UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2016

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

For the transition period from _____ to _____

Commission File No. 001-37627

WAVE LIFE SCIENCES LTD.

(Exact name of registrant as specified in its charter)

Singapore	**Not applicable**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
8 Cross Street #10-00, PWC Building	
Singapore	**048424**
(Address of principal executive offices)	**(Zip code)**

+65 6236 3388

(Registrant's telephone number, including area code)

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

Title of Each Class	**Name of Each Exchange on Which Registered**
$0 Par Value Ordinary Shares	**The NASDAQ Global Market**

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

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

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

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

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

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

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐ (Do not check if a smaller reporting company)	Smaller reporting company	☐

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

The aggregate market value of the registrant's voting and non-voting ordinary shares held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the ordinary shares were last sold as of the last business day of the registrant's most recently completed second fiscal quarter (June 30, 2016) was $221,173,659. The number of outstanding ordinary shares of the registrant as of March 1, 2017 was 23,542,569.

DOCUMENTS INCORPORATED BY REFERENCE

If the Registrant's Definitive Proxy Statement relating to the 2017 Annual General Meeting of Shareholders (the "Proxy Statement") is filed with the Commission within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, then portions of the Proxy Statement will be incorporated by reference into Part III of this Annual Report on Form 10-K. If the Proxy Statement is not filed within such 120-day period, then the Company will file an amendment to this Annual Report within such 120-day period that will contain the information required to be included or incorporated by reference into Part III of this Annual Report.

WAVE LIFE SCIENCES LTD.

ANNUAL REPORT ON FORM 10-K

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Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, the "Exchange Act," that involve substantial risks and uncertainties. In some cases, forward-looking statements are identified by the words "anticipate," "believe," "continue," "could," "estimate," "expect," "future," "goals," "intend," "likely," "may," "might," "ongoing," "objective," "plan," "potential," "predict," "project," "seek," "should," "strategy," "will" and "would" or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report on Form 10-K, such statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain. Forward-looking statements include statements about our ability to fund our working capital requirements; our success, cost and timing of our product development activities and future clinical trials; the timing of and our ability to obtain and maintain regulatory approvals for any of our product candidates; our ability to identify and develop new product candidates; our intellectual property position; our commercialization, marketing and manufacturing capabilities and strategy; our ability to develop sales and marketing capabilities; our estimates regarding future expenses and needs for additional financing; our ability to identify, recruit and retain key personnel; our financial performance; and developments and projections relating to our competitors in the industry. You should refer to the "Risk Factors" section of this Annual Report to Form 10-K and in our other filings with the Securities and Exchange Commission for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure that the forward-looking statements in this Annual Report on Form 10-K will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, these statements should not be regarded as representations or warranties by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

As used in this Annual Report on Form 10-K, unless otherwise stated or the context otherwise indicates, references to "WAVE," the "Company," "we," "our," "us" or similar terms refer to WAVE Life Sciences Ltd. and our wholly owned subsidiaries.

PART I

Item 1. Business

Overview

We are a genetic medicines company with an innovative and proprietary synthetic chemistry drug development platform that we are using to design, develop and commercialize a broad pipeline of first-in-class or best-in-class nucleic acid therapeutic candidates for genetically defined diseases. Nucleic acid therapeutics are a growing and innovative class of drugs that have the potential to address diseases that have historically been difficult to treat with small molecule drugs or biologics. Oligonucleotides are comprised of a sequence of nucleotides that are linked together by a backbone of chemical bonds. We are initially developing oligonucleotides that target genetic defects to either reduce the expression of disease-promoting proteins or transform the production of dysfunctional mutant proteins into the production of functional proteins.

The nucleic acid therapeutics we are developing are stereopure. A stereopure oligonucleotide is comprised of molecules with atoms precisely arranged in three-dimensional orientations at each linkage. We believe controlling the position of the sulfur atom following phosphorothioate ("PS") modification, as described below, will optimize the pharmacological profile of our therapeutics by maximizing therapeutic effect while minimizing the potential for side effects and safety risks. The stereopure therapies we are developing differ from the mixture-based nucleic acid therapeutics currently on the market and in development by others. In nucleic acid therapeutics, the modification of the PS backbone of oligonucleotides is a common alteration, where non-bridging oxygens are replaced with a sulfur atom at each phosphate linkage. Each linkage creates a chiral center that has three-dimensional properties that can either have an "Sp" orientation or an "Rp" orientation. A chiral center is an atom that is bonded to a defined set of pendant groups arranged in a three-dimensional space in a way that is not superimposable on its mirror image. Those chiral configurations are not purposefully designed or controlled, creating mixtures of many thousands of molecules, each having varying three-dimensional atomic arrangements. Such variations may lead to potentially differing pharmacologic properties, with some constituent molecules producing therapeutic effects and others being less beneficial or even contributing to undesirable side effects.

Our preclinical studies have demonstrated that our stereopure nucleic acid therapeutics may achieve superior pharmacologic properties as compared to mixture-based nucleic acid therapeutics. Our platform is designed to enable us to rationally design, optimize and produce stereopure nucleic acid therapeutics, which were previously thought to be too difficult to make and too expensive to manufacture. Through proprietary rational design, we are also able to develop phosphodiester / phosphorothioate ("PO/PS") modified combinations in our nucleic acids, allowing for judicious and specific use of PS modifications, with the ability to reduce the number of PS in a molecule. We believe this ability to selectively employ PS modification where desired may provide further control over pharmacodynamics and may improve the safety of our drugs. Further, our platform has the potential to design therapies that use any of the major molecular mechanisms employed by nucleic acid therapeutics, including antisense, ribonucleic acid interference ("RNAi"), splicing, and exon skipping, as described below.

Our goal is to develop disease-modifying drugs for indications with a high degree of unmet medical need in genetically defined diseases. We are focused on designing single-stranded nucleic acid therapeutics that can distribute broadly within the human body, allowing us to target diseases across multiple organ systems and tissues, through both systemic and local administration. In addition to our current programs in development, we are also leveraging our platform to explore the next generation of stereopure nucleic acid therapeutics that have the potential to selectively target certain cell types. We believe we are well positioned to achieve our goals, because our team is comprised of leaders in the field of nucleic acid therapeutics, including world renowned scientists, leading researchers in the field and executives with a proven track record in drug discovery development and commercialization of innovative therapeutics.

Our Current Programs

Wholly-owned Proprietary Programs				
Tissue	**Disease**	**Target**	**Mechanism of Action**	
CNS	Huntington's disease	HTT SNP-1 (rs362307)	Allele Specific Silencing	Initiating Clinical Trials Mid-2017
CNS	Huntington's disease	HTT SNP-2 (rs362331)	Allele Specific Silencing	Initiating Clinical Trials Mid-2017
Neuromuscular	Duchenne Muscular Dystrophy	Exon 51	Exon Skipping	Initiating Clinical Trials Second Half of 2017
Note: Three additional development candidates are anticipated to be selected by the end of 2017.				
Partnered Programs				
Tissue		**Target**		**Partner**
Hepatic		APOC3		Pfizer
Hepatic		Undisclosed		Pfizer
Hepatic		Undisclosed		Pfizer
Note: Pfizer is entitled to nominate two additional targets by November 2017.				

