resident for tax purposes in a "relevant territory," but is not under the control, whether directly or indirectly, of a person or persons who is or are resident in Ireland;
- a corporate shareholder that is not resident for tax purposes in Ireland and that is ultimately controlled, directly or indirectly, by persons resident in a "relevant territory;"
- a corporate shareholder that is not resident for tax purposes in Ireland and whose principal class of shares, or those of its 75% direct or indirect parent, is substantially and regularly traded on a stock exchange in Ireland, on a recognized share exchange in a "relevant territory" or on such other share exchange as may be approved by the Irish Minister for Finance; or
- a corporate shareholder that is not resident for tax purposes in Ireland and is wholly-owned, directly or indirectly, by two or more companies where the principal class of shares of each of such companies is substantially and regularly traded on a stock exchange in Ireland, on a recognized share exchange in a "relevant territory" or on such other share exchange as may be approved by the Irish Minister for Finance;

and provided, in all cases noted above (but subject to "Shares Held by U.S. Resident Shareholders" below), Strongbridge Biopharma plc or, in respect of Strongbridge Biopharma plc shares held through DTC, any qualifying intermediary appointed by Strongbridge Biopharma plc, has received from the shareholder, where required, the relevant Irish DWT declaration forms prior to the payment of the dividend. In practice, in order to ensure sufficient time to process the receipt of relevant Irish DWT declaration forms, the Strongbridge Biopharma plc shareholder where required should furnish the relevant Irish DWT declaration forms to:

- its broker (and the relevant information is further transmitted to any qualifying intermediary appointed by Strongbridge Biopharma plc) before the record date for the dividend (or such later date before the dividend payment date as may be notified to the shareholder by the broker) if its shares are held through DTC; or
- Strongbridge Biopharma plc's transfer agent at least seven business days before the record date for the dividend if its shares are held outside of DTC.

A list of "relevant territories" for the purposes of DWT, is set forth below and this list is subject to change:

Albania	Czech Republic	Italy	Netherlands	Slovenia
Armenia	Denmark	Japan	New Zealand	South Africa
Australia	Egypt	Republic of Korea	Norway	Spain
Austria	Estonia	Kuwait	Pakistan	Sweden
Bahrain	Ethiopia	Latvia	Panama	Switzerland
Belarus	Finland	Lithuania	Poland	Thailand
Belgium	France	Luxembourg	Portugal	Turkey
Bosnia and Herzegovina	Georgia	Macedonia	Qatar	Ukraine
Botswana	Germany	Malaysia	Romania	United Arab Emirates
Bulgaria	Greece	Malta	Russia	United Kingdom
Canada	Hong Kong	Mexico	Saudi Arabia	United States of America
Chile	Hungary	Moldova	Serbia	Uzbekistan
China	Iceland	Montenegro	Singapore	Vietnam
Croatia	India	Morocco	Slovak Republic	Zambia
Cyprus	Israel			

It is the responsibility of each individual shareholder to determine whether or not they are a "resident" for tax purposes in a "relevant territory."

Prior to paying any future dividend, our company will enter into an agreement with an institution which is recognized by the Irish Revenue Commissioners as a "qualifying intermediary" and which satisfies the requirements for dividends to be paid to certain shareholders free from DWT where such shareholders hold their shares through DTC, as described below. The agreement will generally provide for certain arrangements relating to distributions in respect of those shares that are held through DTC. The agreement will provide that the "qualifying intermediary" shall distribute or otherwise make available to Cede & Co., as nominee for DTC, any cash dividend or other cash distribution to be made to holders of the deposited securities, after we deliver or cause to be delivered to the "qualifying intermediary" the cash to be distributed.

We will rely on the information received directly or indirectly from brokers and their transfer agent in determining where shareholders reside and whether they have furnished the required U.S. tax information, as described below. Shareholders who are required to furnish Irish DWT declaration forms in order to receive their dividends without DWT should note that those declarations forms are only valid until 31 December of the fifth year after the year of issue/certification of the forms and new DWT declarations forms must be completed and filed before the expiration of that period to enable the shareholder continue to receive dividends without DWT.

Shares Held by U.S. Resident Shareholders

Dividends paid on our ordinary shares that are owned by residents of the United States should not be subject to DWT, subject to the completion and delivery of the relevant forms to us.

Residents of the United States who hold their shares through DTC should be entitled to receive dividends without DWT provided that the address of the beneficial owner of the shares in the records of the broker holding such shares is in the United States. We would strongly recommend that such shareholders ensure that their information has been properly recorded by their brokers so that such brokers can further transmit the relevant information to a qualifying intermediary appointed by us.

Residents of the United States who hold their shares outside of DTC will be entitled to receive dividends without DWT provided that the shareholder has completed the relevant Irish DWT declaration form and this declaration form remains valid. Such shareholders must provide the relevant Irish DWT declaration form to our transfer agent at least seven business days before the record date of the dividend payment to which they are entitled. We would strongly

recommend that such shareholders complete the relevant Irish DWT declaration form and provide them to our transfer agent as soon as possible after acquiring shares in our company.

If a U.S. resident shareholder is entitled to an exemption from DWT, but receives a dividend subject to DWT, that shareholder may be entitled to claim a refund of DWT from the Irish Revenue Commissioners, subject to certain time limits and provided the shareholder is beneficially entitled to the dividend.

Shares Held by Residents of "Relevant Territories" Other Than the United States

Shareholders who are residents of "relevant territories" other than the United States, and who are entitled to an exemption from DWT, must complete the relevant Irish DWT declaration form in order to receive dividends without DWT.

Shareholders must provide the relevant Irish DWT declaration form to their brokers so that such brokers can further transmit the relevant information to a qualifying intermediary appointed by us before the record date of the dividend to which they are entitled, in the case of shares held through DTC, or to our transfer agent at least seven business days before such record date, in the case of shares held outside of DTC. We would strongly recommend that such shareholders complete the relevant Irish DWT declaration form and provide that form to their brokers or our transfer agent as soon as possible after acquiring shares in our company.

If a shareholder who is resident in a "relevant territory" and is entitled to an exemption from DWT receives a dividend subject to DWT, that shareholder may be entitled to claim a refund of DWT from the Irish Revenue Commissioners, subject to certain time limits and provided the shareholder is beneficially entitled to the dividend.

Notwithstanding the foregoing, the General Exemptions from DWT referred to above do not apply to an individual shareholder that is resident or ordinarily resident in Ireland or to a corporate entity that is resident in Ireland or that is under the control, whether directly or indirectly, of a person or persons who is or who are resident in Ireland. However, other exemptions from DWT may still be available to such shareholder.

In addition, it may also be possible for certain shareholders to rely on a double tax treaty to limit the applicable DWT.

Shares Held by Other Persons

A shareholder that does not fall within one of the categories specifically mentioned above may nonetheless fall within other exemptions from DWT provided that the shareholder has completed the relevant Irish DWT declaration form and this declaration form remains valid.

If any such shareholder is exempt from DWT but receives a dividend subject to DWT, that shareholder may be entitled to claim a refund of DWT from the Irish Revenue Commissioners, subject to certain time limits.

Income Tax on Dividends Paid

Irish income tax may arise for certain shareholders in respect of any dividends received from us.

Non-Irish Resident Shareholders

A shareholder that is not resident or ordinarily resident in Ireland for Irish tax purposes and who is entitled to an exemption from DWT generally has no liability to Irish income tax or other similar charges with respect to any dividends received from us. An exception to this position may apply where a shareholder holds our ordinary shares through a branch or agency in Ireland through which a trade is carried on.

A shareholder that is not resident or ordinarily resident in Ireland for Irish tax purposes and who is not entitled to an exemption from DWT generally has no additional liability to Irish income tax or other similar charges on any dividends received from us. In these circumstances, the shareholder's liability to Irish tax is effectively limited to the

amount of SWT withheld by us. An exception to this position may apply where a shareholder holds our ordinary shares through a branch or an agency in Ireland through which a trade is carried on.

Capital Acquisitions Tax

Capital acquisitions tax, or CAT, consists principally of gift tax and inheritance tax. A gift or inheritance of our ordinary shares, including where such shares are held in DTC, may attract a charge to CAT irrespective of the place of residence, ordinary residence or domicile of the transferor or the transferee of the shares. This is because a charge to CAT may arise on a gift or inheritance which comprises of property situated in Ireland. Our ordinary shares are regarded as property situated in Ireland for CAT purposes because our share register must be retained in Ireland. The person who receives the gift or inheritance is primarily liable for any CAT that may arise.

CAT is levied at a rate of 33% above certain tax-free thresholds. The appropriate tax-free threshold is dependent upon (1) the relationship between the donor and the donee and (2) the aggregation of the values of previous gifts and inheritances received by the donee from persons within the same group threshold. Gifts and inheritances passing between spouses are exempt from CAT. Shareholders should consult their own tax advisers as to whether CAT is creditable or deductible in computing any domestic tax liabilities.

Irish Stamp Duty

The rate of Irish stamp duty, where 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. Where a charge to Irish stamp duty applies it is generally a liability for the transferee. Irish stamp duty may, depending on the manner in which our ordinary shares are held, be payable in respect of the transfer of our ordinary shares.

Shares held through DTC

On the basis that most of our shares are expected to be held through DTC, or through brokers who hold shares on behalf of their customers through DTC, the transfer of such shares should be exempt from Irish stamp duty based on established practice of Irish Revenue Commissioners. We received written confirmation from the Irish Revenue Commissioners on June 22, 2015 that a transfer of our shares held through DTC and transferred by means of a book-entry interest would be exempt from Irish stamp duty.

Shares Held Outside of DTC or Transferred Into or Out of DTC

A transfer of our ordinary shares where any of the parties to the transfer hold the shares outside of DTC may be subject to Irish stamp duty. A shareholder should be entitled to transfer our ordinary shares into, or out of, DTC without giving rise to Irish stamp duty provided (1) there is no change in beneficial ownership of the shares and (2) at the time of the transfer into, or out of, DTC, is not effected in contemplation of a subsequent sale of such shares by the beneficial owner to a third party.

To avoid Irish stamp duty on transfers of our ordinary shares any directly registered shareholder may wish to consider opening a broker account, and any person who wishes to acquire our ordinary shares may wish to consider holding such shares through DTC.

DTC Requirement

In order for DTC, Cede & Co. and National Securities Clearing Corporation, or NSCC, which provides clearing services for securities that are eligible for the depository and book-entry transfer services provided by DTC and registered in the name of Cede & Co., which entities are referred to collectively as the DTC Parties, to agree to provide services with respect to our ordinary shares, we have entered into a composition agreement with the Irish Revenue Commissioners under which we have agreed to pay or procure the payment of any obligation for any Irish stamp duty or similar Irish transfer or documentary tax with respect to our ordinary shares, on (1) transfers to which any of the DTC Parties is a party or (2) which may be processed through the services of any of the DTC Parties and the DTC Parties have

received confirmation from the Irish Revenue Commissioners that during the period that such composition agreement remains in force, the DTC Parties shall not be liable for any Irish stamp duty with respect to our ordinary shares.

In addition, to assure the DTC Parties that they will not be liable for any Irish stamp duty or similar Irish transfer or documentary tax with respect to our ordinary shares under any circumstances, including as a result of a change in applicable law, and to make other provisions with respect to our ordinary shares required by the DTC Parties, we and our transfer agent have entered into a Special Eligibility Agreement for Securities with DTC, Cede & Co. and NSCC, or the DTC Eligibility Agreement.

The DTC Eligibility Agreement provides for certain indemnities of the DTC Parties by us and Computershare, Inc. (as to which we indemnify Computershare, Inc.) and provides that DTC may impose a global lock on our ordinary shares or otherwise limit transactions in the shares, or cause the shares to be withdrawn, and NSCC may, in its sole discretion, exclude our ordinary shares from its continuous net settlement service or any other service, and any of the DTC Parties may take other restrictive measures with respect to our ordinary shares as it may deem necessary and appropriate, without any liability on the part of any of the DTC Parties, (1) at any time that it may appear to any of the DTC Parties, in any such party's sole discretion, that to continue to hold or process transactions in our ordinary shares will give rise to any Irish stamp duty or similar Irish transfer or documentary tax liability with respect to our ordinary shares on the part of any of the DTC Parties or (2) otherwise as DTC's rules or NSCC's rules provide.

Notwithstanding our entry into a composition agreement with the Irish Revenue Commissioners and the indemnities given pursuant to the DTC Eligibility Agreement, any stamp duty liability resulting from a transfer of our shares will be for the "accountable person" under Irish law (generally the transferee) and, to the extent we or a subsidiary of our company discharges such liability, on any transferee's behalf, we will seek payment or reimbursement of such liability. For further details on this point, shareholders should read the discussion under "Transfer and Registration of Shares" above.

THE IRISH TAX CONSIDERATIONS SUMMARIZED ABOVE ARE FOR GENERAL INFORMATION ONLY. EACH SHAREHOLDER SHOULD CONSULT HIS OR HER OWN TAX ADVISOR AS TO THE PARTICULAR TAX CONSEQUENCES THAT MAY APPLY TO SUCH SHAREHOLDER.

Material U.S. Federal Income Tax Considerations for U.S. Holders

The following is a description of the material U.S. federal income tax consequences to the U.S. Holders described below of owning and disposing of our ordinary shares, but it does not purport to be a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire the ordinary shares. This discussion applies only to a U.S. Holder that holds ordinary shares as capital assets for tax purposes. In addition, it does not describe all of the tax consequences that may be relevant in light of the U.S. Holder's particular circumstances, including alternative minimum tax consequences, any state or local tax considerations, any U.S. federal gift, estate or generation-skipping transfer tax consequences and tax consequences applicable to U.S. Holders subject to special rules, such as:

- certain financial institutions;
- brokers;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- real estate investment trusts;
- insurance companies;
- persons holding ordinary shares as part of a hedging transaction, straddle, wash sale, conversion transaction or integrated transaction or persons entering into a constructive sale with respect to the ordinary shares;
- regulated investment companies;
- persons whose functional currency for U.S. federal income tax purposes is not the U.S. dollar;

- entities classified as partnerships or other pass-through entities for U.S. federal income tax purposes, including persons that will hold our ordinary shares through such an entity;
- tax-exempt entities, including an "individual retirement account" or "Roth IRA;"
- persons that own or are deemed to own ten percent or more of our voting stock;
- persons that are U.S. expatriates;
- persons who acquired our ordinary shares pursuant to the exercise of an employee stock option or otherwise as compensation; or
- persons holding shares in connection with a trade or business conducted outside of the United States.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds ordinary shares, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships holding ordinary shares and partners in such partnerships should consult their tax advisers as to their particular U.S. federal income tax consequences of holding and disposing of the ordinary shares.

This discussion is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code, administrative pronouncements, judicial decisions, and final, temporary and proposed Treasury regulations, all as of the date hereof, any of which is subject to change, possibly with retroactive effect.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of ordinary shares who is:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;
- an estate whose income is includible in gross income for U.S. federal income tax purposes regardless of its source; or
- a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election in effect under applicable Treasury Regulations to be treated as a U.S. person.

U.S. Holders should consult their tax advisers concerning the U.S. federal, state, local and foreign tax consequences of owning and disposing of ordinary shares in their particular circumstances.

Passive Foreign Investment Company Rules

We believe we were classified as a passive foreign investment company " PFIC", in the past and we may be classified as a PFIC for our current taxable year and for the foreseeable future. In addition, we may, directly or indirectly, hold equity interests in other PFICs, or Lower-tier PFICs. In general, a non-U.S. corporation will be considered a PFIC for any taxable year in which (1) 75% or more of its gross income consists of passive income or (2) 50% or more of the average quarterly value of its assets consists of assets that produce, or are held for the production of, passive income. For purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as if it held its proportionate share of the assets of the other corporation and received directly its proportionate share of the income of the other corporation. Passive income generally includes dividends, interest, rents, royalties and capital gains.

We must determine our PFIC status annually based on tests which are factual in nature, and our status will depend on our income, assets and activities each year.

Under attribution rules, if we are a PFIC, U.S. Holders will be deemed to own their proportionate shares of Lower-tier PFICs and will be subject to U.S. federal income tax according to the rules described in the following

paragraphs on (1) certain distributions by a Lower-tier PFIC and (2) a disposition of shares of a Lower-tier PFIC, in each case as if the U.S. Holder held such shares directly, even though holders have not received the proceeds of those distributions or dispositions directly.

If we are a PFIC for any taxable year during which a U.S. Holder holds our shares, the U.S. Holder may be subject to certain adverse tax consequences. Unless a holder makes a timely "mark-to-market" election or "qualified electing fund" election each as discussed below, gain recognized on a disposition (including, under certain circumstances, a pledge) of ordinary shares by the U.S. Holder, or on an indirect disposition of shares of a Lower-tier PFIC, will be allocated ratably over the U.S. Holder's holding period for the shares. The amounts allocated to the taxable year of disposition and to years before we became a PFIC will be taxed as ordinary income. The amounts allocated to each other taxable year will be subject to tax at the highest rate in effect for that taxable year for individuals or corporations, as appropriate, and an interest charge will be imposed on the tax attributable to the allocated amounts. Further, to the extent that any distribution received by a U.S. Holder on our ordinary shares (or a distribution by a Lower-tier PFIC to its shareholder that is deemed to be received by a U.S. Holder) exceeds 125% of the average of the annual distributions on the shares received during the preceding three years or the U.S. Holder's holding period, whichever is shorter, the distribution will be subject to taxation in the same manner as gain, described immediately above and lower rates of taxation applicable to long-term capital gains with respect to dividends paid to certain non-corporate U.S. Holders would not apply.

If we are a PFIC for any year during which a U.S. Holder holds ordinary shares, we generally will continue to be treated as a PFIC with respect to the holder for all succeeding years during which the U.S. Holder holds ordinary shares, even if we cease to meet the threshold requirements for PFIC status. U.S. Holders should consult their tax advisers regarding the potential availability of a "deemed sale" election that would allow them to eliminate this continuing PFIC status under certain circumstances.

If the ordinary shares are "regularly traded" on a "qualified exchange," a U.S. Holder may make a mark-to-market election that would result in tax treatment different from the general tax treatment for PFICs described above. The ordinary shares will be treated as "regularly traded" in any calendar year in which more than a *de minimis* quantity of the ordinary shares is traded on a qualified exchange on at least 15 days during each calendar quarter. The NASDAQ Global Select Market, to which we intend to apply for the listing of our ordinary shares, is a qualified exchange for this purpose. U.S. Holders should consult their tax advisers regarding the availability and advisability of making a mark-to-market election in their particular circumstances. In particular, U.S. Holders should consider carefully the impact of a mark-to-market election with respect to their ordinary shares given that we may have Lower-tier PFICs for which a mark-to-market election may not be available.