Our core focus for our wholly-owned proprietary programs is neurology, which we broadly define as genetic diseases within the central nervous system (the "CNS") and neuromuscular system. We expect to initiate six development programs by the end of 2018. These programs include our three most advanced programs, which are in Huntington's disease ("HD"), and Duchenne Muscular Dystrophy ("DMD"), and three additional development candidates which we expect to select by the end of 2017. Further details regarding our programs are set forth below.

- In HD, we have two separate programs, WVE-120101 and WVE-120102, each targeting two disease-associated single nucleotide polymorphisms ("SNPs"), within the *huntingtin* gene: rs362307 ("HTT SNP-1") and rs362331 ("HTT SNP-2"). SNPs are naturally occurring variations within a given genetic sequence and in certain instances can be used to distinguish between two related copies of a gene where only one is responsible for causing production of a defective protein which causes disease. It has been shown that by targeting HTT SNP-1 and HTT SNP-2, the production of disease-causing proteins associated with HD can be reduced. We expect to initiate clinical development of both WVE-120101 and WVE-120102 in mid-2017.
- In DMD, we have developed WVE-210201, which targets exon 51, a region within the ribonucleic acid, ("RNA"), transcribed from the *dystrophin* gene. DMD is a genetic disorder caused by mutations in the *dystrophin* gene that results in dysfunctional dystrophin protein. We expect to initiate clinical development of WVE-210201 in the second half of 2017.
- In May 2016, we entered into a collaboration with Pfizer focused on the advancement of genetically defined targets for the treatment of metabolic diseases, bringing together our proprietary drug development platform, across antisense and single-stranded RNAi modalities, along with GalNAc and Pfizer's hepatic targeting technology for delivery to the liver. The collaboration seeks to leverage our stereochemistry platform across antisense and RNAi modalities and incorporates GalNAc and Pfizer's hepatic targeting technology. Under the terms of the agreement, Pfizer will select, and we will advance, up to five targets from discovery through to the selection of clinical candidates, at which point Pfizer may elect to exclusively license the programs and undertake further development and potential commercialization. Two targets were declared upon initiation of the agreement, including Apolipoprotein C-III. In the third quarter of 2016, Pfizer nominated its third target. Per the terms of the agreement, Pfizer is entitled to nominate the remaining two targets by November 2017.

Our R&D Platform and Proprietary Technology

We believe that our proprietary synthetic chemistry drug development platform is an engine for nucleic acid development and places us in a unique position to deliver drugs to underserved patient populations. We believe that, based on our candidate design and selection process, our platform technology can potentially be applied to treat a significant number of target indications. These targets span multiple therapeutic areas and may be addressed with various modalities best suited for a given indication.

Our novel platform technology enables the development of PO/PS modified nucleic acid therapeutics in which stereochemistry is precisely controlled. This degree of control enables us to both rationally design and synthesize therapeutically optimized stereopure nucleic acid therapeutics. Prior to the development of our technology, it was not possible to create stereopure PS modified nucleic acid therapeutics, meaning drugs where the configuration of each chiral PS linkage is precisely controlled during chemical synthesis. Our unique approach also enables us to use rational drug design, whereby we employ the conventional wisdom of small molecule drug

discovery and apply these insights to nucleic acid therapeutic development. After identifying the target sequence, we are able to precisely control the oligonucleotide stereochemistry and determine the most suitable modality, such as antisense or exon skipping. We believe that our rational and methodical approach enables the optimization of several key elements of drug design, including stability, specificity, activity, and immunogenicity. We believe our platform technology has broad application as it does not rely upon a particular chemistry or particular nucleotide sequence, thereby creating opportunities to optimize across a larger number of therapeutic areas.

We believe that we have a strong intellectual property position relating to the development and commercialization of our stereopure nucleic acid therapeutic candidates. Our intellectual property portfolio includes filings designed to protect stereopure oligonucleotide compositions generally, as well as filings designed to protect stereopure compositions of oligonucleotides with particular stereochemical patterns (for example, that affect or confer biological activity). Our portfolio also includes filings for both proprietary methods and reagents, as well as various chemical methodologies that enable production of such stereopure oligonucleotide compositions. In addition, our portfolio includes filings designed to protect methods of using stereopure oligonucleotide compositions and filings designed to protect particular stereopure oligonucleotide products, such as those having a particular sequence, pattern of nucleoside and/or backbone modification, pattern of backbone linkages and/or pattern of backbone chiral centers.

Our Strategy

We are leveraging our innovative and proprietary synthetic chemistry drug development platform to design, develop and commercialize optimized disease-modifying nucleic acid therapeutics for indications with a high degree of unmet medical need in genetically defined diseases. We are focused on designing single-stranded nucleic acid therapeutics that can distribute broadly within the human body, allowing us to target diseases across multiple organ systems and tissues, through both systemic and local administration.

The key components of our strategy are as follows:

- ***Maintain and extend our leadership in oligonucleotide stereochemistry***. We intend to establish a dominant position in the field of oligonucleotide stereochemistry, advancing basic research and pharmacology across multiple therapeutic modalities and target classes.
- ***Rapidly advance our development candidates.*** We currently have three development programs in neurology: WVE-120101, WVE-120102 and WVE-210201. These programs in Huntington's disease and Duchenne Muscular Dystrophy are our most advanced therapeutic programs. In HD, we have programs targeting HTT SNP-1 and HTT SNP-2; in DMD, we are targeting exon 51. We expect to advance all three programs into clinical development in 2017.
- ***Maintain our focus on neurology.*** We are committed to maintaining our focus on rare genetic diseases in neurology, which we broadly define as CNS and the neuromuscular system. We believe there are several areas within neurology that we can uniquely address with our stereopure nucleic acid chemistry to reach underserved patient populations who may potentially benefit from our technology.
- ***Further invest to broaden our platform.*** We remain focused and disciplined with investments in our platform that we believe will enable a sustainable engine for future growth. We believe our platform will drive the discovery and advancement of stereopure therapeutic candidates in both our core focus area of neurology and additional therapeutic areas.
- ***Deepen our pipeline.*** We continue to leverage our platform and plan to identify three additional candidates in 2017 that will enable us to potentially broaden our pipeline to six wholly-owned development programs by the end of 2018, as well as additional partnerships and collaborations.
- ***Establish manufacturing leadership in oligonucleotides.*** To provide internal current good manufacturing practice ("cGMP") manufacturing capabilities and increase our control and visibility of our drug product supply chain, we signed a lease in 2016 for a manufacturing facility of approximately 90,000 square feet in Lexington, Massachusetts that we plan to occupy late in the second quarter of 2017. We expect that our internal expertise in cGMP manufacturing will better facilitate our growth and secure availability of drug product for current and future development activities and, potentially, commercial-scale manufacturing. In addition, we believe we have a strong intellectual property position relating to the design, development and commercialization of stereopure nucleic acid therapeutics. We intend to file new patent applications and take other steps to leverage, expand and enforce our intellectual property position.