If a U.S. Holder makes the mark-to-market election, the holder generally will recognize as ordinary income any excess of the fair market value of the ordinary shares at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the ordinary shares over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. Holder makes the election, the holder's tax basis in the ordinary shares will be adjusted to reflect the income or loss amounts recognized. Any gain recognized on the sale or other disposition of ordinary shares in a year when we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). Distributions paid on ordinary shares will be treated as discussed below under "—Taxation of Distributions."

Alternatively, a U.S. Holder can make an election, if we provide the necessary information, to treat us and each Lower-tier PFIC as a qualified electing fund, or a QEF Election, in the first taxable year that we are treated as a PFIC with respect to the holder. A U.S. Holder must make the QEF Election for each PFIC by attaching a separate properly completed IRS Form 8621 for each PFIC to the holder's timely filed U.S. federal income tax return. U.S. Holders should be aware that there can be no assurances that we will satisfy the record keeping requirements that apply to a QEF, or that we will supply U.S. Holders with information that such U.S. Holders are required to report under the QEF rules, in the event that we are a PFIC. Thus, U.S. Holders may not be able to make a QEF Election with respect to their ordinary shares. Further, no assurance can be given that such QEF information will be available for any Lower-tier PFIC. Each U.S. Holder should consult its own tax advisers regarding the availability of, and procedure for making, a QEF Election.

If a U.S. Holder makes a QEF Election with respect to a PFIC, the holder will be taxed on a current basis on its pro rata share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is classified as a PFIC and for which the QEF election is in place and properly maintained. If a U.S. Holder makes a QEF Election with respect to us, any distributions paid by us out of our earnings and profits that were previously included in the holder's income under the QEF Election would not be taxable to the holder. A U.S. Holder will increase its tax basis in its ordinary shares by an amount equal to any income included under the QEF Election and will decrease its tax basis by any amount distributed on the ordinary shares that is not included in the holder's income. In addition, a U.S. Holder will recognize capital gain or loss on the disposition of ordinary shares in an amount equal to the difference between the amount realized and the holder's adjusted tax basis in the ordinary shares. U.S. Holders should note that if they make QEF Elections with respect to us and Lower-tier PFICs, they may be required to pay U.S. federal income tax with respect to their ordinary shares for any taxable year significantly in excess of any cash distributions received on the shares for such taxable year. U.S. Holders should consult their tax advisers regarding making QEF Elections in their particular circumstances.

Furthermore, as discussed below, if we were a PFIC or, with respect to a particular U.S. Holder, were treated as a PFIC for the taxable year in which we paid a dividend or the prior taxable year, the 20% preferential tax rate with respect to dividends paid to certain non-corporate U.S. Holders would not apply.

If we were a PFIC for any taxable year during which a U.S. Holder held ordinary shares, such U.S. Holder would be required to file an annual information report with such U.S. Holder's U.S. Federal income tax return on IRS Form 8621.

U.S. Holders should consult their tax advisers concerning our PFIC status and the tax considerations relevant to an investment in a PFIC.

Taxation of Distributions

Subject to the passive foreign investment company rules described above, distributions paid on ordinary shares, other than certain pro rata distributions of ordinary shares, will be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we do not maintain calculations of our earnings and profits under U.S. federal income tax principles, it is expected that distributions generally will be reported to U.S. Holders as dividends. The amount of a dividend will include any amounts withheld by us in respect of Irish taxes. The amount of the dividend will be treated as foreign-source dividend income to U.S. Holders and will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code. Dividends will be included in a U.S. Holder's income on the date of the U.S. Holder's receipt of the dividend. The amount of any dividend income paid in Euros will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt, which will be "U.S. source" ordinary income or loss.

Dividends paid by us may be taxable to a non-corporate U.S. Holder at the special reduced rate normally applicable to long-term capital gains, provided we are not a PFIC in the taxable year in which the dividends are received or in the preceding taxable year, so long as certain holding period requirements are met. As discussed above under "Passive Foreign Investment Company Rules," we expect to be a PFIC and, as a result, the special reduced rate is unlikely to be available with respect to dividends paid by us.

Subject to applicable limitations, some of which vary depending upon the U.S. Holder's circumstances, Irish income taxes withheld from dividends on ordinary shares may be creditable against the U.S. Holder's U.S. federal income tax liability. The rules governing foreign tax credits are complex, and U.S. Holders should consult their tax advisers regarding the creditability of foreign taxes in their particular circumstances. In lieu of claiming a foreign tax credit, U.S. Holders may, at their election, deduct foreign taxes, including the Irish tax, in computing their taxable income, subject to generally applicable limitations under U.S. law. An election to deduct foreign taxes instead of claiming foreign tax credits applies to all foreign taxes paid or accrued in the taxable year.

Sale or Other Disposition of Ordinary Shares

Subject to the passive foreign investment company rules described above, for U.S. federal income tax purposes, gain or loss realized on the sale or other disposition of ordinary shares will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder held the ordinary shares for more than one year The amount of the gain or loss will equal the difference between the U.S. Holder's tax basis in the ordinary shares disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes.

Net Investment Income Tax

U.S. Holders that are individuals or estates or trusts that do not fall into a special class of trusts that is exempt from such tax, will be required to pay an additional 3.8% tax on the lesser of (1) the U.S. Holder's "net investment income" for the relevant taxable year and (2) the excess of the U.S. Holder's modified adjusted gross income for the taxable year over a certain threshold (which in the case of individuals will be between US $125,000 and US $250,000, depending on the individual's circumstances). A U.S. Holder's "net investment income" will generally include, among other things, dividends and capital gains. Such tax will apply to dividends and to capital gains from the sale or other disposition of the ordinary shares, unless derived in the ordinary course of the conduct of a trade or business (other than a trade or business that consists of certain passive or trading activities). Special rules apply and certain elections are available for certain U.S. Holders that are subject to the 3.8% tax on net investment income and hold shares in a PFIC. Potential investors should consult with their own tax advisers regarding the application of the net investment income tax to them as a result of their investment in our ordinary shares.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (1) the U.S. Holder is a corporation or other exempt recipient or (2) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding.

Backup withholding is not an additional tax. Amounts withheld as backup withholding may be credited against such holder's U.S. federal income tax liability, and such holder may obtain a refund of any excess amounts withheld under the backup withholding rules by filing an appropriate claim for refund with the IRS and furnishing any required information in a timely manner. U.S. Holders of ordinary shares should consult their tax advisers regarding the application of the U.S. information reporting and backup withholding rules.

Information With Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals (and, under proposed regulations, certain entities) may be required to report information relating to an interest in our ordinary shares, subject to certain exceptions (including an exception for ordinary shares held in accounts maintained by certain U.S. financial institutions). U.S. Holders should consult their tax advisers regarding the effect, if any, of this requirement on their ownership and disposition of the ordinary shares.

F. Dividends

Not applicable.

G. Statement by experts

Not applicable.

H. Documents on display

We are subject to the informational requirements of the Exchange Act and are required to file reports and other information with the SEC. Shareholders may read and copy any of our reports and other information at, and obtain copies upon payment of prescribed fees from, the Public Reference Room maintained by the SEC at 100 F Street N.E., Washington, D.C. 20549. The public may obtain information on the operation of the Public Reference Room by calling the U.S. Securities and Exchange Commission at 1-800-SEC-0330.

We are a "foreign private issuer" as such term is defined in Rule 405 under the Securities Act, and are not subject to the same requirements that are imposed upon U.S. domestic issuers by the SEC. Under the Exchange Act, we are subject to reporting obligations that, in certain respects, are less detailed and less frequent than those of U.S. domestic reporting companies. As a result, we do not file the same reports that a U.S. domestic issuer would file with the SEC, although we are required to file or furnish to the SEC the continuous disclosure documents that we are required to file in Ireland under Irish securities laws.

We will provide without charge to each person, including any beneficial owner, on the written or oral request of such person, a copy of any or all documents referred to above which have been or may be incorporated by reference in this Annual Report (not including exhibits to such incorporated information that are not specifically incorporated by reference into such information). Requests for such copies should be directed to us at the following address: 900 Northbrook Drive, Suite 200, Trevose, PA 19053, Attention: Chief Legal Officer, phone number: (610) 254-9225. Additionally, our documents are available for free via our website at www.strongbridgebio.com

I. Subsidiary information

As of March 1, 2017, the Company had the following subsidiaries:

Name	Nature of Business	Group Share %	Registered Office and Country of Incorporation
BioPancreate Inc.	Operating	100%	900 Northbrook Drive Suite 200 Trevose, Pennsylvania 19053 U.S.A.
Cortendo AB (publ)	Operating	100%	Box 47 433 21 Partille Gothenburg Sweden
Cortendo Cayman Ltd	Operating	100%	Maples Corporate Services PO Box 309 Ugland House Grand Cayman KY1-1104
Strongbridge U.S. Inc.	Operating	100%	Corporate Trust Center Lmt 1209 Orange Street Wilmington, Delaware 19801 U.S.A.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

At December 31, 2016, we had cash and cash equivalents of $66.8 million, which consisted 100% of bank deposits in the United States. 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.

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

Not applicable.

PART II

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

None.

ITEM 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

The effective date of the registration statement (File no. 333-206654) for our initial public offering of ordinary shares was October 15, 2015. The offering closed on October 21, 2015.

We received and used net proceeds of approximately $23.5 million from our initial public offering. We have disbursed $1.0 million of the IPO proceeds to fund our purchase of the U.S. marketing rights of Keveyis from Taro Pharmaceuticals. An additional $10.0 million has been used to fund general and administrative expenses.

None of the net proceeds of the offering was paid directly or indirectly to any director, officer, general partner of ours or to their associates, persons owning ten percent or more of any class of our equity securities, or to any of our affiliates.

ITEM 15. 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 Securities Exchange Act of 1934, as amended, or 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 Rule 13a-15(b) under the Exchange Act, our management, under the supervision and with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2016. Based on such evaluation, our management concluded that the Company’s disclosure controls and procedures were not effective as of December 31, 2016.

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, 2016, based on the Internal Control-Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on this assessment and in connection with the preparation of our consolidated financial statements for the year ended December 31, 2016, our management concluded that there was a material weakness in the design and operating effectiveness of our internal control over the valuation of warrants issued in connection with our December 2016 private placement of ordinary shares. Accordingly, our management concluded that the Company's internal control over financial reporting was not effective as of December 31, 2016.

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 independent registered public accounting firm regarding internal control over financial reporting because the Jumpstart Our Business Startups Act provides an exemption from such requirement 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 16. [RESERVED]

ITEM 16A. AUDIT COMMITTEE FINANCIAL EXPERT

Our Board has determined that two of the three members of our audit committee, Mr. Kollender and Dr. Steineger, qualify as an "audit committee financial expert" as defined in Item 16A of Form 20-F under the Exchange Act and that each member is "independent" in accordance with The NASDAQ Global Select Market corporate governance requirements and Rule 10A-3 of the Exchange Act. For information relating to qualifications and experience of each audit committee member, see "Item 6. Directors, Senior Management and Employees."

ITEM 16B. CODE OF ETHICS

We have adopted a Code of Business Conduct and Ethics applicable to all of our directors and employees, including our President and Chief Executive Officer, Chief Financial Officer, controller or principal accounting officer or other persons performing similar functions, which is a "code of ethics" as defined in Item 16B of Annual Report on Form 20-F and as required by The NASDAQ Global Select Market Listing Rules, which refers to Section 406(c) of the Sarbanes-Oxley Act.

The full text of the Code of Business Conduct and Ethics is posted on our website at www.strongbridgebio.com. Information contained on, or that can be accessed through, our website does not constitute a part of this Annual Report on Form 20-F and is not incorporated by reference herein. We will provide a copy of such code of ethics without charge upon request by mail or by telephone. If we make any amendment to the Code of Business Conduct and Ethics or grant any waivers, including any implicit waiver, from a provision of the Code of Business Conduct and Ethics, we will

disclose the nature of such amendment or waiver on our website to the extent required by the rules and regulations of the SEC. We have not made any amendments to our Code of Business Conduct and Ethics or granted any waivers, including any implicit waivers, from a provision of the Code of Business Conduct and Ethics.

ITEM 16C. 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:

Fee Category:	2016	2015
	(in thousands)	
Audit Fees[1]	$ 619	$1,309
Audit-Related Fees[2]	—	70
Tax Fees[3]	118	71
All Other Fees[4]	—	365
Total Fees	$ 737	$1,815

(1) Audit fees consist of fees for the audit of our financial statements, the review of our interim financial statements and statutory audits. For 2015, it also included the audit of Aspireo in 2015 and services associated with our registration statement on Form F-1.

(2) Audit-related fees incurred consist of other services not audited related.

(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.

(4) Other fees consist of fees incurred for the Irish redomicile and other services.

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 16D. EXEMPTIONS FROM THE LISTING STANDARDS FOR AUDIT COMMITTEES

Not applicable.

ITEM 16E. PURCHASES OF EQUITY SECURITIES BY THE ISSUER AND AFFILIATED PURCHASERS

None.

ITEM 16F. CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT

See item 16F of our Annual Report on Form 20-F for the year ended December 31, 2015.

ITEM 16G. CORPORATE GOVERNANCE

We are a foreign private issuer. As a result, in accordance with NASDAQ Listing Rule 5615(a)(3), we may comply with home country governance requirements and certain exemptions thereunder rather than complying with certain of the corporate governance requirements of NASDAQ.

Irish law does not require that a majority of our board of directors consist of independent directors. Our board of directors therefore may include fewer independent directors than would be required if we were subject to NASDAQ Listing Rule 5605(b)(1). In addition, we are not subject to NASDAQ Listing Rule 5605(b)(2), which requires that independent directors must regularly have scheduled meetings at which only independent directors are present.

Our articles of association provide that at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy, but no such proxy shall be voted or acted upon at any subsequent meeting, unless the proxy expressly provides for this. Irish law does not require shareholder approval for the issuance of securities in connection with the establishment of or amendments to equity-based compensation plans for employees. To this extent, our practice varies from the requirements of NASDAQ Listing Rule 5635, which generally requires an issuer to obtain shareholder approval for the issuance of securities in connection with such events.

ITEM 16H. MINE SAFETY DISCLOSURE

Not applicable.

PART III

ITEM 17. Financial Statements.

See Item 18-"Financial Statements".

ITEM 18. Financial Statements.

Please refer to the financial statements beginning on page F-1. The financial statements and related notes are filed as part of this Annual Report on Form 20-F, together with the reports of our independent registered public accounting firms.

ITEM 19. EXHIBITS

EXHIBIT INDEX

3.1*	Constitution of Strongbridge Biopharma plc, incorporated by reference to Exhibit 3.1 to the Company's Form F-1/A filed September 9, 2015
3.2*	Articles of Association of Strongbridge Biopharma plc, incorporated by reference to Exhibit 3.2 to the Company's Form F-1/A filed 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 Company's Form F-1/A filed August 28, 2015
10.2*	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 Company's Form 6-K filed December 23, 2016
10.3*	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 Company's Form F-1/A filed August 28, 2015
10.4†*	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 Company's Form F-3 filed January 12, 2017
10.5†*	Supply Agreement, dated December 12, 2016, between Taro Pharmaceutical North America, Inc. and Strongbridge plc, incorporated by reference to Exhibit 10.4 to the Company's Form F-3 filed January 12, 2017
10.6*	Amended and Restated Employment Agreement, effective August 23, 2014, by and between Cortendo AB and Matthew Pauls, incorporated by reference to Exhibit 10.6 to the Company's Form 20-F filed March 24, 2016
10.7*	Amended and Restated Employment Agreement, effective March 23, 2015, by and between Cortendo AB and A. Brian Davis, incorporated by reference to Exhibit 10.7 to the Company's Form 20-F filed March 23, 2015
10.8†*	Loan and Security Agreement, dated December 28, 2016, 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 10.5 to the Company's Form F-3 filed January 12, 2017
10.9**	Amended and Restated Employment Agreement, effective August 5, 2015, by and between Cortendo AB and Fredrick Cohen, M.D.
10.10*	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/A filed August 28, 2015
10.11*	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/A filed August 28, 2015
10.12*	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/A filed August 28, 2015
10.13*	Form of Indemnification Agreement, incorporated by reference to Exhibit 10.13 to the Company's Form F-1/A filed September 25, 2015
10.14*	Strongbridge Biopharma Plc 2015 Equity Compensation Plan, incorporated by reference to Exhibit 10.14 to the Company's Form 20-F filed March 24, 2016
10.15*	Strongbridge Biopharma Plc Non-Employee Director Equity Compensation Plan, incorporated by reference to Exhibit 10.15 to the Company's Form 20-F filed March 24, 2016

10.16*	Form of Stock Option Agreement under the Strongbridge Biopharma Plc Non-Employee Director Equity Compensation Plan, incorporated by reference to Exhibit 10.16 to the Company's Form 20-F filed March 24, 2016
10.17*	Form of Nonqualified Stock Option Agreement under the Strongbridge Biopharma Plc 2015 Equity Compensation Plan, incorporated by reference to Exhibit 10.17 to the Company's Form 20-F filed March 24, 2016
10.18*	Form of Restricted Stock Unit Award Agreement under the Strongbridge Biopharma Plc 2015 Equity Compensation Plan, incorporated by reference to Exhibit 10.18 to the Company's Form 20-F filed March 24, 2016
10.19*	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 filed December 23, 2016
10.20**	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.
10.21**	Strongbridge Biopharma plc 2017 Inducement Plan
12.1**	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
12.2**	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
13.1**	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
21.1**	Subsidiaries of the Company
23.1**	Consent of Ernst & Young LLP
23.2**	Consent of Ernst & Young AB
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

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* Previously filed.

** Filed herewith.

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

SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on Annual Report on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

STRONGBRIDGE BIOPHARMA PLC

By: /s/ A. BRIAN DAVIS
Name: **A. Brian Davis**
Title: Chief Financial Officer

Date: April 4, 2017

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of Strongbridge Biopharma plc

We have audited the accompanying consolidated statements of operations, shareholders' equity and cash flows of Strongbridge Biopharma plc for the year ended December 31, 2014. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, 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. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated results of operations, shareholders' equity and cash flows of Strongbridge Biopharma plc for the year ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young AB
Gothenburg, Sweden
August 17, 2015 except for Note 1, as to which the date is September 9, 2015

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of Strongbridge Biopharma plc

We have audited the accompanying consolidated balance sheets of Strongbridge Biopharma plc (the Company) as of December 31, 2016 and 2015, and the related consolidated statements of operations and comprehensive loss, changes in shareholders' equity, and cash flows for each of the two years in the period ended December 31, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, 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. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Strongbridge Biopharma plc at December 31, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the two years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Philadelphia, Pennsylvania
April 4, 2017

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

	December 31, 2016	December 31, 2015
ASSETS		
Current assets:		
Cash and cash equivalents	$ 66,837	$ 51,623
Prepaid expenses and other current assets	764	1,253
Total current assets	67,601	52,876
Property and equipment, net	25	35
Deferred tax asset	1,599	—
Intangible assets, net	60,900	36,551
Goodwill	7,256	7,256
Other assets	150	612
Total assets	$ 137,531	$ 97,330
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,089	$ 2,792
Accrued liabilities	14,868	2,685
Total current liabilities	15,957	5,477
Long-term debt	18,434	—
Warrant liability	11,090	—
Supply agreement liability, noncurrent	25,078	—
Deferred tax liabilities	—	926
Total liabilities	70,559	6,403
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Deferred shares, $1.098 par value, 40,000 shares authorized, issued and outstanding at December 31, 2016 and December 31, 2015	44	44
Ordinary shares, $0.01 par value, 600,000,000 shares authorized at December 31, 2016 and December 31, 2015; 35,335,026 and 21,205,382 shares issued and outstanding at December 31, 2016 and December 31, 2015	353	212
Additional paid-in capital	195,975	170,910
Accumulated deficit	(129,400)	(80,803)
Non-controlling interest	—	564
Total stockholders' equity	66,972	90,927
Total liabilities and stockholders' equity	$ 137,531	$ 97,330

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

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

	Year Ended December 31,		
	2016	2015	2014
Operating expenses:			
Research and development	$ 20,023	$ 20,135	$ 5,844
General and administrative	14,875	22,719	4,588
Impairment of intangible assets	15,828	—	—
Total operating expenses	50,726	42,854	10,432
Operating loss	(50,726)	(42,854)	(10,432)
Other (expense) income, net:			
Foreign exchange loss	(69)	(124)	(204)
Unrealized gain on fair value of warrants	638	—	—
Interest expense	(20)	—	—
Other (expense) income, net	(1,180)	(1,105)	486
Total other (expense) income, net	(631)	(1,229)	282
Loss before income taxes	(51,357)	(44,083)	(10,150)
Income tax benefit	2,638	450	480
Net loss	(48,719)	(43,633)	(9,670)
Net loss attributable to non-controlling interest	122	53	—
Net loss attributable to Strongbridge Biopharma	$ (48,597)	$ (43,580)	$ (9,670)
Other comprehensive loss	—	—	—
Comprehensive loss	$ (48,597)	$ (43,580)	$ (9,670)
Net loss attributable to ordinary shareholders:			
Basic	$ (48,597)	$ (43,580)	$ (9,670)
Diluted	$ (49,236)	$ (43,580)	$ (9,670)
Net loss per share attributable to ordinary shareholders:			
Basic	$ (2.26)	$ (2.62)	$ (1.20)
Diluted	$ (2.27)	$ (2.62)	$ (1.20)
Weighted-average shares used in computing net loss per share attributable to ordinary shareholders:			
Basic	21,550,353	16,606,669	8,043,175
Diluted	21,655,564	16,606,669	8,043,175

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

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

	Strongbridge Biopharma plc Shareholders							
	Ordinary Shares		Deferred Shares		Additional Paid-In Capital	Accumulated Deficit	Non-Controlling Interest	Total Shareholders' Equity
	Shares	Amount	Shares	Amount				
Balance—January 1, 2014	7,939,608	$ 79	—	—	$ 45,273	$ (27,553)	$ 24	$ 17,823
Net loss	—	—	—	—	—	(9,670)	—	(9,670)
Shares exchanged for BioPancreate non-controlling interest	5,272	—	—	—	19	—	(24)	(5)
Stock-based compensation	—	—	—	—	480	—	—	480
Issuance of shares	1,755,909	18	—	—	10,175	—	—	10,193
Balance—December 31, 2014	9,700,789	97	—	—	55,947	(37,223)	—	18,821
Net loss	—	—	—	—	—	(43,580)	(53)	(43,633)
Stock-based compensation	—	—	—	—	3,581	—	—	3,581
Reclass of stock-based liability award to equity	—	—	—	—	1,542	—	—	1,542
Issuance of shares	9,108,169	91	—	—	91,418	—	—	91,509
U.S. non-accredited shares repurchased	(24,955)	—	—	—	(412)	—	—	(412)
Issuance of shares in initial public offering, net	2,500,000	25	—	—	19,450	—	—	19,475
Non-controlling interest resulting from exchange offer	(78,621)	(1)	—	—	(616)	—	617	—
Beneficial shares issued	—	—	40,000	$ 44	—	—	—	44
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

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,		
	2016	2015	2014
Cash flows from operating activities:			
Net loss	$ (48,719)	$ (43,633)	$ (9,670)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	10	11	9
Stock-based compensation	4,606	3,940	251
Deferred income tax benefit	(2,638)	(450)	(480)
Impairment of intangible assets	15,828	—	
Impairment/loss on investment in Antisense Therapeutics	550	551	—
Change in fair value of warrant liability	(638)	—	—
Change in fair value of foreign currency forward contracts	—	438	(279)
Changes in operating assets and liabilities:			
Accounts payable	(1,702)	1,737	236
Accrued liabilities and other liabilities	475	1,263	736
Other assets	(88)	(52)	2
Prepaid expenses and other current assets	602	(1,165)	(309)
Net cash used in operating activities	(31,714)	(37,360)	(9,504)
Cash flows from investing activities:			
Payments for acquisitions	(3,392)	(3,168)	—
Investment in Antisense Therapeutics	—	(1,101)	—
Purchase of equipment	—	(25)	(24)
Net cash used in investing activities	(3,392)	(4,294)	(24)
Cash flows from financing activities:			
Proceeds from initial public offering, net	—	19,475	—
Proceeds from issuance of ordinary shares and warrants, net	32,298	58,341	10,193
Proceeds from exercise of stock options	120	—	—
Proceeds from long-term debt	19,316	—	—
Acquisition of non-controlling interest	(1,414)	(412)	—
Net cash provided by financing activities	50,320	77,404	10,193
Effect of exchange rate changes on cash and cash equivalents	—	241	70
Net increase in cash and cash equivalents	15,214	35,991	735
Cash and cash equivalents—beginning of period	51,623	15,632	14,897
Cash and cash equivalents—end of period	$ 66,837	$ 51,623	$ 15,632
Supplemental Disclosures of Cash Flow Information			
Cash paid during the year for:			
Income taxes other, net of refunds			
Interest	$ 20	$ —	$ —
Supplemental non-cash investing and financing activities:			
Ordinary shares issued for acquisition of COR-005	$ —	$ 33,211	$ —
Ordinary shares exchanged for BioPancreate	$ —	$ —	$ 43
Supply agreement liability for intangible asset	$ 29,285	$ —	$ —

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

STRONGBRIDGE BIOPHARMA plc
Notes to Consolidated Financial Statements

1. Organization

Strongbridge Biopharma plc is 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 ("FDA") for hyperkalemic, hypokalemic, and related variants of primary periodic paralysis. Keveyis, for which we hold the U.S. marketing rights, has orphan drug exclusivity status in the United States through August 7, 2022. In addition to this neuromuscular disease product, we have two clinical-stage product candidates for rare endocrine diseases, Recorlev and veldoreotide. Recorlev (levoketoconazole, and formerly called COR-003) is a cortisol synthesis inhibitor currently being studied for the treatment of endogenous Cushing's syndrome. Veldoreotide (formerly called COR-005) is a next-generation somatostatin analog (SSA) being investigated for the treatment of acromegaly, with potential additional applications in Cushing's syndrome and neuroendocrine tumors. Both Recorlev and veldoreotide have received orphan designation from the FDA and the European Medicines Agency ("EMA").

Given the well-identified and concentrated prescriber base addressing our target markets, we intend to use a small, focused sales force to effectively market our products, if approved, in the United States, the European Union and other key global markets. We believe that our ability to execute on this strategy is enhanced by the significant commercial and clinical development experience of key members of our management team. We will continue to identify and evaluate the acquisition of products and product candidates 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.

On October 15, 2015, a registration statement was declared effective by the U.S. Securities and Exchange Commission and on October 16, 2015 we initiated our initial U.S. public offering (IPO) of 2,500,000 ordinary shares at a price of $10.00 per share. The aggregate net proceeds received by us from the IPO were $19.5 million. Our shares began trading on The NASDAQ Global Select Market under the symbol "SBBP". On October 20, 2015, trading ceased on the Norwegian Over-The-Counter Market, or NOTC.

Exchange offer

On May 26, 2015, Strongbridge Biopharma plc (then named Cortendo plc), was incorporated under the laws of Ireland.

On August 7, 2015, Strongbridge Biopharma plc initiated an exchange offer for the outstanding shares of Cortendo AB. The exchange offer was structured as a one-for-one exchange offer in which shareholders of Cortendo AB exchanged their common shares, with a par value of $0.15, for beneficial interests in ordinary shares of Strongbridge Biopharma plc, with a par value of $0.01, in the form of Norwegian depositary receipts and, as the case may be, Swedish depositary receipts (except for non-accredited investors who hold Cortendo AB shares located in the United States, who were offered cash in an amount equivalent to the value of the Strongbridge Biopharma plc shares such investors would otherwise receive for their Cortendo AB shares exchanged).

The exchange offer was settled on September 8, 2015, and Cortendo AB became a subsidiary with 99.582% of its shares being owned by Strongbridge Biopharma plc. Accordingly, Strongbridge Biopharma plc is a continuation of Cortendo AB, the predecessor, and the consolidated financial statements represent the assets, liabilities and results of operations of Cortendo AB, for all periods presented.

On September 8, 2015, Strongbridge Biopharma plc effected a 1-for-11 reverse stock split of its ordinary shares. Accordingly, the consolidated financial statements and notes retroactively reflect the capital structure of Strongbridge Biopharma plc after giving effect to the exchange offer and the reverse stock split. With affect from September 8, 2015, the 0.418% of Cortendo AB not owned by Strongbridge Biopharma plc, is accounted for as a non-controlling interest. In September 2016, we acquired the non-controlling interest in Cortendo AB, after which

Cortendo AB became a wholly-owned subsidiary of Strongbridge Biopharma plc. Total consideration paid per share was $13.66 resulting in an aggregate payment of $1.4 million.

Liquidity

We believe that our cash resources of $66.8 million at December 31, 2016 will be sufficient to allow us to fund planned operations into 2019, which is after the expected receipt of data from the Recorlev SONICS and LOGICS Phase 3 clinical trials. We expect our funding requirements for operating activities to increase in 2017 and possibly beyond due to expenses associated with the commercialization of Keveyis, the execution of the Phase 3 SONICS and LOGICS clinical trials for Recorlev, and selling, general and administrative expenses. We also expect our cash needs to increase to fund potential in-licenses, acquisitions or similar transactions as we pursue our strategy. These expenses may be offset only in part by sales of Keveyis. In addition, beginning in June 2018, we will be required to make monthly principal payments to repay amounts borrowed under our credit facility.

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. There can be no assurances, however, that additional funding will be available on terms acceptable to us.

Our loan and security agreement, under which outstanding borrowings were $20.0 million at December 31, 2016, contains financial and non-financial covenants including minimum amounts of net revenue in 2017 and beyond. Failure to comply with the covenants could result in the lenders declaring the loan immediately due and payable. Our liquidity requirements are predicated on maintaining compliance with the debt covenants and repaying outstanding borrowings in accordance with the 48 month loan term (see Note 6).

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, BioPancreate Inc. (Trevose, Pennsylvania, United States), 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 Financial Accounting Standards Board (FASB).

Foreign currency translation

The consolidated financial statements are reported in United States dollars, which is the functional currency of our subsidiaries and Cortendo AB. 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.

Segment information

Operating segments are identified as components of an enterprise about which separate discrete 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. Our material long-lived assets, which primarily consists of in-process research and development, reside in the United States, Sweden and Cayman Islands.

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.. We consider both the initial valuation as well as our year-end valuation under Level 3 of the fair value hierarchy. The change in the fair value of the level 3 warrant liabilities is reflected in the statement of operations and comprehensive loss for the year ended December 31, 2016.

Through June 30, 2015, we entered into foreign currency forward contracts to offset some of the foreign exchange risks we bear on operating expenses that were not denominated in U.S. dollars. These instruments were not entered into for speculative purposes and, although we believe they served as effective economic hedges, we did not seek to qualify for hedge accounting. The forward contracts settled on June 30, 2015, and we have not entered into new forward contracts.

These forward contracts were recorded at fair value on the accompanying consolidated balance sheets as prepaid expenses and other current assets. These forward contracts were measured using observable quoted prices for similar instruments. The gain and loss recognized in other income, net, for these forward contracts was a loss of $0.4 million and a gain of $0.3 million for the years ended December 31, 2015 and 2014, respectively. These amounts represent the net gain or loss on the forward contracts and do not include changes in the related exposures, which generally offset a portion of the gain or loss on the forward contracts. We considered our foreign currency forward contracts under Level 2 of the fair value hierarchy.

On May 13, 2015, as part of our agreement to acquire an exclusive license agreement from Antisense Therapeutics Limited (Antisense), we purchased 15,025,075 shares of Antisense common stock that had a fair value of $0.095 per share, which was the quoted market price of the Antisense common stock on the Australian Securities Exchange (ASX). Because we were contractually prohibited from selling the shares for 24 months from the date of purchase, we estimated a discount for the lack of marketability of $0.022 per share using an option pricing model that estimated the value of a protective put option using inputs that included quoted market prices and observable inputs other than quoted market prices. We initially recorded the net fair value amount of $1.1 million as a non-current other asset in our consolidated balance sheet. As of December 31, 2015, the non-current other asset was valued using the ASX closing market price of $0.051 per share and an updated discount for the lack of marketability of $0.014 per share using an option pricing model, resulting in an impairment charge recorded as a valuation allowance against the non-current other asset of $550,000. We considered both the initial valuation as well as our year-end valuation under Level 2 of the fair value hierarchy. In April 2016, we executed an agreement (the "Settlement Agreement") with Antisense to terminate the exclusive license agreement. Pursuant to the terms of the Settlement Agreement, we made a one-time payment of approximately $770,000 to Antisense and returned to Antisense, for no consideration, the shares of Antisense owned by us. Therefore no remeasurement was needed as of December 31, 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, 2016 and 2015 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

Business combinations

When acquiring new enterprises over which we obtain control, the acquisition method is applied. Under this method, we identify assets and liabilities of these enterprises and measure them at fair value at the acquisition date. Allowance is made for the tax effect of the adjustments made.

The excess of the consideration transferred, the amount of the non-controlling interest in the acquiree and the acquisition date fair value of previous equity interest in the acquiree over the fair value of the identifiable net assets acquired is recorded as goodwill.

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, such as our in-process research and development, 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.

To test these assets for impairment, we compare the fair value of the asset to its carrying value. The method we use to estimate the fair value measurements of indefinite-lived intangible assets is based on the income approach. For the impairment analysis for the year ended December 31, 2016, significant unobservable inputs used in the income approach valuation method including a discount rates, royalty rates and probabilities of product candidate advancement from one clinical trial phase to the next. The determination of fair value of indefinite lived assets is considered Level 3 for fair value measurement.

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 the years ended December 31, 2016, 2015 and 2014.

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 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 account for non-employee and liability-classified stock-based awards based on the then-current fair values at each financial reporting date until the performance is complete for non-employee awards, or until the award is settled (exercised) for liability-classified awards. Changes in the amounts attributed to these awards between the reporting dates are included in stock-based compensation expense (credit) in our statements of operations. We include liability-classified stock options in non-current liabilities in our balance sheets as their settlement (exercise) does not require use of cash, cash equivalents or other current assets.

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 common stock, 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 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 are also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from estimates. We record stock-based compensation expense only for those awards

that are expected to vest. To the extent that actual forfeitures differ from our estimates, the differences are recorded as a cumulative adjustment in the period the estimates were revised.

Income taxes

We use the asset and liability method of accounting for income taxes in accordance with FASB ASC Topic 740, Income Taxes (ASC 740). Under this method, income tax expense is recognized for the amount of (1) taxes payable or refundable for the current year and (2) deferred tax consequences of temporary differences resulting from matters that have been recognized in an entity's financial statements or tax returns.

Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the results of operations in the period that includes the enactment date. A valuation allowance is provided to reduce the deferred tax assets reported if, based on the weight of the available positive and negative evidence, it is more likely than not some portion or all of the deferred tax assets will not be realized.

ASC 740 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements and prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. ASC 740 also provides guidance on de-recognition, classification, interest and penalties, accounting in interim periods, disclosure and transition. We have no material uncertain tax positions for any of the reporting periods presented.

We recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2016, 2015 and 2014, we had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in our statements of operations.

Net loss per share

Basic net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period. Diluted net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding for the period, including any dilutive effect from outstanding stock options or other equity-based awards. Shares used in the diluted net loss per share calculations exclude anti-dilutive common equivalent shares, which currently consist of outstanding stock options and warrants. Due to the Company operating at a net loss these anti-dilutive shares of common stock totaled 3,249,784 shares, 2,591,520 shares and 925,077 shares for the years ended December 31, 2016, 2015 and 2014, respectively. While these common equivalent shares are currently anti-dilutive, they could be dilutive in the future.

Recently adopted accounting pronouncements

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers*, which requires entities to recognize revenue in a way that depicts the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled to in exchange for those goods or services. The new guidance also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. The FASB has subsequently issued ASU No. 2016-10, *Revenue from Contracts with Customer* (Topic 606): Identifying Performance Obligations and Licensing, to address issues arising from implementation of the new revenue recognition standard. ASU 2014-09 and ASU 2016-10 are effective for interim and annual periods beginning January 1, 2018, and may be adopted earlier. The revenue standards are required to be adopted by taking either a full retrospective or a modified retrospective approach. The Company currently is evaluating the effect that this guidance may have on its consolidated financial statements as it relates to our launch of Keveyis.