Nucleic Acid Therapeutics

The majority of traditional therapeutics, such as small molecule drugs and biologics, work by interacting with proteins that contribute to the disease. However, there are thought to be a limited number of "druggable" proteins; it is currently estimated that approximately 80% of human protein targets cannot be addressed by these conventional approaches. By contrast, we believe that directing medicines

to the ribonucleic acid ("RNA"), which is critical to the production of proteins, rather than to the proteins themselves, has the potential to significantly increase the number of druggable targets.

Nucleic acid therapeutics is an innovative class of drugs that can modulate the function of target RNAs to ultimately affect the production of disease-associated proteins. Nucleic acid therapeutics employ a number of different molecular mechanisms to regulate protein production. These mechanisms can be broadly categorized as silencing, those that promote degradation of the target RNA, including antisense and RNAi, and splicing, those that involve binding to the target RNA and modulating its function by promoting exon skipping and RNA-guided gene editing.

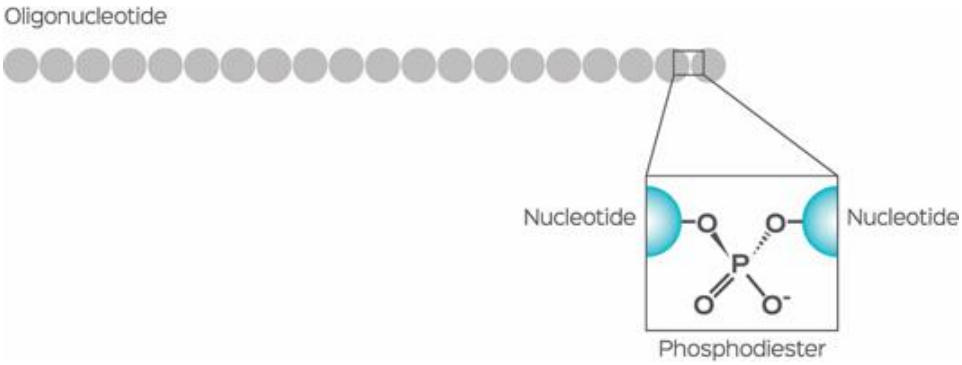
The unique capability of nucleic acid therapeutics to address a wide range of genomic targets across multiple therapeutic areas has the potential to create potentially significant market opportunities to develop drugs to treat a broad spectrum of human diseases, including diseases where no medicines currently exist or for which existing treatments are not optimal.

The nucleic acid therapeutics we are currently developing employ the following molecular mechanisms:

- **Antisense**, which uses a therapeutic oligonucleotide designed to bind to a specific sequence in a target RNA strand that encodes a disease-associated protein. The resulting two-stranded molecule ("duplex") is then recognized by a cellular enzyme called RNase H, which cleaves, or cuts, the target RNA in the duplex, thereby preventing the disease-associated protein from being made.
- **RNA interference** ("RNAi") which uses a therapeutic oligonucleotide designed to recognize a specific sequence and engages RNA interference machinery known as RISC complex to silence target RNA that encodes a disease-associated protein, thereby preventing the protein from being made.
- **Splicing**, which is the processing of the nascent precursor messenger RNA ("pre-mRNA") transcript into messenger RNA ("mRNA"). After splicing, introns are removed and exons are joined together, or ligated.
- **Exon skipping**, which uses a therapeutic oligonucleotide designed to bind to a particular sequence within a target RNA and direct the cellular machinery to delete, or splice, certain specific regions out of that RNA. Often, the underlying mutation in the target RNA leads to a "stop" instruction, so that, absent the therapeutic oligonucleotide, non-productive mRNA is produced. Use of the exon skipping oligonucleotide permits the cellular machinery to correct the "stop" instruction and assemble a partially functional protein, thereby mitigating or alleviating the disease that would otherwise result from the genetic mutation.

Design of Nucleic Acid Therapeutics

A large subset of nucleic acid therapeutics is comprised of chemically modified, short-length RNA or deoxyribonucleic acid ("DNA") strands, commonly known as oligonucleotides. Oligonucleotides are comprised of a sequence of nucleotides—the building blocks of RNA and DNA—that are linked together by a backbone of chemical bonds. In nucleic acid molecules that have not been modified for therapeutic use, the nucleotides are linked by phosphodiester (PO) bonds, as shown below.



Such unmodified nucleic acid molecules are unsuitable for use as therapeutics because they are rapidly degraded by enzymes called nucleases that are widely present in the human body, are rapidly cleared by the kidneys and have poor uptake into targeted cells. The industry has employed chemical modifications of the nucleotides and phosphodiester bonds to improve the stability, biodistribution and cellular uptake of nucleic acid therapeutics.

Phosphorothioate ("PS") modification was one of the earliest and remains one of the most common backbone modifications used in nucleic acid therapeutics. In PS modification, one of the nonbridging oxygen (O) atoms bonded to a phosphorus (P) atom is replaced with a sulfur (S) atom. PS modification has been shown to improve the stability of oligonucleotides by making them less susceptible

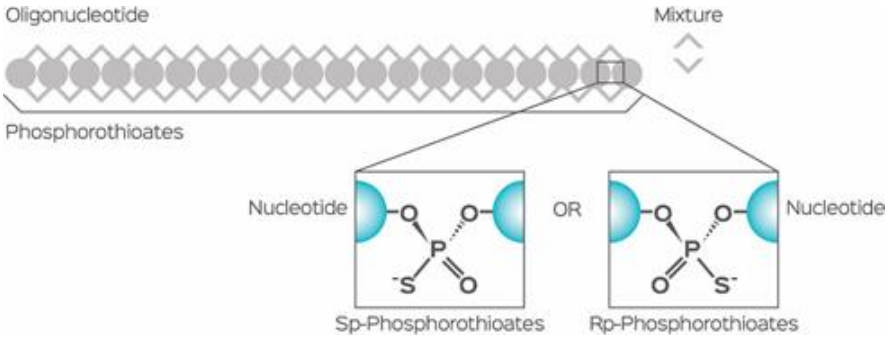
to enzymatic degradation. Further, PS bond-containing oligonucleotides increase binding to plasma proteins, which improves biodistribution by preventing rapid renal excretion of these molecules.

Whereas traditional modifications require full replacement of the naturally occurring phosophodiester (PO) with phosphorothioate (PS), we are able to judiciously use a combination of PO and PS in our steropure nucleic acids. We believe this ability to selectively employ PS modification where desired may provide further control over pharmacodynamics and may improve the safety of our drugs.

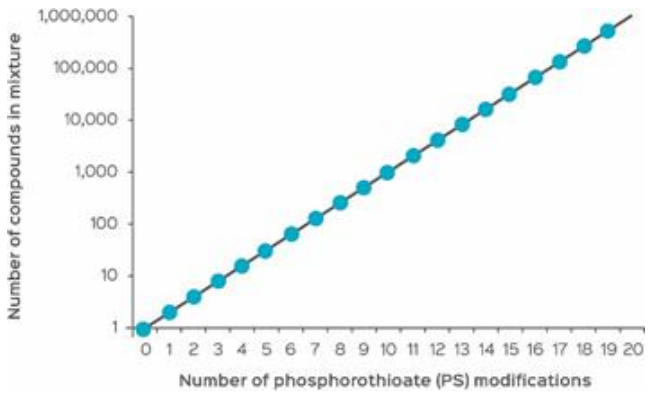
Nucleic acid therapeutics are a relatively "new" class of drugs from the perspective of regulatory approvals. The first approval of a nucleic acid therapeutic by the U.S. Food and Drug Administration ("FDA"), occurred in 1998, and the most recent FDA approval of a nucleic acid therapeutic occurred in 2016. Nucleic acid therapeutic candidates that employ PS modification are being developed by several different companies. PS modification is accepted as state-of-the-art advancement in the field of nucleic acid therapeutics. We believe that PS modification will remain a key component of nucleic acid therapeutic development.

PS Modification Results in Complex Drug Mixtures

A consequence of using PS modification in oligonucleotide synthesis is that it creates a chiral center at each phosphorus, each of which is designated as either an "Sp" or "Rp" configuration. This chirality creates stereoisomers, which, as shown below, have identical chemical composition but different three-dimensional arrangement of their atoms and consequently different chemical and biological properties.



The configuration of each PS modification occurs randomly during conventional nucleic acid synthesis. Because oligonucleotides are comprised of numerous nucleotides and associated PS modifications—with each PS modification having a random chiral configuration—the synthesis process generates an exponentially large number of stereoisomers of the synthesized oligonucleotide. Specifically, each linkage of an additional nucleotide residue doubles the number of stereoisomers of the product, so that a conventional preparation of a PS-containing oligonucleotide is in fact a highly heterogeneous mixtures of 2^N stereoisomers, where N represents the number of PS modifications. For instance, as shown below, a conventional fully PS modified oligonucleotide (20 nucleotides in length, 19 PS modifications) in fact is a mixture of over 500,000 stereoisomers, each having the same nucleotide sequence but differing in the stereochemistry along their backbones.



Stereoisomers often possess different chemical and pharmacologic properties. For example, certain stereoisomers can drive the therapeutic effects of a drug while others can be less beneficial or can even contribute to undesirable side effects. The greater the variation among a drug's constituent stereoisomers, the greater the potential to diminish the drug's efficacy and safety.

Prior to the development of our technology, it was not possible to create stereopure PS modified nucleic acid therapeutics, meaning drugs where the configuration of each chiral PS linkage is precisely controlled during chemical synthesis. Moreover, because of the sheer number of stereoisomers present in a mixture, it would be impractical, if not impossible, to physically isolate the most therapeutically optimal stereoisomer from within a mixture. For these reasons, all of the PS modified nucleic acid therapeutics currently on the market and in development by others are mixtures of many stereoisomers, which we believe are not optimized for stability, catalytic activity, efficacy or toxicity.

In small molecule therapeutics, U.S. regulators have long sought to eliminate the risks potentially posed by drug mixtures containing multiple stereoisomers. Since 1992, the FDA has recommended full molecular characterization of stereoisomers within small molecule drug mixtures. Historically, it has not been possible to achieve such characterization of nucleic acid therapeutic drug mixtures, which can contain tens of thousands to millions of distinct pharmacologic entities. Based on our preclinical studies, we believe we have the ability to design and synthesize stereopure PS modified nucleic acid therapeutics, which in preclinical models have shown superior drug properties compared with mixture-based nucleic acid therapeutics. We believe our drug development platform has the potential to set a new industry standard for the molecular characterization of complex nucleic acid therapeutic drug mixtures.

Our Solution: Controlling Stereochemistry and Employing Rational Design in Nucleic Acid Therapeutics

We have developed proprietary chemistry that, for the first time, enables the development of PO/PS modified nucleic acid therapeutics in which stereochemistry is precisely controlled. This degree of control enables us to both rationally design and synthesize therapeutically optimized stereopure nucleic acid therapeutics.

In addition, our rational drug design process of stereopure oligonucleotides employs selective and judicious use of PS modifications, which allows us to retain naturally occurring PO nucleic acids in our therapeutics. We believe the inclusion of phosphodiesters in our nucleic acid designs may contribute to increased safety and reduced renal accumulation.

We have discovered and expect to continue to identify fundamental relationships between pharmacology and the three-dimensional orientation or arrangement of atoms within an oligonucleotide, including stability, catalytic activity, specificity, safety and immunogenicity, which we believe have the potential to lead to improved efficacy and durability of effect. We have rationally designed and synthesized stereopure PO/PS modified drugs that, in preclinical studies, have demonstrated superior stability or potency, or both, as compared to their respective parent drug mixtures, which may result in increased durability of effect, as well as increased specificity and decreased immune activity. Therefore, we expect our stereopure PO/PS modified drugs to have improved safety profiles and to be dosed at lower concentrations or less frequently, or both, compared with mixture-based nucleic acid therapeutics. We are using these discoveries to guide our drug development activities.

Advantages of Our Approach

We believe that our innovative and proprietary synthetic chemistry drug development platform is a significant advance in the development of nucleic acid therapeutics. The advantages of our approach include:

- ***Ability to rationally design drugs with optimized pharmacological properties***. Our platform reduces susceptibility to enzymatic degradation and renal clearance and optimizes interactions with proteins that mediate activity as well as those that affect safety and tolerability. Our ability to improve pharmacologic stability and reduce clearance can enhance the biodistribution of single-stranded oligonucleotides to multiple tissues following systemic administration without the need for additional delivery technology.
- ***Broad applicability***. Our platform is applicable to multiple RNA-targeting approaches, including antisense, RNAi, exon skipping, splicing, RNA-guided gene editing, microRNA and others, and is compatible with a broad range of chemical modifications and targeting moieties.
- ***Proprietary production of stereopure nucleic acid therapeutics***. Our scientists have developed expertise in the techniques required to produce adequate supplies of PS modified stereopure nucleic acid therapeutic materials for our preclinical and planned clinical activities. In addition, we believe we have the intellectual property position and know-how necessary to protect, advance and scale these production processes to support our clinical trials and potential future commercial supply.