In September 2014, the FASB issued ASU No. 2014-15*, Presentation of Financial Statements—Going Concern: Disclosures of Uncertainties about an Entity's Ability to Continue as a Going Concern*. The new guidance addresses management's responsibility to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. Management's evaluation should be based on relevant conditions and events that are known and reasonably knowable at the date that the financial statements are issued. The Company adopted ASU 2014-15 and it did not have an impact on our financial position or results of operations.

In September 2015, the FASB issued ASU 2015-16, *Business Combinations—Simplifying the Accounting Measurement-Period Adjustments* that eliminates the requirement to restate prior period financial statements for measurement period adjustments for business combinations. The new guidance requires that the cumulative impact of a measurement period adjustment (including the impact on prior periods) be recognized in the reporting period in which the adjustment is identified. The guidance is effective for fiscal years beginning on or after December 15, 2015, and interim periods within those years and should be applied prospectively to measurement period adjustments that occur after the effective date. The Company will prospectively apply the guidance to applicable transactions.

In November 2015, the FASB issued ASU 2015-17, *Income Taxes: Balance Sheet Classification of Deferred Taxes* that amends the balance sheet classification of deferred taxes. The new guidance requires that deferred tax liabilities and assets be classified as noncurrent on the balance sheet. Previous guidance required deferred tax liabilities and assets to be separated into current and noncurrent amounts on the balance sheet. The guidance is effective for fiscal years beginning on or after December 15, 2016, and interim periods within those years. The Company is currently evaluating the impact that the new guidance will have on our consolidated financial statements.

In January 2016, the FASB issued ASU No. 2016-01, *Financial Instruments – Overall: Recognition and Measurement of Financial Assets and Financial Liabilities*, that modifies certain aspects of the recognition, measurement, presentation, and disclosure of financial instruments. The accounting standard update is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017, and early adoption is permitted. The Company are currently assessing the impact that adopting this new accounting guidance will have on our consolidated financial statements.

In March 2016, the FASB issued ASU 2016-09, *Compensation – Stock Compensation: Improvements to Employee Share-Based Payments Accounting*, which effects all entities that issue share-based payment awards to their employees. The amendments in this ASU cover such areas as the recognition of excess tax benefits and deficiencies, the classification of those excess tax benefits on the statement of cash flows, an accounting policy election for forfeitures, the amount an employer can withhold to cover income taxes and still qualify for equity classification and the classification of those taxes paid on the statement of cash flows. This ASU is effective for annual and interim periods beginning after December 15, 2016. This guidance can be applied either prospectively, retrospectively or using a modified retrospective transition method. Early adoption is permitted. The Company does not expect that this new guidance will have a material impact on the Company's Consolidated Financial Statements.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments,* which simplifies certain elements of cash flow classification. The new guidance is intended to reduce diversity in practice in how certain transactions are classified in the statement of cash flows. The ASU is effective for annual periods beginning after December 15, 2017. The Company is currently evaluating the impact the adoption of the ASU will have on its consolidated financial statements.

In January 2017, the FASB issued ASU 2017-01, *Business Combinations - Clarifying the Definition of a Business,* which clarified the definition of a business to assist entities with evaluating whether transactions should be accounted for as acquisitions of assets or businesses. The guidance is effective for interim and annual periods beginning after December 31, 2017, and early adoption is permitted. The Company elected to early adopt this guidance in the current period and has applied it to its evaluation of our asset purchase from Taro Pharmaceutical Industries Ltd. (see note 4).

In January 2017, the FASB issued 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 the Company beginning in the first quarter of fiscal year 2021, 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. The Company is currently evaluating the impact this standard will have on its financial statements.

3. 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. The noncurrent asset comprising of our investment in Antisense common stock, up until the time our investment was returned to Antisense was classified as Level II as we discounted the active market quoted price of the security to reflect our contractual restriction on selling the investment. Level 3 instruments consist of the common stock 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.

Because of their short term nature, the amounts reported in the balance sheet for cash and cash equivalents, and accounts payable approximate fair value.

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, 2016			
	Level I	**Level II**	**Level III**	**Total**
Warrant Liabilities	—	—	11,090	11,090
Total liabilities	$ —	$ —	$ 11,090	$ 11,090

	As of December 31, 2015			
	Level I	**Level II**	**Level III**	**Total**
Assets				
Cash equivalents	$ 45,296	$ —	$ —	$ 45,296
Noncurrent asset	—	550	—	550
Total assets	$ 45,296	$ 550	$ —	$ 45,846

4. 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, 2016			
	Beginning of Period	Additions	Impairment	End of Period
IPR&D	$ 36,551	$ —	$ (15,828)	$ 20,723
Acquired product rights	—	40,177	—	40,177
Goodwill	7,256	—	—	7,256
Total	$ 43,807	$ 40,177	$ (15,828)	$ 68,156

	As of December 31, 2015			
	Beginning of Period	Additions	Impairment	End of Period
IPR&D	$ 5,228	$ 31,323	$ —	$ 36,551
Acquired product rights	—	—	—	—
Goodwill	2,200	5,056	—	7,256
Total	$ 7,428	$ 36,379	$ —	$ 43,807

Goodwill and in-process research and development as of December 31, 2016 and 2015 resulted from our acquisition of BioPancreate and our 2015 acquisition of veldoreotide (formerly called COR-005) from Aspireo Pharmaceuticals, Ltd. (see Note 8). In-process research and development is initially measured at its fair value and is not amortized until commercialization. Once commercialization occurs, in-process research and development will be amortized over its estimated useful life. We recorded $5.2 million of impairment relating to our BioPancreate IPR&D (See note 8) and $10.6 million impairment for our veldoreotide IPR&D during the year ended December 31, 2016. 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 is due to increased costs estimated 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 consist of acquired developed product rights obtained from the asset acquisition of Keveyis® (dichlorphenamide) from a subsidiary of Taro Pharmaceutical Industries Ltd. (“Taro”). Keveyis is approved in the U.S. to treat hyperkalemic, hypokalemic and related variants of primary periodic paralysis, a group of rare hereditary disorders that cause episodes of muscle weakness or paralysis. Keveyis has received orphan drug exclusivity status in the U.S through August 7, 2022. In connection with the Asset Purchase and Supply Agreement we entered into with Taro Pharmaceutical Industries Ltd, we have 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 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 will be amortized as units are sold over an estimated 8 year period.

5. Accrued liabilities

Accrued liabilities consist of the following (in thousands):

	December 31, 2016	December 31, 2015
Consulting and professional fees	$ 1,110	$ 1,288
Accrued payable due Taro Pharmaceuticals Industries Ltd.	7,500	—
Supply agreement - current portion	4,207	—
Employee compensation	1,554	1,172
Other	497	225
Total accrued liabilities	$ 14,868	$ 2,685

6. Long Term Debt

On December 28, 2016, the Company entered into a loan and security agreement (the “Loan Agreement”) with Oxford Finance LLC (“Oxford”) and Horizon Technology Finance Corporation (“Horizon”). The Loan Agreement provided for a $40 million credit facility, of which $20 million was borrowed initially. Under the Loan Agreement, the Company has access to two additional tranches of $10 million each, which would be available to the Company subject to the achievement of certain specified milestones.

The borrowings pursuant to the Loan Agreement mature after 48 months. The Loan Agreement provides for interest-only payments initially for the first 18 months of the loan followed by an amortization period of 30 months, a final payment fee equal to 8% of the amount borrowed, and interest payable at an annual rate equal to the sum of 8.22% plus the greater of 0.53% or the 30-day US LIBOR rate. The credit facility provides that if the Company satisfies certain milestones and borrows the final $10 million tranche, the interest-only period would be extended by an additional six months and the amortization period would be 24 months. The Company has granted a security interest in substantially all of its existing assets and assets acquired by the Company in the future, including intellectual property. The Loan Agreement contains facility and prepayment fees, and customary affirmative and negative covenants, including a financial covenant regarding minimum amounts of net revenue and events of default and restricts the payment of cash dividends. The Loan Agreement contains a material adverse change clause whereby a material adverse change in the Company's business, operations or financial condition would be considered an event of default whereby the lenders could declare all amounts under the Loan Agreement as immediately due and payable. We incurred $1.3 million in debt discounts and $0.3 million of debt issuance costs relating to this Loan Agreement which have been recorded as a reduction to the long-term debt. These amounts will be amortized over the outstanding period of the debt to interest expense using the effective interest rate method.

In connection with the execution of the Loan Agreement, we issued warrants to the Lenders to purchase an aggregate of 428,571 ordinary shares at an exercise price equal to $2.45 per share. The warrants are immediately exercisable and expire after ten years. We accounted for these warrants as equity, and the fair value was recorded into APIC.

Future principal payments due under the Loan Agreement are as follows (in thousands):

	Principal Payments
2017	$ —
2018	4,667
2019	8,000
2020	7,333
Total future payments	$ 20,000

7. Warrants

Common stock 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, 2016 is as follows:

	Classification	Exercise Price	Expiration Date	Warrants Issued	Warrants Exercised	December 31, 2016
Warrants in connection with private equity placement	Liability	$ 2.50	6/28/2022	7,000,000	—	7,000,000
Warrants in connection with loan agreement	Equity	$ 2.45	12/28/2026	428,571	—	428,571
				7,428,571		7,428,571

8. Commitments and contingencies

(a) Lease

On April 22, 2014, we entered into a 48-month building lease for approximately 3,000 square feet of space in Radnor, Pennsylvania. The lease has annual rent escalations. We obtained access to the newly leased space on August 1,

2014, and this 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.

In March 2015, the Company 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. As a result of this lease, we vacated the previously leased Radnor, Pennsylvania facility as of April 13, 2015 and determined that the Radnor, Pennsylvania facility was not likely to be utilized during the remaining lease term and as such we commenced efforts to sublease the facility. The Company recorded a liability as of the April 13, 2015 cease-use date of $0.1 million for the estimated fair value of its obligations under the lease. The most significant assumptions used in determining the amount of the estimated liability are the potential sublease revenues and the credit-adjusted risk-free rate utilized to discount the estimated future cash flows.

As of December 31, 2016, future minimum commitments under facility operating leases were as follows (in thousands):

	Operating leases
2017	$ 311
2018	319
2019	184
Total minimum lease payments	$ 814

Rent expense recognized under our operating lease, including additional rent charges for utilities, parking, maintenance and real estate taxes, was $275,000, $254,000 and $83,000 for the years ended December 31, 2016, 2015 and 2014, respectively.

(b) License Agreements

Cornell Center for Technology Enterprise and Commercialization

In 2011, a license agreement was executed between BioPancreate and the Cornell Center for Technology Enterprise and Commercialization (CCTEC). Under the terms of the license agreement, BioPancreate obtained certain rights from the CCTEC for commercial development, use and sale of products that use the technology associated with the license. We are obligated to make milestone payments upon the achievement of certain regulatory and clinical milestones up to $2.6 million in the aggregate. For years in which licensed products are sold, we are required to pay a royalty based on a low single-digit percentage of net sales. The minimum annual royalty in such years is $100,000. In the event the product is sublicensed, up to $3.5 million of certain fees we receive that are not earned royalties or reimbursements for direct costs are due to CCTEC upon achievement of certain regulatory and clinical milestones.

In October 2016, our wholly owned subsidiary, BioPancreate Inc., provided a notice to Cornell University, through its Cornell Center for Technology Enterprise and Commercialization ("CCTEC"), in accordance with the terms of its agreement with CCTEC entered into in March 2011, of the termination of the agreement. The notice was provided in accordance with our decision to terminate our development program for BP-2002, a gene-modified probiotic in pre-clinical development for the potential treatment of type 1 and 2 diabetes that was the subject of the agreement. We recorded an impairment charge of $5.2 million during the year ended December 31, 2016, which represented the value of the intangible asset we had previously capitalized related to the license agreement.

Antisense Therapeutics

In May 2015, we entered into an exclusive license agreement, or the Antisense License Agreement, with Antisense Therapeutics that provided us with development and commercialization rights to Antisense Therapeutics' product candidate, ATL1103, for endocrinology applications (specifically excluding the treatment of any form of cancer and the treatment of any complications of diabetes). We refer to this product candidate as COR-004. Under the terms of

the Antisense License Agreement, we paid Antisense Therapeutics an initial upfront license fee of $3.0 million in cash which was recorded as research and development expenses. We also invested $2.0 million in Antisense Therapeutics equity which was initially recorded as a non-current other asset for $1.1 million with the difference constituting the cost of the license which was recorded as research and development expense. The terms of the Antisense License Agreement provided that we could terminate the Antisense License Agreement upon 90 days' prior written notice to Antisense Therapeutics if we believed the further development and commercialization of COR-004 was no longer feasible due to a material change that was beyond our control. If, however, it is determined that we terminated the Antisense License Agreement for convenience, we would be required to pay Antisense Therapeutics a $2.0 million termination fee.

In April 2016, we executed an agreement (the "Settlement Agreement") with Antisense Therapeutics ("Antisense") to terminate the exclusive license agreement (the "Antisense License Agreement") that we and Antisense entered into in May 2015. Pursuant to the terms of the Settlement Agreement, we have made a one-time payment of approximately $770,000 to Antisense and returned to Antisense, for no consideration, the shares of Antisense owned by us. We also agreed to transfer to Antisense all data, reports, records and materials resulting from our development activities and all ATL1103 drug compound in our possession. The settlement agreement provides for the release by each party of all obligations and liabilities under the Antisense License Agreement. In connection with the settlement and return of shares, we recorded $1.1 million of expense within other (expense)/income.

(c) Commitments to Taro Pharmaceuticals Industries Ltd.

In December 2016, we acquired the U.S. marketing rights to Keveyis® (dichlorphenamide) from a subsidiary of Taro Pharmaceutical Industries Ltd. ("Taro"). Keveyis is approved in the U.S. to treat hyperkalemic, hypokalemic and related variants of primary periodic paralysis, a group of rare hereditary disorders that cause episodes of muscle weakness or paralysis. Keveyis has received orphan drug exclusivity status in the U.S through August 7, 2022. 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. 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.

9. Business combinations

BioPancreate

On October 29, 2013, we exercised our option to acquire the remaining interest in BioPancreate. As consideration for this acquisition of shares, we issued 336,136 shares of our ordinary shares in October 2013 and an additional 5,272 ordinary shares in January 2014. The transaction was recorded as an equity transaction and the previously held non-controlling interest in BioPancreate was reclassified to equity.

Aspireo Pharmaceuticals Ltd. Acquisition

On June 30, 2015, we acquired veldoreotide from Aspireo Pharmaceuticals Ltd., an Israeli company. Veldoreotide was formerly called COR-005 by us and DG3173 by Aspireo Pharmaceuticals. We also acquired from Aspireo the rights and obligations to the on-going research and development contracts, which combined with veldoreotide represented "substantially all" of the Aspireo business. Under the terms of the acquisition agreement, we issued to Aspireo 2,062,677 common shares, which had a value of $33.2 million on June 30, 2015. In connection with this acquisition, we also made a payment to the Office of the Chief Scientist of the Israeli Ministry of Economy, or OCS, in the amount of $3.0 million, which represents the repayment of amounts granted by the OCS to Aspireo, plus interest, that were used in support of research and development conducted by Aspireo for the development of DG3173.

The acquisition was accounted for using the acquisition method of accounting for business combinations. The total consideration transferred was allocated to the assets acquired and liabilities assumed based on their respective fair values. The fair value of $16.10 per ordinary share of the 2,062,677 ordinary shares issued was determined based on the closing market price on the NOTC of our ordinary shares on the acquisition date. To determine the fair value of the acquired in-process research and development intangible asset, we applied the income approach using the multi-period excess earnings method. The following table summarizes the fair values of the assets acquired and liabilities assumed (in thousands):

In process research and development	$ 31,323
Liabilities assumed:	
Other liabilities (net)	(195)
OCS liability	(2,973)
Total fair values of assets and liabilities	28,155
Fair value of total consideration transferred	(33,211)
Goodwill	$ (5,056)

The excess of the consideration transferred over net assets acquired was assigned to goodwill in an amount of $5.1 million and is primarily related to expected synergies. A deferred tax liability was not recorded for the difference between the book and cost basis of the in-process research and development intangible asset because the asset is domiciled in the Cayman Islands and therefore we do not expect to pay income tax. The goodwill is not deductible for income tax purposes.

We incurred $2.2 million in acquisition-related transaction costs for the period ended December 31, 2015, which is included as general and administration expense in the accompanying consolidated statements of operations.

10. Income taxes

For the years ended December 31, 2016, 2015 and 2014, the components of loss before income taxes were as follows (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Sweden	$ (16,433)	$ (33,960)	$ (9,165)
Ireland	(11,653)	(191)	—
Cayman Islands	(19,550)	(8,722)	—
U.S.	(3,721)	(1,210)	(985)
Total	$ (51,357)	$ (44,083)	$ (10,150)

The components of income tax expense (benefit) for the years ended December 31, 2016, 2015 and 2014 were as follows (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Current tax expense (benefit):			
Sweden	$ —	$ —	$ —
Ireland	22	—	—
U.S.			
Federal	151	—	—
State	73	—	—
Total	$ 246	$ —	$ —
Deferred tax expense (benefit):			
Sweden	$ —	$ 212	$ (648)
Ireland	—	(24)	—
U.S.			
Federal	(5,793)	(17,543)	(2,433)
State	(678)	(1,233)	(720)
Change in valuation allowance	3,587	18,138	3,321
Total	$ (2,638)	$ (450)	$ (480)

With the exception of Strongbridge U.S. Inc., we have incurred net operating losses since inception. For the Ireland and Swedish operations, we have not reflected any benefit of net operating loss carryforwards (NOLs) in the accompanying financial statements. For Strongbridge U.S. Inc., as a result of the intercompany service agreements, it is more likely than not this entity will have taxable income and recognize all deferred tax assets. Due to the recording of a full impairment of the BioPancreate intellectual property in the current year at BioPancreate, we have established a full valuation allowance against all prior deferred tax assets.