- ***Scalability and Manufacturing.*** Our manufacturing process and technical expertise in designing stereopure oligonucleotides is unique in nucleic acid therapeutics. We believe that our scalable synthesis processes will allow us to meet demand for cGMP-qualified clinical trial supply, as well as the potential for commercial manufacturing at a cost of goods and potential cost-per-patient that are comparable to traditional methods.

Our Proprietary Chemistry – Proof of Concept

We have demonstrated in preclinical models, predictive of human biology, that direct relationships exist between stereochemistry and pharmacology, and that these relationships can be used to rationally design and construct nucleic acid therapeutics. In proof-of-concept studies, we examined diverse sets of oligonucleotides designed and synthesized using our platform, which allowed us to characterize and compare the behavior of various stereoisomers. These preclinical studies have demonstrated that by controlling stereochemistry, we can optimize multiple aspects of pharmacology, including stability, catalytic activity, specificity, safety and immunogenicity, which we believe have the potential to lead to improved efficacy and durability of effect. As with any drug under development, we cannot be certain that our stereopure nucleic acid therapeutics will demonstrate in humans the same favorable pharmacologic properties we have observed in the preclinical studies we have conducted to date. See "Risk Factors—Risks Related to the Discovery, Manufacturing, Development and Commercialization of Our Product Candidates" for a discussion of the risks associated with the development of pharmaceuticals, and nucleic acid therapeutics in particular.

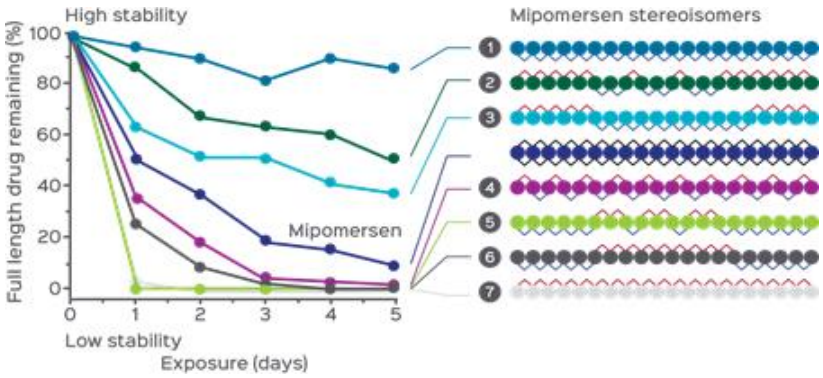
To assess the relationship between stereochemistry and pharmacology, we conducted studies of mipomersen using a diverse set of stereoisomers alongside the parent mixture. We chose to study mipomersen because at the time it was the only systemically administered nucleic acid therapeutic approved for commercialization and because of the public availability of documents from the regulatory bodies that have evaluated mipomersen for marketing approval. Mipomersen, which is currently marketed by Kastle Therapeutics and was marketed by Genzyme Corporation, a Sanofi Company, under the brand name KYNAMRO, is approved for the treatment of homozygous familial hypercholesterolemia and is designed to silence production of apolipoprotein B ("ApoB"). While mipomersen received marketing authorization in the United States, concerns about the drug's tolerability and liver and cardio-vascular safety led the European Medicines Agency ("EMA") in 2012 to refuse to grant marketing authorization for mipomersen in the European Union. One of the EMA's central concerns about mipomersen was that a high proportion of patients stopped taking the drug within two years, mainly due to side effects such as flu-like symptoms, injection site reactions and liver toxicity. The EMA considered these side effects important because mipomersen is intended for long-term treatment in order to maintain its cholesterol-lowering effect.

Mipomersen is an oligonucleotide that contains 20 nucleotides and 19 PS modifications. The chirality of each PS modification has the effect of doubling the number of stereoisomers at each phosphorus and, therefore, mipomersen is actually a mixture of over 500,000 different stereoisomers ($2^{19} = 524,288$), or a stereomixture. We rationally designed and synthesized individual stereoisomers of mipomersen, each having specific and different stereochemistry, and conducted studies comparing the stereoisomers with the mipomersen stereomixture.

Stability

We investigated the relationship between stereochemistry and stability by exposing our panel of individual mipomersen stereoisomers and the mipomersen stereomixture to metabolic enzymes, including nucleases, in homogenate rat liver and rat serum. Each stereoisomer and the mipomersen stereomixture were incubated separately in rat whole-liver homogenate for five days at physiological temperature and the percentage of each full-length stereoisomer and the mipomersen stereomixture remaining was measured daily.

As shown in the graph below, by day five, less than 15% of the stereomixture remained. In contrast, at day five, over 50% of our stereopure isomers 1 and 2 remained, indicating that these individual stereoisomers have greater stability than the stereomixture. However, the mipomersen stereomixture was more stable than stereoisomers 4, 5, 6 and 7.



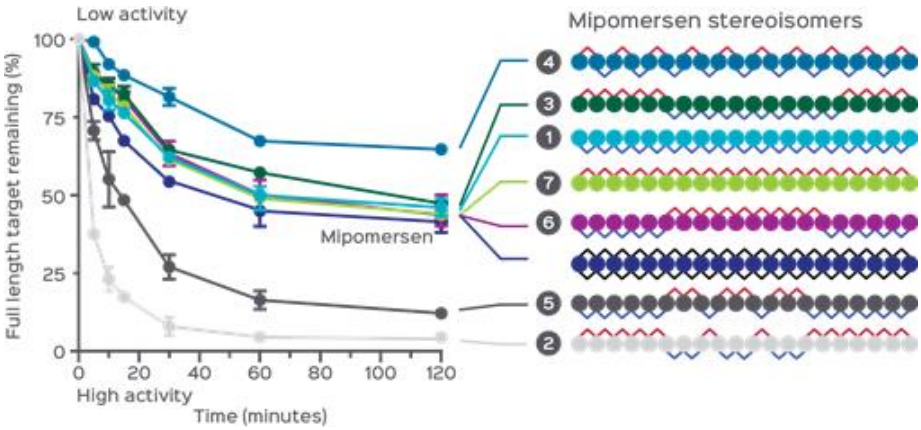
Similar results were observed when the stability of the stereomixture and selected stereoisomers were compared in rat serum.

Catalytic Activity

We investigated the relationship between stereochemistry and catalytic activity, which, in the case of antisense, is a measure of the efficiency with which the drug can knockdown the target. Efficient catalytic activity is critical for optimized pharmacology of drugs like mipomersen.