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,	
	2016	2015
Deferred tax assets:		
Net operating loss carryforwards	$ 24,433	$ 22,039
Stock based compensation	1,870	—
Other deferred activity	96	—
Tax credits	9,135	9,135
Capitalized research and development costs	161	161
Total deferred tax assets	35,695	31,335
Valuation allowance	(33,738)	(30,150)
Deferred tax assets recognized	1,957	1,185
Deferred tax liabilities:		
Warrants	(358)	—
Acquired intangible assets	—	(2,111)
Total deferred tax liabilities	(358)	(2,111)
Net deferred tax assets (liabilities)	$ 1,599	$ (926)

We have evaluated the positive and negative evidence bearing upon the realizability of our deferred tax assets. Based on our history of operating losses in Ireland and Sweden, we have concluded that it is more likely than not that the benefit of our deferred tax assets will not be realized. Currently, as a result of intercompany service agreements that provide a source of taxable income going forward, Strongbridge U.S. Inc. is more likely than not to realize its deferred

tax assets. Separately, as a result of recording a full impairment of the BioPancreate intellectual property, we have recorded a full valuation allowance against the prior federal attributes and all existing state attributes related to BioPancreate. The valuation allowance increased by approximately $3.6 million and $18.1 million during the year ended December 31, 2016 and 2015, respectively, due primarily to net operating losses.

The Company's 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, 2016 and 2015. In December 31, 2014, the effective income tax rate differs from the previous ultimate parent company, Cortendo AB's, Swedish domestic tax rate of 22% as follows:

	Year Ended December 31,		
	2016	2015	2014
Ireland statutory income tax rate	12.50 %	12.50 %	—
Swedish statutory income tax rate	—	—	22.00 %
Foreign tax differential between Sweden, U.S., Cayman Island and Ireland	2.28	15.70	(4.60)
Federal tax credits	—	12.10	20.90
Change in valuation allowance	(6.69)	(41.20)	(32.70)
State income taxes	0.92	—	—
Permanent differences	1.59	—	—
Fx remeasurement of Swedish DTS	(5.42)	(5.41)	—
Other	(0.04)	7.31	(0.90)
Effective income tax rate	5.14 %	1.00 %	4.70 %

At December 31, 2016, we had approximately $70.4 million of Swedish NOLs and approximately $12.5 million of Ireland NOLs, which have an indefinite life, and approximately $37.1 million of U.S. federal and $37.2 million of state NOLs, which begin to expire in 2031. Through December 31, 2015 we operated through a permanent establishment in both Sweden and the United States. Relief is granted by way of crediting the U.S. tax against the Swedish tax. This tax credit can never exceed the Swedish tax on the income. Since the tax rate is higher in the United States than in Sweden, the Swedish taxable carryforward losses of $70.4 million can only generate a tax benefit if income is derived from sources other than the permanent establishment in the United States. Beginning January 1, 2016, the US operations that were not part of BioPancreate Inc occurred in a newly formed US corporation. There were no operating losses generated during 2016 in the U.S. except for a minor state NOL at BioPancreate.

At December 31, 2016, we had $8.9 million of U.S. federal orphan drug tax credit carryforwards, which begin to expire in 2032, and $167,000 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.

11. Ordinary shares

Voting rights and privileges

As of December 31, 2016, and December 31, 2015, there are 600,000,000 authorized shares and 35,335,026 and 21,205,382 outstanding shares, respectively.

The holders of shares 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 euro 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 22, 2016, we raised $32.7 million, net of transaction costs, in a private placement of ordinary shares and warrants. We issued and sold 14,000,000 ordinary shares of common stock at a purchase price of $2.50 per ordinary share as well as warrants to purchase 7,000,000 shares. The warrants are exercisable at a price of $2.50 per share beginning on June 28, 2017 and expire in five years from June 28, 2017. In the event of a sale of the Company, the terms of the warrants 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). Therefore we are required to account for these warrants as liabilities and record at fair value at each reporting period. Fair value for these warrants was initially determined upon issuance using the Black-Scholes Model and were revalued at fair value as of December 31, 2016. The resulting decrease in fair value resulted in an unrealized gain of $0.6 million. As of December 31, 2016, the fair value of these warrants of $11.1 million was recorded as a long-term liability on our consolidated balance sheet.

On October 22, 2015, we closed on our initial U.S. public offering of 2,500,000 ordinary shares at a price to the public of $10.00 per ordinary share for aggregate gross proceeds of $25 million, before deducting the underwriting commission and estimated offering expenses of $5.5 million. In June 2015, we raised $32.6 million, net of transaction costs, in a private placement of 2,284,414 shares of our common stock. The subscription price was $14.54 per share. In February 2015, we raised $25.8 million, net of transaction costs, in a private placement of 4,761,078 shares of our common stock. The subscription price was $5.54 per share.

Shares reserved for issuance

There were 1,951,022 and 2,591,520 shares of common stock reserved for future issuance upon exercise of stock options as of December 31, 2016 and 2015, respectively. As of December 31, 2016, we have 7,428,571 shares reserved for outstanding warrants.

12. Stock-based compensation

The Board of Directors approve the granting of awards to our officers, directors, employees and third party-consultants. Under these grants, the beneficiaries are given the right to acquire new shares of common stock at a pre-determined option price. The purpose of the grants is to assist us in attracting, retaining and motivating officers, employees, directors and consultants. In addition, these awards provide us with the ability to provide incentives that are directly linked to the performance of our business and the related increase in shareholder value.

Our awards have terms that range from five to ten years. As determined by our Board of Directors, our awards vest over service periods ranging up to four years or upon achievement of defined performance or market criteria such as the vesting of certain awards upon our IPO or awards that are accelerated when the fair value of our stock price reaches defined targets.

The exercise price for each stock option is determined by the Board of Directors based upon considerations such as the fair value of the underlying ordinary shares and certain market conditions. For options granted prior to our October 22, 2015, IPO, the determination of the fair value of our common stock takes into account the price at which our shares were being quoted on the NOTC, recent equity financings and our valuations calculated with the assistance of third-parties.

On July 21, 2015, we cancelled 465,262 of our options for certain employees that were not vested and for which service was expected to be rendered and concurrently replaced these with 586,710 options. We accounted for the cancellation and replacement as a modification whereby we determined value of the original options based on current assumptions, without regard to the assumptions made on the grant date. We then compared the fair value of the modified award to the fair value of the original options immediately before the terms were modified, measured based on the share price and other pertinent factors on the date of the modification The incremental value of $468,000 was recorded over the remaining requisite service periods as these awards are expected to vest.

On September 8, 2015, we effected a 1-for-11 reverse stock split of our ordinary shares. In conjunction with the reverse stock split, we adjusted our outstanding stock options by the same ratio.

On October 22, 2015, we converted all of our Cortendo AB awards which were previously denominated in Swedish Krona (SEK) and Norwegian Kroner (NOK), into awards to acquire shares in Strongbridge Biopharma plc which were denominated in U.S. dollars. For the stock options denominated in NOK, the calculation was based on 8.1935 NOK per U.S. dollars. Due to the effects of foreign exchange related to the exercise price, we accounted for the conversion as a modification whereby we determined value of the original options based on current assumptions, without regard to the assumptions made on the grant date. We then compared the fair value of the modified award to the fair value of the original options immediately before the terms were modified, measured based on the share price and other pertinent factors on the date of the modification. Because the effected options were vested, the incremental value of $325,000 was recorded as expense during the period ended December 31, 2015.

For the awards denominated in SEK which were classified as liability awards, we accounted for the conversion as a modification whereby we determined the value of the original options based on current assumptions, without regard to the assumptions made on the grant date. We then compared the fair value of the modified award to the fair value of the original options immediately before the terms were modified, measured based on the share price and other pertinent factors on the date of the modification. The incremental value was recorded as expense in the statement of operations. The liability awards were fully vested as of October 22, 2015 and therefore the resulting liability after modification of $1.5 million, was reclassified from liability to additional paid-in capital on October 22, 2015. As these stock options are now equity-classified and fully vested, we will not remeasure these stock options in the future.

A summary of the outstanding stock options activity for the year ended December 31, 2016 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, 2016	2,591,520	$ 13.59	5.97	$ 1,844
Granted	1,169,600	$ 4.28		
Forfeited and cancelled	(329,518)	$ 12.85		
Expired	—	—		
Exercised	181,818	$ 1.32		
Outstanding—December 31, 2016	3,249,784	$ 11.00	6.89	$ —
Vested and exercisable—December 31, 2016	1,158,660	$ 11.37	4.91	$ —
Vested and expected to vest—December 31, 2016	2,860,743	$ 10.73	6.52	$ —

Included in the stock options outstanding at December 31, 2016, are unvested stock options to purchase 88,909 shares at a weighted average exercise $18.80 per share for which the vesting of certain tranches will accelerate if the fair value per share of our stock reaches $16.11, $31.46 or $37.62 for the respective grantee. In addition, the options outstanding include 97,652 shares that vest upon a market appreciation event so long as it occurs prior to May 26, 2019 of which all were unvested as of December 31, 2016 and 97,652 shares that will vest upon the one year anniversary of the market appreciation event of which all were unvested as of December 31, 2016. The market appreciation event is

defined as the last trading day in the period in which the 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.

The aggregate intrinsic values of options outstanding, vested and exercisable, and vested and expected to vest were calculated as the difference between the exercise price of the options and the estimated fair value of our common stock as of December 31, 2016, since the estimated fair value is less than the exercise price for all stock options, there is not any intrinsic value.

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,		
	2016	2015	2014
Research and development	$ 601	$ 793	$ 268
General and administrative	4,005	3,147	(17)
Total stock-based compensation	$ 4,606	3,940	$ 251

Included in these amounts was stock compensation expense (credit) attributed to liability-classified awards of, $0, $359,000 and $(229,000), for the years ended December 31, 2016, 2015 and 2014, respectively. The total income tax benefit recognized in the income statement for share-based compensation arrangements was $1.9 million, $0, and $0 for 2016, 2015 and 2014, respectively.

As of December 31, 2016, the total unrecognized compensation expense related to unvested options, net of estimated forfeitures, was $6.8 million, which we expect to recognize over an estimated weighted-average period of 2.46 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,		
	2016	2015	2014
Expected term (in years)	5.9	3.23	3.23
Risk-free interest rate	1.21% - 2.23%	0.0% - 0.6%	0.0% - 0.6%
Expected volatility	78.1% - 83.6%	79.0% - 83.1%	68.3% - 80.7%
Dividend rate	—%	—%	—%

Exhibit 10.20

THIS WARRANT AND THE SHARES ISSUABLE HEREUNDER HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "**ACT**"), OR THE SECURITIES LAWS OF ANY STATE AND, EXCEPT AS SET FORTH IN SECTIONS 5.3 AND 5.4 BELOW, MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED UNLESS AND UNTIL REGISTERED UNDER SAID ACT AND LAWS OR, IN THE OPINION OF LEGAL COUNSEL IN FORM AND SUBSTANCE SATISFACTORY TO THE COMPANY, SUCH OFFER, SALE, PLEDGE OR OTHER TRANSFER IS EXEMPT FROM SUCH REGISTRATION.

WARRANT TO SUBSCRIBE FOR SHARES

Company:	STRONGBRIDGE BIOPHARMA PUBLIC LIMITED COMPANY, a public limited company incorporated under the laws of Ireland
Number of Shares:	
Class of Share:	Ordinary Shares of nominal value US$0.01
Warrant Price:	$2.45 per Share
Issue Date:	December 28, 2016
Expiration Date:	December 28, 2026 See also Section 5.1(b).
Credit Facility:	This Warrant to Subscribe for Shares ("**Warrant**") is issued in connection with that certain Loan and Security Agreement, dated December 28, 2016, by and among Oxford Finance LLC, as Lender and Collateral Agent, the Lenders from time to time party thereto, including _____ and the Company (as modified, amended and/or restated from time to time, the "**Loan Agreement**").

THIS WARRANT CERTIFIES THAT, for good and valuable consideration, _____ (" _____" and, together with any successor or permitted assignee or transferee of this Warrant or of any shares issued upon exercise hereof, "**Holder**") is entitled to subscribe for the number of fully paid and non-assessable (which term, when used herein, means that no further sums are required to be paid in connection with such Shares by the holder(s) thereof) shares (the "**Shares**") of the above-stated Class of Shares (the "**Class**") of the above-named company (the "**Company**") at the above-stated Warrant Price, all as set forth above and as adjusted pursuant to Section 2 of this Warrant, subject to the provisions and upon the terms and conditions set forth in this Warrant. The Company has, by resolution of its board of directors, agreed to issue this Warrant to _____ to subscribe for the Shares on the terms set out in this Warrant.

SECTION 1. EXERCISE.

1 . 1 Method of Exercise. Holder may at any time and from time to time exercise this Warrant, in whole or in part, by delivering to the Company the original of this Warrant together with a duly executed Notice of Exercise in substantially the form attached hereto as Appendix 1 and a check, wire transfer of same-day funds (to an account designated by the Company), or other form of payment acceptable to the Company for the aggregate price to be paid for the Shares being subscribed for pursuant to such exercise as determined pursuant to Section 1.2 below (the "Subscription Price"). Thereupon, the Company shall issue to the Holder such number of fully paid and non-assessable shares determined in accordance with Section 1.2 below.

1.2 Exercise. On any exercise of this Warrant:

(a) if Holder does not elect in the applicable Notice of Exercise to effect that exercise pursuant to Section 1.2(b) below, the number of Shares to be issued by the Company pursuant to that exercise shall be the number of Shares specified in paragraph 1 of the applicable Notice of Exercise and the Subscription Price payable in respect of that exercise shall be the product of the Warrant Price multiplied by the number specified in paragraph 1 of the applicable Notice of Exercise; and

(b) if Holder does elect in the applicable Notice of Exercise to effect that exercise pursuant to this Section 1.2(b), the number of Shares to be issued by the Company pursuant to that exercise shall be calculated in accordance with the following formula:

$$X = S - Y$$

where:

X is the number of Shares to be issued by the Company pursuant to that exercise;

S is the number of Shares specified in paragraph 1 of the applicable Notice of Exercise; and

Y is calculated in accordance with the following formula:

$$Y = S(WP - N)/FMV$$

where:

S is the number of Shares specified in paragraph 1 of the applicable Notice of Exercise;

WP is the Warrant Price;

N is the then nominal value of a Share; and

FMV is the Fair Market Value (as determined pursuant to Section 1.3 below) of one Share,

and the Subscription Price payable in respect of that exercise shall be the product of the then nominal value of a Share multiplied by the number specified in paragraph 1 of the applicable Notice of Exercise.

1.3 Fair Market Value. If the Company's ordinary shares are then traded or quoted on a nationally recognized securities exchange, inter-dealer quotation system or over-the-counter market (a "**Trading Market**") and the Class is ordinary shares, the fair market value of a Share shall be the closing price or last sale price of an ordinary share of the Company reported for the Business Day immediately before the date on which Holder delivers this Warrant together with its Notice of Exercise to the Company. If the Company's ordinary shares are then traded in a Trading Market, the fair market value of a Share shall be the closing price or last sale price of an ordinary share of the Company reported for the Business Day immediately before the date on which Holder delivers this Warrant together with its Notice of Exercise to the Company. If the Company's ordinary shares are not traded in a Trading Market,

the Board of Directors of the Company shall determine the fair market value of a Share in its reasonable good faith judgment.

1.4 Delivery of Certificate and New Warrant. Within a reasonable time after Holder exercises this Warrant in the manner set forth in Sections 1.1 and 1.2 above, the Company shall deliver to Holder a certificate representing the Shares issued to Holder upon such exercise and, if this Warrant has not been fully exercised and has not expired, a new warrant of like tenor representing the Shares not so acquired.

1.5 Replacement of Warrant. On receipt of evidence reasonably satisfactory to the Company of the loss, theft, destruction or mutilation of this Warrant and, in the case of loss, theft or destruction, on delivery of an indemnity agreement reasonably satisfactory in form, substance and amount to the Company or, in the case of mutilation, on surrender of this Warrant to the Company for cancellation, the Company shall, within a reasonable time, execute and deliver to Holder, in lieu of this Warrant, a new warrant of like tenor and amount.

1.6 Treatment of Warrant Upon Acquisition of Company.

(a) Acquisition. For the purpose of this Warrant, "**Acquisition**" means any transaction or series of related transactions involving: (i) the sale, lease, exclusive license, or other disposition of all or substantially all of the assets of the Company (ii) any merger or consolidation of the Company into or with another person or entity (other than a merger or consolidation effected exclusively to change the Company's domicile), or any other corporate reorganization, in which the stockholders of the Company in their capacity as such immediately prior to such merger, consolidation or reorganization, own less than a majority of the Company's (or the surviving or successor entity's) outstanding voting power immediately after such merger, consolidation or reorganization (or, if such Company stockholders beneficially own a majority of the outstanding voting power of the surviving or successor entity as of immediately after such merger, consolidation or reorganization, such surviving or successor entity is not the Company); or (iii) any one or more offers by any person or group of persons acting in concert (in either case, the "**Offeror**") which is publicly disclosed and which, if completed, would result in the Offeror holding or controlling more than 50% of the voting and other equity securities of the Company.

(b) Treatment of Warrant at Acquisition. In the event of an Acquisition in which the consideration to be received by the Company's shareholders consists solely of cash, solely of Marketable Securities or a combination of cash and Marketable Securities (a "**Cash/Public Acquisition**"), either (i) Holder shall exercise this Warrant pursuant to Section 1.1 and 1.2 and such exercise will be deemed effective immediately prior to and contingent upon the consummation of such Acquisition or (ii) if Holder elects not to exercise the Warrant, this Warrant will expire immediately prior to the consummation of such Acquisition.

(c) The Company shall provide Holder with written notice of its request relating to the Cash/Public Acquisition (together with such reasonable information as Holder may reasonably require regarding the treatment of this Warrant in connection with such contemplated Cash/Public Acquisition giving rise to such notice), which is to be delivered to Holder not less than twenty-one (21) days prior to the closing of the proposed Cash/Public Acquisition. In the

event the Company does not provide such notice, then if, immediately prior to the Cash/Public Acquisition, the fair market value of one Share (or other security issuable upon the exercise hereof) as determined in accordance with Section 1.3 above would be greater than the Warrant Price in effect on such date, then this Warrant shall automatically be deemed on and as of such date to be exercised pursuant to Section 1.2(b) above as to all Shares (or such other securities) for which it shall not previously have been exercised, and the Company shall promptly notify the Holder of the number of Shares (or such other securities) issued upon such exercise to the Holder and Holder shall pay to the Company in the manner prescribed in Section 1.1 above an amount equal to the Subscription Price in respect of such exercise and be deemed to have restated each of the representations and warranties in Section 4 of the Warrant as the date thereof.

(d) Upon the closing of any Acquisition other than a Cash/Public Acquisition defined above, the acquiring, surviving or successor entity shall assume the obligations of this Warrant, and this Warrant shall thereafter be exercisable for the same securities and/or other property as would have been paid for the Shares issuable upon exercise of the unexercised portion of this Warrant as if such Shares were outstanding on and as of the closing of such Acquisition, subject to further adjustment from time to time in accordance with the provisions of this Warrant.

(e) As used in this Warrant, "**Marketable Securities**" means securities meeting all of the following requirements: (i) the issuer thereof is then subject to the reporting requirements of Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), and is then current in its filing of all required reports and other information under the Act and the Exchange Act; (ii) the class and series of shares or other security of the issuer that would be received by Holder in connection with the Acquisition were Holder to exercise this Warrant on or prior to the closing thereof is then traded in Trading Market, (iii) the issuer thereof has a market cap of at least Five Hundred Million Dollars ($500,000,000) and (iv) following the closing of such Acquisition, Holder would not be restricted from publicly re-selling all of the issuer's shares and/or other securities that would be received by Holder in such Acquisition were Holder to exercise or convert this Warrant in full on or prior to the closing of such Acquisition, except to the extent that any such restriction (x) arises solely under federal or state securities laws, rules or regulations, and (y) does not extend beyond six (6) months from the closing of such Acquisition.

SECTION 2. ADJUSTMENTS TO THE SHARES AND WARRANT PRICE.

2 . 1 Stock Dividends, Splits, Etc. If the Company declares, pays or makes a dividend, distribution or bonus issue on the issued shares of the Class payable in shares or other securities or property (other than cash), then upon exercise of this Warrant, for each Share acquired, Holder shall receive, without additional cost to Holder, the total number and kind of securities and property which Holder would have received had Holder owned the Shares of record as of the date the dividend or distribution occurred. If the Company subdivides the issued shares of the Class by reclassification or otherwise into a greater number of shares, the number of Shares subscribable hereunder shall be proportionately increased and the Warrant Price shall be proportionately decreased. If the issued shares of the Class are combined or consolidated, by reclassification or otherwise, into a lesser number of shares, the Warrant Price shall be proportionately increased and the number of Shares shall be proportionately decreased.

2.2 Reclassification, Exchange, Combinations or Substitution. Upon any event whereby all of the issued shares of the Class are reclassified, exchanged, combined, substituted, or replaced for, into, with or by Company securities of a different class and/or series, then from and after the consummation of such event, this Warrant will be exercisable for the number, class and series of Company securities that Holder would have received had the Shares been in issue on and as of the consummation of such event, and subject to further adjustment thereafter from time to time in accordance with the provisions of this Warrant. The provisions of this Section 2.2 shall similarly apply to successive reclassifications, exchanges, combinations substitutions, replacements or other similar events.

2.3 Intentionally Left Blank.

2.4 Intentionally Left Blank.

2.5 No Fractional Share. No fractional Share shall be issuable upon exercise of this Warrant and the number of Shares to be issued shall be rounded down to the nearest whole Share. If a fractional Share interest arises upon any exercise of the Warrant, the Company shall eliminate such fractional Share interest by paying Holder in cash the amount computed by multiplying the fractional interest by (i) the fair market value (as determined in accordance with Section 1.3 above) of a full Share, less (ii) the then-effective Warrant Price.

2.6 Notice/Certificate as to Adjustments. Upon each adjustment of the Warrant Price, Class and/or number of Shares, the Company, at the Company's expense, shall notify Holder in writing within a reasonable time setting forth the adjustments to the Warrant Price, Class and/or number of Shares and facts upon which such adjustment is based. The Company shall, upon written request from Holder, furnish Holder with a certificate of its Chief Financial Officer, including computations of such adjustment and the Warrant Price, Class and number of Shares in effect upon the date of such adjustment and each reference in this Warrant to the Warrant Price, Class and/or number of Shares shall, unless expressly provided otherwise herein, be construed as a reference to the Warrant Price, Class and/or number of Shares respectively as adjusted in accordance with the terms of this Warrant.

SECTION 3. REPRESENTATIONS AND COVENANTS OF THE COMPANY.

3.1 Representations and Warranties. The Company represents and warrants to, and agrees with, the Holder as follows:

(a) The Company has full power and authority to execute and deliver this Warrant and to comply with the provisions of, and perform its obligations under, this Warrant.

(b) The Company has taken all necessary action to authorize the execution, delivery and performance of this Warrant and this Warrant constitutes legal, valid and binding obligations enforceable against it.

(c) The execution of this Warrant and the performance by the Company of its obligations hereunder do not and will not conflict with its constitution or law or regulation applicable to it.

(d) The initial Warrant Price referenced on the first page of this Warrant is not greater than the price per share at which shares of the Class were last sold and issued prior to the Issue Date hereof in an arms-length transaction in which at least $500,000 of such shares were sold.

(e) All Shares which may be issued upon the exercise of this Warrant, and all securities, if any, issuable upon conversion of the Shares, shall, upon issuance, be duly authorized, validly issued, fully paid and non-assessable, and free of any liens and encumbrances except for restrictions on transfer provided for herein or under applicable federal and state securities laws and shall rank pari passu in all respects with all other Shares in issue on the date of such issuance and conform to the rights attached to such shares set out in the constitution of the Company. The Company covenants that it shall at all times cause to be reserved and kept available out of its authorized and unissued share capital such number of shares of the Class, ordinary shares and other securities as will be sufficient to permit the exercise in full of this Warrant and the conversion of the Shares into ordinary shares or such other securities.

(f) The Company's capitalization table attached hereto as Schedule 1 is true and complete, in all material respects, as of the Issue Date.

3.2 Notice of Certain Events. If the Company proposes at any time to:

(a) declare, pay or make any dividend, distribution or bonus issue upon the issued shares of the Class or its ordinary shares, whether in cash, property, stock, or other securities and whether or not a regular cash dividend;

(b) offer for subscription or sale pro rata to the holders of the issued shares of the Class any additional shares of any class or series of the Company's share capital (other than pursuant to contractual pre-emptive rights);

(c) effect any reclassification, exchange, combination, substitution, reorganization or recapitalization of the issued shares of the Class; or

(d) effect an Acquisition or to liquidate, dissolve or wind up;

then, in connection with each such event, the Company shall give Holder:

(1) at least seven (7) Business Days prior written notice of the date on which a record will be taken for such dividend, distribution, or subscription rights (and specifying the date on which the holders of outstanding shares of the Class will be entitled thereto) or for determining rights to vote, if any, in respect of the matters referred to in (a) and (b) above; and

(2) in the case of the matters referred to in (c) and (d) above at least seven (7) Business Days prior written notice of the date when the same will take place (and specifying the date on which the holders of outstanding shares of the Class will be entitled to exchange their shares for the securities or other property deliverable upon the occurrence of such event).

Reference is made to Section 1.6(c) whereby this Warrant will be deemed to be exercised pursuant to Section 1.2(b) hereof if the Company does not give written notice to Holder of a Cash/Public Acquisition as required by the terms hereof. Company will also provide information requested by Holder that is reasonably necessary to enable Holder to comply with Holder's accounting or reporting requirements.

SECTION 4. REPRESENTATIONS, WARRANTIES OF THE HOLDER.

The Holder represents and warrants to the Company as follows:

4.1 Acting for Own Account. This Warrant and the securities to be acquired upon exercise of this Warrant by Holder are being acquired for investment for Holder's account, not as a nominee or agent, and not with a view to the public resale or distribution within the meaning of the Act. Holder also represents that it has not been formed for the specific purpose of acquiring this Warrant or the Shares.

4.2 Disclosure of Information. Holder is aware of the Company's business affairs and financial condition and has received or has had full access to all the information it considers necessary or appropriate to make an informed investment decision with respect to the acquisition of this Warrant and its underlying securities. Holder further has had an opportunity to ask questions and receive answers from the Company regarding the terms and conditions of the offering of this Warrant and its underlying securities and to obtain additional information (to the extent the Company possessed such information or could acquire it without unreasonable effort or expense) necessary to verify any information furnished to Holder or to which Holder has access.

4.3 Investment Experience. Holder understands that the purchase of this Warrant and its underlying securities involves substantial risk. Holder has experience as an investor in securities of companies in the development stage and acknowledges that Holder can bear the economic risk of such Holder's investment in this Warrant and its underlying securities and has such knowledge and experience in financial or business matters that Holder is capable of evaluating the merits and risks of its investment in this Warrant and its underlying securities and/or has a preexisting personal or business relationship with the Company and certain of its officers, directors or controlling persons of a nature and duration that enables Holder to be aware of the character, business acumen and financial circumstances of such persons.

4.4 Accredited Investor Status. Holder is an "accredited investor" within the meaning of Regulation D promulgated under the Act.

4.5 The Act. Holder understands that this Warrant and the Shares issuable upon exercise hereof have not been registered under the Act in reliance upon a specific exemption therefrom, which exemption depends upon, among other things, the bona fide nature of the Holder's investment intent as expressed herein. Holder understands that this Warrant and the Shares issued upon any exercise hereof must be held indefinitely unless subsequently registered under the Act and qualified under applicable state securities laws, or unless exemption from such registration and qualification are otherwise available. Holder is aware of the provisions of Rule 144 promulgated under the Act.

4.6 No Voting Rights. Holder, as a Holder of this Warrant, will not have any voting rights until the exercise of this Warrant.

SECTION 5. MISCELLANEOUS.

5.1 Term; Automatic Exercise Upon Expiration.

(a) Term. Subject to the provisions of Section 1.6 above, this Warrant is exercisable in whole or in part at any time and from time to time on or before 6:00 PM, Eastern time, on the Expiration Date and shall be void thereafter.

(b) Automatic Exercise upon Expiration. In the event that, upon the Expiration Date, the fair market value of one Share (or other security issuable upon the exercise hereof) as determined in accordance with Section 1.3 above is greater than the Warrant Price in effect on such date, then this Warrant shall automatically be deemed on and as of such date to be exercised pursuant to Section 1.2(b) above as to all Shares (or such other securities) for which it shall not previously have been exercised, and, subject to receipt by the Company of the Subscription Price in respect of the Shares issuable pursuant to such exercise in accordance with Section 1.1, the Company shall, within a reasonable time deliver a certificate representing the Shares (or such other securities) issued upon such exercise to Holder.

5 . 2 Legends. Each certificate evidencing Shares (and each certificate evidencing the securities issued upon conversion of any Shares, if any) shall be imprinted with a legend in substantially the following form:

> THE SHARES EVIDENCED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "**ACT**"), OR THE SECURITIES LAWS OF ANY STATE AND, EXCEPT AS SET FORTH IN THAT CERTAIN WARRANT TO PURCHASE STOCK ISSUED BY THE ISSUER TO _____ DATED DECEMBER 28, 2016, MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED UNLESS AND UNTIL REGISTERED UNDER SAID ACT AND LAWS OR, IN THE OPINION OF LEGAL COUNSEL IN FORM AND SUBSTANCE SATISFACTORY TO THE ISSUER, SUCH OFFER, SALE, PLEDGE OR OTHER TRANSFER IS EXEMPT FROM SUCH REGISTRATION.

5 . 3 Compliance with Securities Laws on Transfer. This Warrant and the Shares issued upon exercise of this Warrant (and the securities issuable, directly or indirectly, upon conversion of the Shares, if any) may not be transferred or assigned in whole or in part except in compliance with applicable federal and state securities laws by the transferor and the transferee (including, without limitation, the delivery of investment representation letters and legal opinions reasonably satisfactory to the Company, as reasonably requested by the Company). The Company shall not require Holder to provide an opinion of counsel if the transfer is to an affiliate of Holder, provided that any such transferee is an "accredited investor" as defined in Regulation D promulgated under the Act. Additionally, the Company shall also not require an opinion of counsel if there is no material question as to the availability of Rule 144 promulgated under the Act.

5.4 Transfer Procedure. After receipt by Holder of the executed Warrant, Holder may transfer all or part of this Warrant to one or more of Holder's affiliates (each, a "**Holder Affiliate**"), by execution of an Assignment substantially in the form of Appendix 2. Subject to the provisions of Section 5.3 and upon providing the Company with written notice, Holder, any such Holder Affiliate and any subsequent Holder, may transfer all or part of this Warrant or the Shares issuable upon exercise of this Warrant (or the Shares issuable directly or indirectly, upon conversion of the Shares, if any) to any other transferee, provided, however, in connection with any such transfer, the Holder Affiliate(s) or any subsequent Holder will give the Company notice of the portion of the Warrant being transferred with the name, address and taxpayer identification number of the transferee and Holder will surrender this Warrant to the Company for reissuance to the transferee(s) (and Holder if applicable).

5.5 Warrant Register. The Company will maintain a register in respect of this Warrant on which shall be entered the name(a) and addresse(s) of the Holders and the particulars of this Warrant held by them and of all cancellations and transfers (in accordance with Section 5.4 above) and exercise of this Warrant.

5.6 Notices. All notices and other communications hereunder from the Company to the Holder, or vice versa, shall be deemed delivered and effective (i) when given personally, (ii) on the third (3rd) Business Day after being mailed by first-class registered or certified mail, postage prepaid, (iii) upon actual receipt if given by facsimile or electronic mail and such receipt is confirmed in writing by the recipient, or (iv) on the first Business Day following delivery to a reliable overnight courier service, courier fee prepaid, in any case at such address as may have been furnished to the Company or Holder, as the case may be, in writing by the Company or such Holder from time to time in accordance with the provisions of this Section 5.6. All notices to Holder shall be addressed as follows until the Company receives notice of a change of address in connection with a transfer or otherwise:

_____
_____
_____
_____
Attn:
Telephone:
Facsimile:
Email:

Notice to the Company shall be addressed as follows until Holder receives notice of a change in address

STRONGBRIDGE BIOPHARMA PUBLIC LIMITED COMPANY
900 Northbrook Drive
Suite 200
Trevose, Pennsylvania 19053
Attn: Chief Legal Officer
Fax: 215-355-7389
Email: s.long@strongbridgebio.com

With a copy (which shall not constitute notice) to:

Reed Smith LLP
599 Lexington Avenue
New York, New York 10022
Attn: Lee Ann Dillon
Fax: 212-521-5450
Email: ldillon@reedsmith.com

5.7 Waiver. This Warrant and any term hereof may be changed, waived, discharged or terminated (either generally or in a particular instance and either retroactively or prospectively) only by an instrument in writing signed by the party against which enforcement of such change, waiver, discharge or termination is sought.

5.8 Attorneys' Fees. In the event of any dispute between the parties concerning the terms and provisions of this Warrant, the party prevailing in such dispute shall be entitled to collect from the other party all costs incurred in such dispute, including reasonable attorneys' fees.

5.9 Counterparts; Facsimile/Electronic Signatures. This Warrant may be executed in counterparts, all of which together shall constitute one and the same agreement. Any signature page delivered electronically or by facsimile shall be binding to the same extent as an original signature page with regards to any agreement subject to the terms hereof or any amendment thereto.

5.10 Governing Law. This Warrant shall be governed by and construed in accordance with the laws of the State of Delaware, without giving effect to its principles regarding conflicts of law.

5.11 Headings. The headings in this Warrant are for purposes of reference only and shall not limit or otherwise affect the meaning of any provision of this Warrant.

5.12 Business Days. "**Business Day**" is any day that is not a Saturday, Sunday or a day on which _____ is closed.

5.13 Rights as Shareholders; Information. No holder of this Warrant, as such, shall be entitled to vote or receive dividends or be deemed the holder of Ordinary shares which may at any time be issuable upon the exercise hereof for any purpose, nor shall anything contained herein be construed to confer upon the holder of this Warrant, as such, any of the rights of a shareholder of the Company or any right to vote for the election of directors or upon any matter submitted to shareholders at any meeting thereof, or to receive notice of meetings, or to receive dividends or subscription rights or otherwise until this Warrant shall have been exercised and the Shares purchasable upon the exercise hereof shall have become deliverable, as provided herein. Notwithstanding the foregoing, the Company will transmit to the holder of this Warrant such information, documents and reports as are generally distributed to the holders of any class or series of the securities of the Company concurrently with the distribution thereof to the shareholders.

5.14 Binding Effect on Successors. This Warrant shall be binding upon any corporation succeeding the Company by merger, consolidation or acquisition of all or substantially all of the Company's assets, and all of the obligations of the Company relating to the Shares issuable upon the exercise or conversion of this Warrant shall survive the exercise, conversion and termination of this Warrant and all of the covenants and agreements of the Company shall inure to the benefit of the successors and assigns of the holder hereof.

5.15 Registration Rights. The Shares issuable hereunder initially shall be exempt from registration under the Act. Following the Date of Grant, and in any case within ninety (90) days thereof, Company shall promptly prepare, file and use its reasonable efforts to cause to become effective as soon as practicable thereafter, a registration statement on Form F-3 or such other form as may be appropriate to be filed with the SEC by Company under the Act (together with any amendments or supplements thereto, whether prior to or after the effective date thereof, the "**Registration Statement**") covering the public resale in the United States of the Shares to be issued pursuant to this Warrant, and Company shall use its reasonable efforts to keep the Registration Statement continuously effective during the Term. Any such registration shall be subject to the customary terms and conditions used in connection with resale prospectuses. Company's obligations under this Section are contingent upon Holder providing promptly all information concerning such Holder and its proposed plan of distribution as Company may reasonably request in connection with any of the foregoing.

[Remainder of page left blank intentionally]

[Signature page follows]

IN WITNESS WHEREOF, the parties have caused this Warrant to Subscribe for Shares to be executed by their duly authorized representatives effective as of the Issue Date written above.

"Company"

STRONGBRIDGE BIOPHARMA PUBLIC LIMITED COMPANY

By: _____

Name: Stephen Long

Title: Chief Legal Officer

IN WITNESS WHEREOF, the parties have caused this Warrant to Subscribe for Shares to be executed by their duly authorized representatives effective as of the Issue Date written above.

"COMPANY"

STRONGBRIDGE BIOPHARMA PLC

By: _____

Name: _____
(Print)

Title: _____

"HOLDER"

_____

By: _____

Name: _____
(Print)

Title: _____

APPENDIX 1

NOTICE OF EXERCISE

1. The undersigned Holder hereby exercises its right to subscribe for _____ ordinary shares in the capital of Strongbridge Biopharma plc (the "**Company**") in accordance with the attached Warrant To Subscribe for Shares, and tenders payment of the aggregate Warrant Price for such shares as follows:

[ ] check in the amount of $_____ payable to order of the Company enclosed herewith

[ ] Wire transfer of immediately available funds to the Company's account

[ ] Net issuance exercise pursuant to Section 1.2(b) of the Warrant

[ ] Other [Describe] _____

2. [Please issue a certificate or certificates representing the Shares in the name specified below:]

_____
Holder's Name

_____

_____
(Address)

3. By its execution below and for the benefit of the Company, Holder hereby restates each of the representations and warranties in Section 4 of the Warrant to Subscribe for Shares as of the date hereof.