In the body, mipomersen uses a cellular enzyme called RNase H to degrade or knockdown ApoB mRNA. Using *in vitro* assays of human RNase H, we evaluated the catalytic activity of the same panel of stereoisomers described above compared with the stereomixture. Stereoisomers or stereomixtures were bound to target ApoB mRNA and incubated with human RNase H to initiate the catalytic reaction. The reaction was stopped at various time-points and the amount of full-length target ApoB mRNA remaining was measured.

As shown below, stereoisomers and the stereomixture exhibited large differences in their catalytic activity, as demonstrated by their efficiency in reducing the amount of the full-length target remaining over time. Certain stereoisomers, most notably stereoisomer 2, demonstrated catalytic activity at levels far superior to that of the stereomixture. Also, importantly, we identified stereoisomers that exhibited lower efficiency levels, most notably isomer 4.



Based on these and other data, we have established key design principles relating stereochemistry and catalytic efficiency using RNase H-mediated antisense. These principles can be applied across antisense therapeutics and are compatible with a broad range of chemical modifications to the drug molecule.

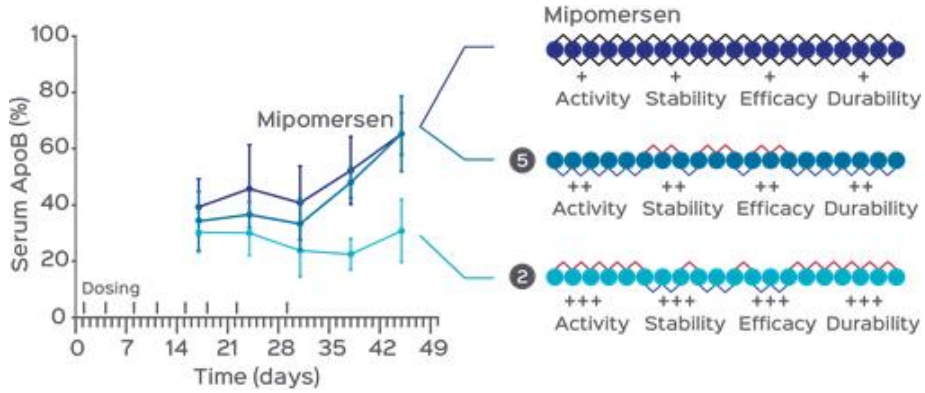
We believe that, based on these studies and others we have conducted, it is possible to synthesize stereopure nucleic acid therapies possessing increased stability and catalytic activity for any PS modified nucleic acid therapeutic independent of nucleotide sequence composition.

Efficacy

We assessed whether improved stability and catalytic activity of our stereoisomers will translate into greater efficacy in an *in vivo* pharmacological study. We administered our panel of stereoisomers and the stereomixture to transgenic mice that express human ApoB. This validated animal model was included in the preclinical package used for the regulatory approval of mipomersen in the United States.

Mice were injected twice weekly with 10 milligrams per kilogram of our stereoisomer 2, our stereoisomer 5 or the stereomixture over a four-week period. ApoB protein levels in the mice's serum were measured on a weekly basis. This treatment protocol and study design replicates the preclinical in vivo pharmacology study for mipomersen included in the regulatory submission for mipomersen.

As shown in the graph below, during the treatment period (up to day 28), stereoisomers 2 and 5, which as described above demonstrated increased catalytic activity *in vitro* compared with the stereomixture, also achieved greater reduction in serum ApoB compared with the stereomixture. In the graph below, levels of ApoB in serum are expressed as a percentage of ApoB at baseline, which was 100%. Knockdown of ApoB by the stereomixture decreased dramatically following final dose. This effect was also observed for stereoisomer 5, which had increased catalytic activity compared with the stereomixture but lowered stability. In comparison, stereoisomer 2, which had superior catalytic activity and stability, demonstrated durable knockdown of serum ApoB for over two weeks after the final dose.



These results demonstrate our ability to rationally design PS modified nucleic acid therapeutics that, in a preclinical setting, have greater stability and catalytic activity, which we believe have the potential to lead to improved efficacy and durability of effect.

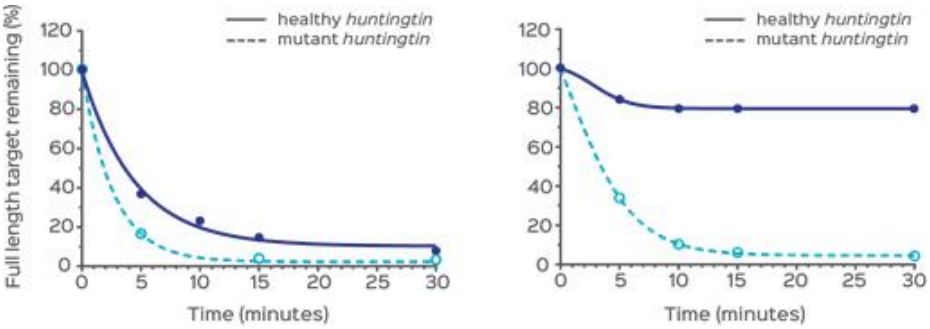
Specificity

By controlling stereochemistry, we have discovered that the pattern of cleavage caused by PS modified antisense, within the target RNA, can be changed, including directing cleavage toward specific sites within the target. This unique capability enables the cleavage of target RNA to be sensitive to small differences between similar targets, where cleavage may be undesirable or potentially unsafe.

For example, Huntington's disease is caused by mutations in one allele (which is one of two or more versions of a gene) of the *huntingtin* gene, resulting in the production of a disease-causing protein, while the other allele encodes a healthy protein. By optimizing stereochemistry, we are able to direct cleavage towards single-nucleotide differences between these alleles and silence the disease-causing *huntingtin* RNA while leaving the healthy *huntingtin* RNA intact.

Stereoisomers or stereomixtures were bound to mutant and healthy *huntingtin* RNA and incubated with human RNase H to initiate the catalytic reaction. The reaction was stopped at various time-points and the amount of full-length mutant and healthy *huntingtin* RNA remaining was measured.

Using these *in vitro* assays of human RNase H, we observed that the stereomixture (left figure) caused substantial reductions in both the mutant and healthy *huntingtin* RNA, while the optimized stereoisomers (right figure) preferentially cleaved mutant huntingtin RNA while sparing the healthy *huntingtin* RNA.



We believe our unique ability to change the cleavage pattern of PS modified nucleic acid therapies with stereochemistry will create opportunities to mitigate unwanted cleavage and also open allele-specific targeting (meaning the preferential interaction of an oligonucleotide with target RNA transcribed from one allele of a given gene) involving causative or associated non-causative genetic variations.