HOLDER:

_____

By:_____

Name:_____

Title:_____

Date:_____

APPENDIX 2

ASSIGNMENT

For value received, _____ hereby sells, assigns and transfers unto

Name: [_____ TRANSFEREE]

Address: _____

Tax ID: _____]

that certain Warrant to Subscribe for Shares issued by Strongbridge Biopharma plc (the "**Company**"), on [DATE] (the "**Warrant**") together with all rights, title and interest therein.

[_____]

By:_____

Name:_____

Title:_____

Date:_____

By its execution below, and for the benefit of the Company, [TRANSFEREE] makes each of the representations and warranties set forth in Article 4 of the Warrant and agrees to all other provisions of the Warrant as of the date hereof.

[TRANSFEREE]

By:_____

Name:_____

Title:_____]

SCHEDULE 1

Company Capitalization Table

21,205,382 Ordinary shares were issued and outstanding as of March 10, 2016.

Exhibit 10.21

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 1,000,000 (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.

Exhibit10.9

AMENDED AND RESTATED EMPLOYMENT AGREEMENT

THIS AMENDED AND RESTATED EMPLOYMENT AGREEMENT (the "Agreement") is made by and between Strongbridge U.S. Inc. (the "Company"), and Fredric J. Cohen ("Executive") as of November 23, 2016.

W I T N E S S E T H:

WHEREAS, Cortendo AB, an affiliate of the Company, and Executive entered into an original employment agreement dated August 5, 2015 (the "Effective Date"), which agreement was subsequently assigned to the Company (such agreement, the "Prior Agreement");

WHEREAS, the Company desires to continue to retain the services of Executive as set forth in this Agreement, and Executive desires to serve the Company in such capacity, subject to the terms and conditions of this Agreement; and

WHEREAS, the Company and Executive intend for this Agreement to replace the Prior Agreement except as otherwise set forth herein.

NOW, THEREFORE, for and in consideration of the mutual promises, covenants and obligations contained herein, Company and Executive agree as follows:

ARTICLE I

EMPLOYMENT AND DUTIES

Section 1.01 Employment and Term. Executive shall be employed by the Company for the period commencing on the Effective Date and expiring on the second anniversary of the Effective Date, unless sooner terminated as set forth in this Agreement (the "Term"); provided, however, that the Term shall thereafter be automatically extended for additional one-year periods unless, at least ninety (90) days prior to expiration of the Term, either (a) the Company gives notice to Executive not to extend the Term or (b) Executive gives notice to the Company not to extend the Term.

Section 1.02 Position and Duties. Executive shall serve as the Chief Medical Officer of the Company, or in such other positions as the parties may agree. Executive shall have the duties and responsibilities customarily associated with such position and will perform such other duties as reasonably directed by the Chief Executive Officer of the Company (the "CEO") consistent with such position(s).

Section 1.03 Scope. Executive will devote substantially all of his business time, attention, skills and efforts to the performance of his duties. Executive acknowledges that his

duties and responsibilities require Executive's full-time business efforts and agrees to not engage in any other business activity or interests which materially interfere or conflict with the performance of Executive's duties. Notwithstanding the foregoing, Executive may (a) serve on corporate, civic or charitable boards or committees of entities that do not compete with the Company, with the approval of the CEO, (b) deliver a reasonable number of lectures or fulfill speaking engagements, with the approval of the CEO, or (c) manage personal investments, so long as such activities do not significantly interfere with the performance of Executive's duties.

ARTICLE II

COMPENSATION AND BENEFITS

Section 2.01 **Base Salary**. During the Term, the Company will pay Executive a base salary (the "Base Salary") at an initial rate of $380,000 per year in accordance with the Company's standard payroll practices. The Base Salary will be reviewed at least annually by the Board of Directors of the Company (the "Board") or a committee thereof and may be adjusted (in which case such adjusted amount shall be the "Base Salary").

Section 2.02 **Annual Incentive**. During Executive's employment with the Company, and as determined by the Board in its sole discretion, Executive shall be eligible for an annual cash incentive (the "Annual Incentive") with a target of 40% of the Base Salary (such percentage, the "Target Annual Incentive"). The Annual Incentive shall be based on the achievement of predetermined performance goals as determined annually by the CEO and the Board. The actual Annual Incentive earned in any particular year may be greater or lower than the Target Annual Incentive, depending on the level of achievement of the applicable performance goals and the discretion of the Board. The Annual Incentive shall be paid to Executive as soon as practicable, but in no event later than the date that is two-and-one-half months following the end of the taxable year (of Executive, or the Company, whichever is later) in which such incentive is earned.

Section 2.03 **Long Term Incentive Plans.** Executive shall be eligible to receive grants under the Company's long term incentive plans (including stock option, restricted stock and other equity compensation plans and any other long-term incentive plans) at the discretion of the CEO and the Board.

Section 2.04 **Business and Entertainment Expenses**. Subject to the Company's standard policies and procedures for expense reimbursement as applied to its executive employees generally, the Company shall reimburse Executive for, or pay on behalf of Executive, reasonable out-of-pocket business expenses incurred by Executive on behalf of the Company.

Section 2.05 **Other Company Benefits**. Executive shall be entitled to participate in all employee benefit plans, practices and programs maintained by the Company and made available to its similarly situated executives, including the Company's paid time-off policy. Executive shall also be entitled to paid time-off for all holidays in the U.S. in accordance with the applicable Company policy.

ARTICLE III

TERMINATION

Section 3.01 General. The Company may terminate Executive's employment for any reason or no reason, and Executive may terminate his employment for any reason or no reason, in either case subject only to the terms of this Agreement. For purposes of this Agreement, the following terms have the following meanings:

(a) "Accrued Obligations" shall mean: (i) Executive's earned but unpaid Base Salary through the Termination Date; (ii) payment of any annual, long-term, or other incentive award which relates to a completed fiscal year or performance period, as applicable, and is payable (but not yet paid) on or before the Termination Date; (iii) a lump-sum payment in respect of accrued but unused vacation days at Executive's per-business-day Base Salary rate in effect as of the Termination Date; and (iv) any unpaid expense or other reimbursements due pursuant to Section 2.04 hereof.

(b) "Cause" shall mean (i) Executive's conviction of, or plea of guilty or nolo contendere to, any felony or any crime involving theft, embezzlement, dishonesty or moral turpitude; (ii) any act by Executive constituting willful misconduct, deliberate malfeasance, dishonesty, unethical conduct or gross negligence in the performance of his duties; (iii) Executive's willful and continued failure to perform any of the duties of his position (which has not been cured within thirty (30) days following the first written notice from the Company describing such failure in reasonable detail); or (iv) any material breach (which has not been cured within thirty (30) days following the first written notice from the Company describing such breach in reasonable detail) by Executive of this Agreement or any other agreement between Executive and the Company or any of its affiliates.

(c) "Change in Control" shall mean the occurrence of any of the following:

(i) 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 (a "Majority of the 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 in Control;

(ii) the stockholders of the Company approve a plan of complete liquidation of the Company;

(iii) the sale or disposition of all or substantially all of the Company's assets;

(iv) 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.

(v) Notwithstanding the foregoing, the following acquisitions shall not constitute a Change in 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.

(d) "Disability" shall mean Executive's becoming incapacitated for a period of at least one hundred eighty (180) days by accident, sickness or other circumstance that renders Executive mentally or physically incapable of performing the material duties and services required of Executive hereunder on a full-time basis during such period. A termination of Executive's employment due to a Disability shall be effective only if the party terminating Executive's employment first gives at least fifteen (15) days' written notice of such termination to the other party.

(e) "Good Reason" shall mean, without Executive's express written consent, the occurrence of any one or more of the following: (i) a material diminution by the Company of Executive's Base Salary, other than any diminution that is also applicable in a substantially similar manner and proportion to the other senior executives of the Company; (ii) the assignment to Executive of duties or responsibilities which are materially inconsistent with Executive's position; (iii) a change in the principal location at which Executive performs his duties for the Company to a new location that is more than fifty (50) miles from the prior location; or (iv) an action or inaction that constitutes a material breach of this Agreement by the Company.

A termination of employment by Executive for Good Reason shall be effectuated by giving the Company written notice ("Notice of Termination for Good Reason"), not later than thirty (30) days following the occurrence of the circumstance that constitutes Good Reason, setting forth in reasonable detail the specific conduct of the Company that constitutes Good Reason and the specific provision(s) of this Agreement on which Executive relied. The Company shall be entitled, during the forty-five (45) day period following receipt of a Notice of Termination for Good Reason, to cure the circumstances that gave rise to Good Reason, provided that the Company shall be entitled to waive its right to cure or reduce the cure period by delivery of written notice to that effect to Executive (such forty-five (45) day or shorter period, the "Cure Period"). If, during the Cure Period, such circumstance is remedied, Executive will not be permitted to terminate employment for Good Reason as a result of such circumstance. If, at the end of the Cure Period, the circumstance that constitutes Good Reason has not been remedied, Executive will be entitled to terminate employment for Good Reason during the thirty (30) day period that follows the end of the Cure Period. If Executive does not terminate employment during such thirty (30) day period, Executive will not be permitted to terminate employment for Good Reason as a result of such event.

(f) "Pro-Rata Annual Incentive" shall mean an amount equal to (i) the Annual Incentive that Executive would have been entitled to receive for the calendar year that includes the Termination Date if his employment hereunder had continued (as determined by the Board based upon the actual achievement of the applicable performance goals), multiplied by (ii) a fraction, the

numerator of which is the number of days he was employed hereunder during such year and the denominator of which is the number of days in such year.

(g) "Termination Date" shall mean the date on which Executive's employment hereunder terminates (which, in the case of a notice of non-renewal of the Term in accordance with Article I hereof, shall mean the date on which the Term expires, provided that Executive's employment is terminated on such date due to the non-renewal of the Term).

Section 3.02 Termination Without Cause or by Executive With Good Reason. If the Company terminates Executive's employment without Cause, or Executive terminates for Good Reason, the Term shall expire on the Termination Date and Executive shall be entitled to: (a) the Accrued Obligations; (b) an amount equal to the sum of (i) twelve (12) months of the annual Base Salary as in effect immediately prior to the Termination Date and (ii) the Target Annual Incentive, paid in equal installments on the normal payroll cycle over the twelve (12) month period that begins on the sixtieth (60^{th}) day following the Termination Date; (c) the Pro-Rata Annual Incentive, payable in a cash lump sum to Executive on the date Company pays its annual incentive compensation bonuses for the year that includes the Termination Date if Executive's employment continued; and (d) medical, dental benefits provided by the Company to Executive and Executive's spouse and dependents (in each case, as provided in any applicable plan) at least equal to the levels of benefits provided to other similarly situated active employees of the Company and its subsidiaries until the earlier of (i) the one-year anniversary of the Termination Date or (ii) the date that Executive becomes covered under a subsequent employer's medical and dental plans.

Section 3.03 Termination Due to Non-Renewal of the Term by the Company. If Executive's employment is terminated due to the non-renewal of the Term by the Company pursuant to Section 1.01, Executive shall be entitled to: (a) the Accrued Obligations; (b) an amount equal to the sum of (i) six (6) months of the annual Base Salary as in effect immediately prior to the Termination Date and (ii) one-half of the Target Annual Incentive, paid in equal installments on the normal payroll cycle over the six (6) month period that begins on the sixtieth (60^{th}) day following the Termination Date; (c) the Pro-Rata Annual Incentive, payable in a cash lump sum to Executive on the date Company pays its annual incentive compensation bonuses for the year that includes the Termination Date if Executive's employment had continued; and (d) medical, dental benefits provided by the Company to Executive and Executive's spouse and dependents (in each case, as provided in any applicable plan) at least equal to the levels of benefits provided to other similarly situated active employees of the Company and its subsidiaries until the earlier of (i) the six-month anniversary of the Termination Date or (ii) the date that Executive becomes covered under a subsequent employer's medical and dental plans.

Section 3.04 Termination Without Cause, by Executive With Good Reason, or Due to Non-Renewal of the Term by the Company following a Change in Control of the Company. If the Company terminates Executive's employment without Cause, Executive terminates for Good Reason, or Executive's employment is terminated due to the non-renewal of the Term by the Company pursuant to Section 1.01, in any case, within twenty four (24) months following the occurrence of Change in Control, the Term shall expire on the Termination Date and, in lieu of the benefits set forth in Section 3.02 or 3.03, Executive shall be entitled to: (a) the Accrued Obligations; (b) an amount equal to the sum of (i) eighteen (18) months of the annual Base Salary as in effect immediately prior to the Termination Date and (ii) the Target Annual

Incentive, paid in equal installments on the normal payroll cycle over the eighteen (18) month period that begins on the sixtieth (60^{th}) day following the Termination Date; (c) the Pro-Rata Annual Incentive, payable in a cash lump sum to Executive on the date Company pays its annual incentive compensation bonuses for the year that includes the Termination Date if Executive's employment continued; (d) medical, dental benefits provided by the Company to Executive and Executive's spouse and dependents (in each case, as provided in any applicable plan) at least equal to the levels of benefits provided to other similarly situated active employees of the Company and its subsidiaries until the earlier of (i) the one-year anniversary of the Termination Date or (ii) the date that Executive becomes covered under a subsequent employer's medical and dental plans; and (e) the acceleration of vesting of all unvested equity or equity-based awards held by Executive as of the Termination Date.

Section 3.05 Other Terminations. If Executive's employment hereunder is terminated (a) by Executive without Good Reason; (b) by the Company for Cause; (c) due to non-renewal of the Term by Executive; or (d) due to Executive's death or Executive's Disability, the Term shall expire as of the Termination Date and Executive and/or Executive's estate or beneficiaries shall be entitled to the Accrued Obligations.

Section 3.06 Release. Executive's entitlement to the payments (other than the Accrued Obligations) and benefits described in this Article III is expressly contingent upon Executive providing the Company with a signed release that is attached hereto as **Attachment A** (the "Release"). To be effective, such Release must be delivered by Executive to the Company no later than forty-five (45) days following the Termination Date and must not be revoked during the seven (7) days following such delivery. If such Release is not executed in a timely manner or is revoked, all such payments and benefits shall immediately cease and Executive shall be required to repay to the Company any such payments that have already been paid to Executive.

ARTICLE IV

RESTRICTIVE COVENANTS

Section 4.01 Confidentiality.

(a) Company Information. Executive agrees at all times during the Term of this Agreement and thereafter, to hold in strictest confidence, and not to use, except in connection with the performance of Executive's duties, and not to disclose to any person or entity without written authorization of the Company, any Confidential Information of the Company. As used herein, "Confidential Information" means any Company proprietary or confidential information, technical data, trade secrets or know-how, including, but not limited to, research, product plans, products, services, customer lists and customers, markets, software, developments, inventions, processes, formulas, technology, designs, drawings, engineering, marketing, distribution and sales methods and systems, sales and profit figures, finances and other business information disclosed to Executive by the Company, either directly or indirectly in writing, orally or by drawings or inspection of documents or other tangible property. However, Confidential Information does not include any of the foregoing items which has become publicly known and made generally available through no wrongful act of Executive.

(b) Executive-Restricted Information. Executive agrees that during the Term of this Agreement Executive will not improperly use or disclose any proprietary or confidential information or trade secrets of any person or entity with whom Executive has an agreement or duty to keep such information or secrets confidential.

(c) Third Party Information. Executive recognizes that the Company has received and in the future will receive from third parties their confidential or proprietary information subject to a duty on the Company's part to maintain the confidentiality of such information and to use it only for certain limited purposes. Executive agrees at all times during the Term of this Agreement and thereafter, to hold in strictest confidence, and not to use, except in connection with the performance of Executive's duties, and not to disclose to any person or entity, or to use it except as necessary in performing Executive's duties, consistent with the Company's agreement with such third party.

Section 4.02 Non-Competition.

(a) Executive acknowledges that, during the Term, Executive has had access to information concerning the Company's critical business strategies, engineering and technology development plans, competitive analyses, organizational structure. Accordingly, in consideration of the compensation provided under this Agreement, Executive agrees that during the Term and for the one (1) year period thereafter, Executive will not directly or indirectly, own, manage, operate, control (including indirectly through a debt or equity investment), provide services to, or be employed by, any person or entity engaged in any business that is (i) located in or provides services or products to a region in which the Company does business, and (ii) competitive with the business activities of the Company as they existed during the period that Executive provided services to the Company.

(b) Executive acknowledges that the restrictions contained under this Section 4.02 are reasonable and necessary to protect the legitimate interests of the Company, that the Company would not have executed this Agreement in the absence of such restrictions, and that any violation of any provision of this paragraph will result in irreparable injury to the Company. In the event the provisions under this Section 4.02 shall ever be deemed to exceed the time, scope or geographic limitations permitted by applicable laws, then such provisions shall be reformed to the maximum time, scope or geographic limitations, as the case may be, permitted by applicable laws.

Section 4.03 Injunctive Relief. Executive agrees that it is impossible to measure in money the damages which will accrue to the Company by reason of a failure by Executive to perform any of Executive's obligations under this Article IV. Accordingly, if Company or any of its affiliates institutes any action or proceeding to enforce its rights under this Article IV, to the extent permitted by applicable law, Executive hereby waives the claim or defense that the Company or its affiliates has an adequate remedy at law, and Executive shall not claim that any such remedy at law exists.

ARTICLE V

MISCELLANEOUS

Section 5.01 Withholding. The Company shall withhold all applicable federal, state and local taxes, social security and workers' compensation contributions and other amounts as may be required by law with respect to compensation payable to Executive.

Section 5.02 Modification of Payments.

(a) In the event it shall be determined that any payment, right or distribution by the Company or any other person or entity to or for the benefit of Executive pursuant to the terms of this Agreement or otherwise, in connection with, or arising out of, his employment with the Company or a change in ownership or effective control of the Company or a substantial portion of its assets (a "Payment") is a "parachute payment" within the meaning of Section 280G of the Internal Revenue Code of 1986, as amended (the "Code") on account of the aggregate value of the Payments due to Executive being equal to or greater than three times the "base amount," as defined in Section 280G(b)(3) of the Code, (the "Parachute Threshold") so that Executive would be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax") and the net after-tax benefit that Executive would receive by reducing the Payments to the Parachute Threshold is greater than the net after-tax benefit Executive would receive if the full amount of the Payments were paid to Executive, then the Payments payable to Executive shall be reduced (but not below zero) so that the Payments due to Executive do not exceed the amount of the Parachute Threshold, reducing first any Payments under Section 3.02(b) hereof.