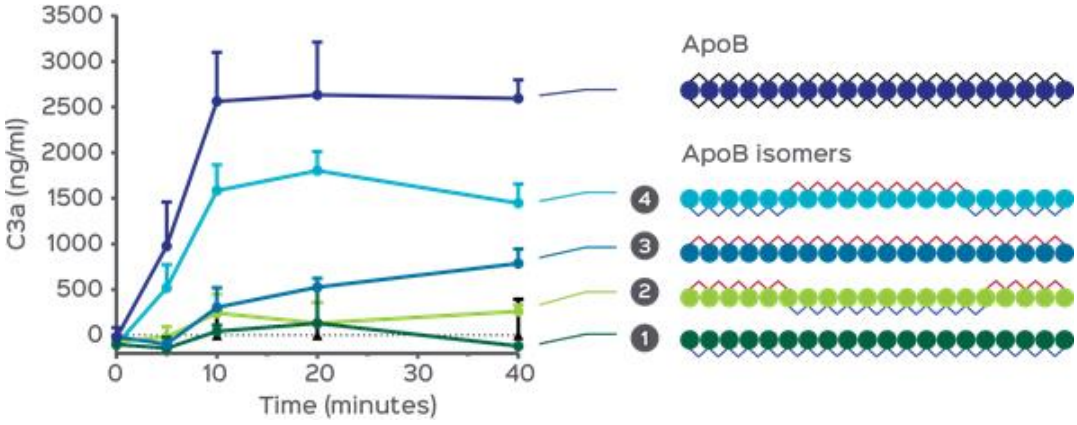
Through these studies, we have demonstrated an ability to use stereochemistry in the preclinical setting to control cleavage and reduce off-target cleavage. We believe these findings can be applied in the design of nucleic acid therapies that target a range of variation-specific disease targets.

Immunogenicity

We investigated the relationship between stereochemistry and immunogenicity, which is the ability of a substance to activate an immune response. Immune activation has been observed with PS modified oligonucleotides in preclinical toxicology studies, and flu-like symptoms and injection-site reactions in clinical studies are believed to be immune mediated.

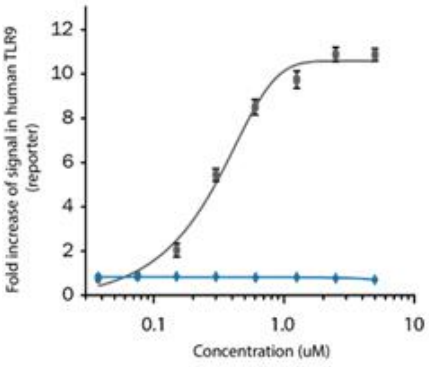
Using non-human primate serum we analyzed the activation of the complement system following exposure to our panel of individual stereoisomers and the parent stereomixtures. Each isomer and parent stereomixture were incubated at physiological temperature in non-human primate serum from three individual animals. Samples were removed at the indicated times and complement activation was measured by measuring the increase in the amount of protein C3a. Protein C3a is formed by the cleavage of complement component 3 upon activation of the complement system, and its levels in serum increase in direct proportion to the amount of activation. Such measurements were taken using the enzyme-linked immunosorbent assay ("ELISA") analytical method, a technique used to determine the amount of a specific protein present in a biological sample and which requires an antibody that is specific to the protein of interest, which is linked to an enzyme whose activity can be used to quantify the amount of protein present.

As shown below, equal concentrations of stereoisomers and the stereomixture exhibited differences in the levels of C3a. Certain stereoisomers showed greater than twice the reduction in C3a compared to the stereomixture. We believe that, based on these studies, it is possible to modulate complement activation and potentially reduce immunogenicity of PS modified oligonucleotides by controlling stereochemistry.

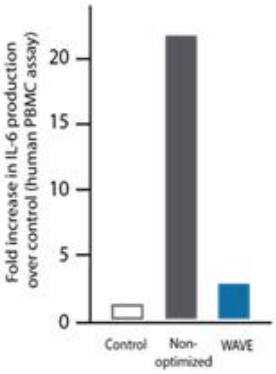


In addition, human TLR9 reporter assay and human PBMC cytokine panel (IL-6 and MIP-1b are key cytokines in B-cell and macrophage activation, respectively) provide further validation of stereochemistry impact on immunogenicity. Conventional wisdom states that 5-methyl C (5mC) and 2' modification are sufficient to avoid immune activation. However, substantial immune activation exists within highly stable compounds despite the incorporation of these modifications, as seen below. The WAVE chemistry platform enables reduced activation of the immune system.