(b) The Company hereby agrees that, for purposes of determining whether any payment and benefits set forth in Section 3.04 above would be subject to the Excise Tax, the non-compete set forth in in Section 4.02 above shall be treated as an agreement for the performance of personal services. The Company hereby agrees to indemnify, defend, and hold harmless Executive from and against any adverse impact, tax, penalty, or excise tax resulting from the Company or accountant's attribution of a value to the non-compete set forth in in Section 4.02 above that is less than the total compensation amount that would be disclosed under Item 402(c) of Securities and Exchange Commission Regulation S-K if Executive had been a "named executive officer" of the Company in the year prior to year of the event that triggers the Excise Tax, to the extent the use of such lesser amount results in a larger Excise Tax than Executive would have been subject to had the Company or accountant attributed a value to the non-compete set forth in in Section 4.02 above that is at least equal to the total compensation amount disclosed under Item 402(c) of Securities and Exchange Commission Regulation S-K for such year.

Section 5.03 Section 409A.

(a) Notwithstanding anything herein to the contrary, this Agreement is intended to be interpreted and applied so that the payment of the benefits set forth herein either shall either be exempt from the requirements of Section 409A of the Code ("Section 409A") or shall comply with the requirements of such provision.

(b) Notwithstanding any provision of this Agreement to the contrary, if Executive is a "specified employee" within the meaning of Section 409A, any payments or arrangements due upon a termination of Executive's employment under any arrangement that constitutes a "nonqualified deferral of compensation" within the meaning of Section 409A and which do not otherwise qualify under the exemptions under Treas. Regs. Section 1.409A-1 (including without limitation, the short-term deferral exemption or the permitted payments under Treas. Regs. Section 1.409A-1(b)(9)(iii)(A)), shall be delayed and paid or provided, without interest, on the earlier of (i) the date which is six (6) months after Executive's "separation from service" (as such term is defined in Section 409A and the regulations and other published guidance thereunder) for any reason other than death, and (ii) the date of Executive's death.

(c) After any Termination Date, Executive shall have no duties or responsibilities that are inconsistent with having a "separation from service" within the meaning of Section 409A and, notwithstanding anything in the Agreement to the contrary, distributions upon termination of employment of nonqualified deferred compensation may only be made upon a "separation from service" as determined under Section 409A and such date shall be the Termination Date for purposes of this Agreement. Each payment under this Agreement or otherwise shall be treated as a separate payment for purposes of Section 409A. In no event may Executive, directly or indirectly, designate the calendar year of any payment to be made under this Agreement which constitutes a "nonqualified deferral of compensation" within the meaning of Section 409A and to the extent an amount is payable within a time period, the time during which such amount is paid shall be in the discretion of the Company.

Section 5.04 **Merger Clause**. Effective as of the date hereof, this Agreement contains the complete, full, and exclusive understanding of Executive and the Company as to its subject matter and shall, on such date, and supersede any prior employment agreement between Executive and the Company (and its affiliates), including the Prior Agreement. Any amendments to this Agreement shall be effective and binding on Executive and the Company only if any such amendments are in writing and signed by both Parties.

Section 5.05 **Assignment**.

(a) This Agreement is personal to Executive and, without the prior written consent of the Company, shall not be assigned by Executive otherwise than by will or the laws of descent and distribution, and any assignment in violation of this Agreement shall be void.

(b) Notwithstanding the foregoing Section 5.05(a), this Agreement and all rights of Executive hereunder shall inure to the benefit of, and be enforceable by, Executive's personal or legal representatives, executors, administrators, successors, heirs, distributees, devisees and legatees. If Executive should die while any amounts would still be payable to him or her hereunder if he or she had continued to live, all such amounts, unless otherwise provided herein, shall be paid in accordance with the terms of this Agreement to Executive's devisee, legatee or other designee or, should there be no such designee, to Executive's estate.

(c) The Company may assign this Agreement to any affiliate or subsidiary of the Company without the consent of Executive and shall require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business

or assets of the Company (a "Successor") to assume and agree to perform this Agreement in the same manner and to the same extent that the Company would have been required to perform it if no such succession had taken place. As used in this Agreement, (i) the term "Company" shall mean the Company as hereinbefore defined and any Successor and any permitted assignee to which this Agreement is assigned and (ii) the term "Board" shall mean the Board as hereinbefore defined and the board of directors or equivalent governing body of any Successor and any permitted assignee to which this Agreement is assigned.

Section 5.06 Dispute Resolution. Except for any proceeding brought pursuant to Section 5.05 above, the parties agree that any dispute arising out of or relating to this Agreement or the formation, breach, termination or validity thereof, will be settled by binding arbitration by a panel of three arbitrators in accordance with the commercial arbitration rules of the American Arbitration Association. The arbitration proceedings will be located in Philadelphia, Pennsylvania. The arbitrators are not empowered to award damages in excess of compensatory damages and each party irrevocably waives any damages in excess of compensatory damages. Judgment upon any arbitration award may be entered into any court having jurisdiction thereof and the parties consent to the jurisdiction of any court of competent jurisdiction located in the Eastern District of Pennsylvania.

Section 5.07 GOVERNING LAW. THIS AGREEMENT SHALL BE DEEMED TO BE MADE IN THE COMMONWEALTH OF PENNSYLVANIA, INTERPRETATION, CONSTRUCTION AND PERFORMANCE OF THIS AGREEMENT IN ALL RESPECT SHALL BE GOVERNED BY THE LAWS OF THE COMMONWEALTH OF PENNSYLVANIA WITHOUT REGARD TO ITS PRINCIPLES OF CONFLICTS OF LAW.

Section 5.08 Amendment; No Waiver. No provision of this Agreement may be amended, modified, waived or discharged except by a written document signed by Executive and duly authorized officer of the Company. The failure of a party to insist upon strict adherence to any term of this Agreement on any occasion shall not be considered as a waiver of such party's rights or deprive such party of the right thereafter to insist upon strict adherence to that term or any other term of this Agreement. No failure or delay by any party in exercising any right or power hereunder will operate as a waiver thereof, nor will any single or partial exercise of any other right or power. No agreements or representations, oral or otherwise, express or implied, with respect to the subject matter hereof have been made by any party, which are not set forth expressly in this Agreement.

Section 5.09 Severability. If any term or provision of this Agreement is invalid, illegal or incapable of being enforced by any applicable law or public policy, all other conditions and provisions of this Agreement shall nonetheless remain in full force and effect so long as the economic and legal substance of the transactions contemplated by this Agreement is not affected in any manner materially adverse to any party. Upon any such determination that any term or other provision is invalid, illegal or incapable of being enforced, the parties hereto shall negotiate in good faith to modify this Agreement so as to effect the original intent of the parties as closely as possible in a mutually acceptable manner in order that the transactions contemplated hereby be consummated as originally contemplated to the fullest extent possible.

Section 5.10 **Survival**. The rights and obligations of the parties under the provisions of this Agreement that relate to post-termination obligations shall survive and remain binding and enforceable, notwithstanding the expiration of the term of this Agreement, the termination of Executive's employment with the Company for any reason or any settlement of the financial rights and obligations arising from Executive's employment hereunder, to the extent necessary to preserve the intended benefits of such provisions.

Section 5.11 **Notices.** All notices and other communications required or permitted by this Agreement will be made in writing and all such notices and communications will be deemed to have been duly given when delivered or (unless otherwise specified) mailed by United States certified or registered mail, return receipt requested, postage prepaid, addressed, if to the Company, at its principal office, and if to Executive, at Executive's last address on file with the Company. Either party may change such address from time to time by notice to the other**.**

Section 5.12 **Headings and References**. The headings of this Agreement are inserted for convenience only and neither constitute a part of this Agreement nor affect in any way the meaning or interpretation of this Agreement. When a reference in this Agreement is made to a Section, such reference shall be to a Section of this Agreement unless otherwise indicated.

Section 5.13 **Counterparts**. This Agreement may be executed in one or more counterparts (including via facsimile), each of which shall be deemed to be an original, but all of which together shall constitute one and the same instrument.

[signature page follows]

IN WITNESS WHEREOF, this Agreement has been executed by the parties as of the date first written above.

STRONGBRIDGE U.S. INC.

By: /s/ Matthew Pauls
Name: Matthew Pauls
Title: President & CEO

EXECUTIVE

/s/ Fredric J. Cohen
Fredric J. Cohen

ATTACHMENT A

GENERAL RELEASE

1. Fredric J. Cohen ("Executive"), for and in consideration of the commitments of Strongbridge U.S. Inc. (the "Company") as set forth in Article III of the Amended and Restated Employment Agreement dated as of November 23, 2016 (the "Employment Agreement"), and intending to be legally bound, does hereby REMISE, RELEASE AND FOREVER DISCHARGE the Company and its present and former divisions, subsidiaries, parents, predecessor and successor corporations, officers, directors, and their respective successors, predecessors, assigns, heirs, executors, and administrators (collectively, "Releasees") from all causes of action, suits, debts, claims and demands whatsoever in law or in equity, which Executive ever had, now has, or hereafter may have, whether known or unknown, or which Executive's heirs, executors, or administrators may have, by reason of any matter, cause or thing whatsoever, up to the date of Executive's execution of this General Release, particularly, but without limitation of the foregoing general terms, any claims arising from or relating in any way to Executive's employment relationship with the Company and Releasees, the terms and conditions of that relationship, and the termination of that relationship, including, but not limited to, any claims arising under any applicable Company employee benefit plan(s), the Age Discrimination in Employment Act, the Older Workers' Benefit Protection Act, Title VII of The Civil Rights Act of 1964, the Civil Rights Act of 1991, Sections 1981 through 1988 of Title 42 of the United States Code, the Americans with Disabilities Act, the Employee Retirement Income Security Act of 1974, the Family and Medical Leave Act, the Worker Adjustment and Retraining Notification Act, Pennsylvania employment laws, and any other federal, state and local employment laws, as amended, and any other claims under any federal, state or local common law, statutory, or regulatory provision, now or hereafter recognized, and any claims for attorneys' fees and costs. This General Release is effective without regard to the legal nature of the claims raised and without regard to whether any such claims are based upon tort, equity, implied or express contract or discrimination of any sort.

2. To the fullest extent permitted by law, and subject to the provisions of Paragraph 3 below, Executive represents and affirms that (i) Executive has not filed or caused to be filed on Executive's behalf any claim for relief against the Company or any Releasee and, to the best of Executive's knowledge and belief, no outstanding claims for relief have been filed or asserted against the Company or any Releasee on Executive's behalf; and (ii) Executive has no knowledge of any improper, unethical or illegal conduct or activities that Executive has not already reported to any supervisor, manager, department head, human resources representative, agent or other representative of the Company, to any member of the Company's legal or compliance departments, or to the ethics hotline; and (iii) Executive will not file, commence, prosecute or participate in any judicial or arbitral action or proceeding against the Company or any Releasee based upon or arising out of any act, omission, transaction, occurrence, contract, claim or event existing or occurring on or before the date of execution of this General Release.

3. The release of claims described in Paragraph 1 of this General Release does not preclude Executive from filing a charge with the U.S. Equal Employment Opportunity Commission. However, Executive agrees and hereby waives any and all rights to any monetary relief or other personal recovery from any such charge, including costs and attorneys' fees.

4. Subject to the provisions of Paragraph 3 of this General Release, in further consideration of the commitments of the Company as described in the Employment Agreement, Executive agrees that Executive will not file, claim, sue or cause or permit to be filed, any civil action, suit or legal proceeding seeking equitable or monetary relief (including damages, injunctive, declaratory, monetary or other relief) for himself involving any matter released in Paragraph 1. In the event that suit is filed in breach of this release of claims, it is expressly understood and agreed that this release of claims shall constitute a complete defense to any such suit. In the event any Releasee is required to institute litigation to enforce the terms of this paragraph, Releasees shall be entitled to recover reasonable costs and attorneys' fees incurred in such enforcement. Executive further agrees and covenants that should any person, organization, or other entity file, claim, sue, or cause or permit to be filed any civil action, suit or legal proceeding involving any matter occurring at any time in the past, Executive will not seek or accept personal equitable or monetary relief in such civil action, suit or legal proceeding. Nothing in this General Release shall prohibit or restrict Executive from: (i) making any disclosure of information required by law; (ii) providing information to, or testifying or otherwise assisting in any investigation or proceeding brought by any federal regulatory or law enforcement agency or legislative body, any self-regulatory organization, or the Company's designated legal, compliance or human resources officers; or (iii) filing, testifying, participating in or otherwise assisting in a proceeding relating to an alleged violation of any federal, state or municipal law relating to fraud, or any rule or regulation of the Securities and Exchange Commission or any self-regulatory organization.

5. Executive understands and agrees that the payments, benefits and agreements provided in the Employment Agreement are being provided to Executive in consideration for Executive's acceptance and execution of, and in reliance upon Executive's representations in, the Employment Agreement and this General Release, and that they are greater than the payments, benefits and agreements, if any, to which Executive would have received if Executive had not executed the Employment Agreement and this General Release. In addition, Executive acknowledges and agrees that Executive has been paid all amounts owed to Executive as of the date of Executive's signing of this General Release.

6. Executive and the Company agree and acknowledge that the agreement by the Company described in the Employment Agreement, and the settlement and termination of any asserted or unasserted claims against the Releasees, are not and shall not be construed to be an admission of any violation of any federal, state or local statute or regulation, or of any duty owed by any of the Releasees to Executive.

7. This General Release and the obligations of the parties hereunder shall be construed, interpreted and enforced in accordance with and be governed by the laws of Pennsylvania without reference to its conflicts of laws principles.

8. Executive certifies and acknowledges as follows:

a. that Executive has read the terms of this General Release, and that Executive understands its terms and effects, including the fact that Executive has agreed to RELEASE AND FOREVER DISCHARGE the Company and each and every one of its affiliated entities from any legal action arising out of Executive's relationship with the Company and the termination of that relationship;

b. that Executive has signed this Release voluntarily and knowingly in exchange for the consideration described herein and in the Employment Agreement, which Executive acknowledges is adequate and satisfactory to Executive and to which Executive acknowledges that Executive would not otherwise be entitled;

c. that Executive has been and is hereby advised in writing to consult with an attorney prior to signing this General Release;

d. that Executive does not waive rights or claims that may arise after the date this General Release is executed;

e. that the Company has provided Executive with at least 21 (twenty-one) days within which to consider this General Release, that any modifications, material or otherwise, made to this General Release have not restarted or affected in any manner the original 21 (twenty-one) day consideration period, and that Executive has signed on the date indicated below after concluding that this General Release is satisfactory to Executive;

f. that Executive acknowledges that this General Release may be revoked by Executive within seven (7) days after Executive's execution, and it shall not become effective until the expiration of such seven day revocation period. If the last day of the revocation period is a Saturday, Sunday, or legal holiday in the state in which Executive resides, then the revocation period shall not expire until the next following day which is not a Saturday, Sunday, or legal holiday. In the event of a timely revocation by Executive, this General Release and the Employment Agreement will be deemed null and void and the Company will have no obligations hereunder; and

g. that this General Release may not be signed prior to the third calendar day before the last day of the Term of the Employment Agreement. If this General Release is signed prior to the last day of the Term of the Employment Agreement, the Company reserves the right to have Executive ratify the General Release on or after the last day of the Term.

Intending to be legally bound hereby, Executive executed the foregoing General Release on the date indicated below.

Fredric J. Cohen

_____

Signature

Date:_____

Exhibit 12.1

CERTIFICATION

I, Matthew Pauls, certify that:

1. I have reviewed this Annual Report on Form 20-F of Strongbridge Biopharma plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;

4. The Company'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)) for the Company 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 Company, 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) Evaluated the effectiveness of the Company'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

    c) Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and

5. The Company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company'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 Company'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 Company's internal control over financial reporting.

Date: April 4, 2017

/s/ MATTHEW PAULS
Name: Matthew Pauls
Title: Chief Executive Officer (principal executive officer)

Exhibit 12.2

CERTIFICATION

I, A. Brian Davis, certify that:

1. I have reviewed this Annual Report on Form 20-F of Strongbridge Biopharma plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;

4. The Company'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)) for the Company 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 Company, 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) Evaluated the effectiveness of the Company'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

    c) Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and

5. The Company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company'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 Company'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 Company's internal control over financial reporting.

Date: April 4, 2017

/s/ A. BRIAN DAVIS
Name: A. Brian Davis
Title: Chief Financial Officer (principal financial officer and principal accounting officer)

Exhibit 13.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT 2002

In connection with the Annual Report of Strongbridge Biopharma plc (the "Company") on Form 20-F for the period ended December 31, 2016 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), we, Matthew Pauls, Chief Executive Officer (principal executive officer) of the Company, and A. Brian Davis, Chief Financial Officer (principal financial officer and principal accounting officer) of the Company, certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that:

1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: April 4, 2017

By: /s/ MATTHEW PAULS
Matthew Pauls
Chief Executive Officer (principal executive officer)

By: /s/ A. BRIAN DAVIS
A. Brian Davis
Chief Financial Officer (principal financial officer and principal accounting officer)

Exhibit 21.1

Subsidiaries of the Company

BioPancreate Inc.

Cortendo AB (publ)

Cortendo Cayman Ltd.

Strongbridge U.S. Inc.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statements (Form S-8 No. 333-215532 and Form F-3 No. 333-215531) of our report dated April 4, 2017, with respect to the consolidated financial statements of Strongbridge Biopharma plc included in this Annual Report (Form 20-F) for the year ended December 31, 2016.

/s/ Ernst & Young LLP

Philadelphia, Pennsylvania
April 4, 2017

Exhibit 23.2

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form F-3 No. 333-215531) of Strongbridge BioPharma plc; and

(2) Registration Statement (Form S-8 No. 333-215532) pertaining to the Employees' Savings Plan of Strongbridge BioPharma plc.

of our report dated August 17, 2015, with respect to the consolidated financial statements of Strongbridge BioPharma Plc For the year ended December 31, 2014, included in this Annual Report (Form 20-F) of Strongbridge BioPharma plc. for the year ended December 31, 2016.

/s/ Ernst & Young AB

Gothenburg, Sweden

April 4, 2017