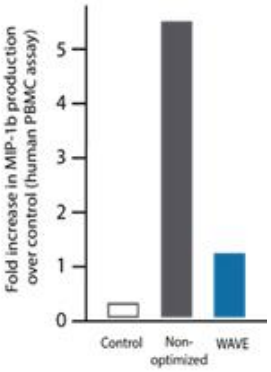
Human TLR9 assay



PBMC IL-6 activation



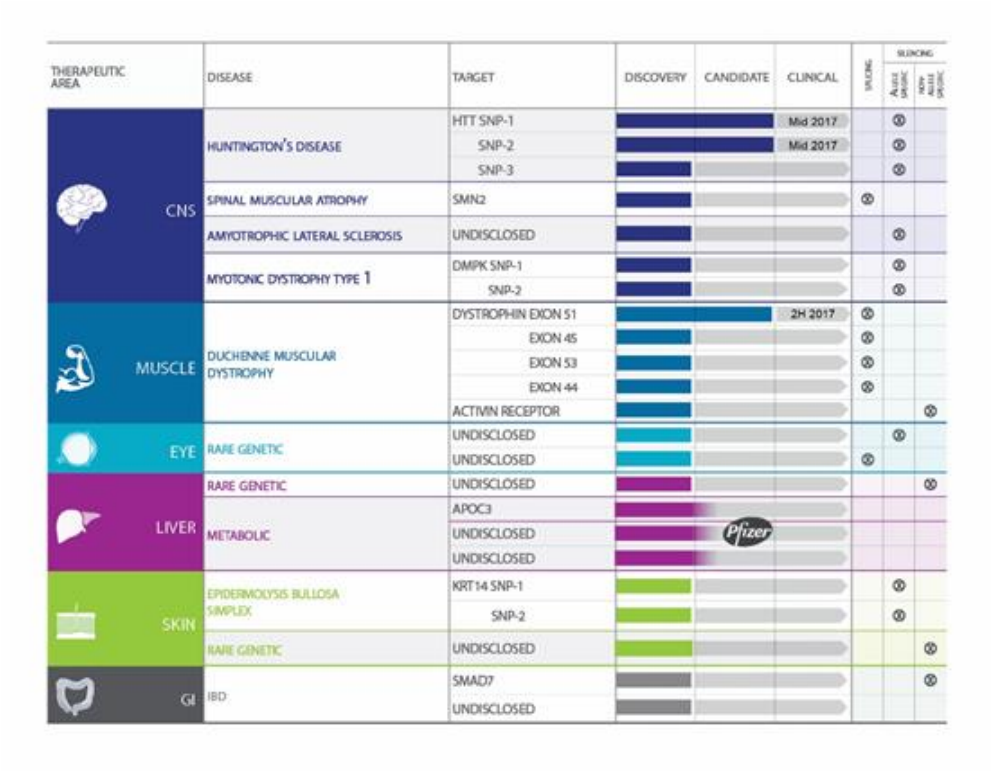
PBMC MIP-1b activation



Our Pipeline

We are developing nucleic acid therapeutics for genetically defined diseases that we believe are capable of targeting a wide range of organ systems and tissues. Based on our design principles, we have demonstrated in preclinical studies our ability to rapidly design and select lead therapeutic candidates with optimized pharmacological properties. We believe that our platform can potentially be used in the near-term to develop treatments for several other target indications. Our most advanced therapeutic programs are in Huntington's disease and Duchenne Muscular Dystrophy. In HD, we have programs targeting HTT SNP-1 and HTT SNP-2; in DMD, we are targeting exon 51. We anticipate initiating clinical development of all three programs in 2017. See "Our Initial Therapeutic Candidates" for more information about these targets. We also have early-stage discovery programs in which we are focused on screening activities and lead optimization for potential drug candidates targeting various areas, including eye, hepatic and neuromuscular and central nervous system diseases.

Our current programs in development and our exploratory portfolio are summarized in the table below:



Our Initial Therapeutic Candidates

Our lead development programs target Huntington's disease (WVE-120101 and WVE-120102) and Duchenne Muscular Dystrophy (WVE-210201).

Huntington's Disease

Background and Market Opportunity

Huntington's disease ("HD"), is an orphan hereditary neurodegenerative disease that is fatal and for which there is no cure. HD results from the accumulation of the defective gene product mutant huntingtin ("mHTT"), which promotes the degeneration of neurons. This accumulation is caused by an expanded CAG triplet repeat in the HTT gene, which results in production of mutant HTT (mHTT) protein. Accumulation of mHTT causes progressive loss of neurons in the brain, and can lead to neuronal cell death, causing motor, cognitive and psychiatric disability. HD patients still possess wild type (healthy) HTT protein, which is believed to be critical for neuronal function, and suppression may have detrimental long-term consequences. Absence of healthy huntingtin protein has been shown to be embryonic lethal. Symptoms typically appear between the ages of 30 and 50 and worsen over the next 10 to 20 years.

Many describe the symptoms of HD as having amyotrophic lateral sclerosis ("ALS"), Parkinson's disease and Alzheimer's disease simultaneously. Patients experience a reduction in motor function and psychological disturbances. Life expectancy after symptom onset is approximately 20 years. In the later stages, often lasting over ten years, movements become increasingly difficult to control. Affected persons become fully dependent upon others for assistance with activities of daily living ("ADLs"), lose the ability to walk, and often require placement in a long-term care facility. We estimate that approximately 30,000 people in the United States have symptomatic HD and more than 200,000 others have a 50% chance of inheriting the disorder from their affected parent.

Current Treatments

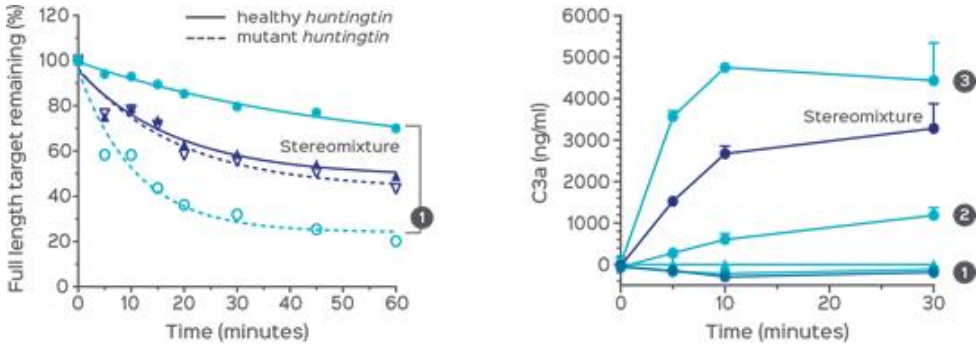
Currently, there are no approved treatments that can reverse or slow down the course of HD. Some of the symptoms of HD can be managed with medication and therapies. Antipsychotics and other drugs affecting the dopamine pathways are used for symptom control. Lowering the levels of mHTT protein has demonstrated therapeutic effects in animal models. Roche and Ionis Pharmaceuticals have antisense oligonucleotides that are non allele specific to silence the huntingtin gene in Phase 1/2a clinical development, with human trials having commenced in July 2015.

Our Programs

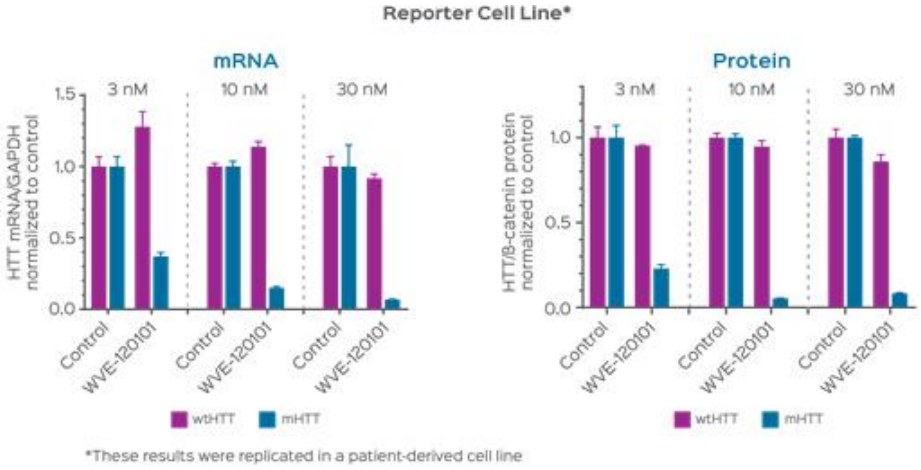
We are advancing two therapeutic candidates, WVE-120101 and WVE-120102, targeting single nucleotide polymorphisms ("SNPs"), associated with the mutant alleles of the *huntingtin* gene. The precise targeting of mutant alleles by stereochemically controlled ("stereopure") oligonucleotides should allow discrimination and selective silencing of the mutant *huntingtin* messenger RNA transcripts that lead to the production of the mutant protein associated with manifestations of the disease while leaving normal *huntingtin* transcripts and protein relatively intact. Each SNP has a particular demographic distribution, and defines a subpopulation of patients suited for allele-specific interventions. More than two-thirds of the HD patient population possess one of the two most common SNPs. Therefore, we are attempting to develop oligonucleotides targeting these two SNPs. If approved, WVE-120101 and WVE-120102 would be the first allele-specific therapies for HD patients. If approved, our allele-specific approach may also enable us to address the pre-manifest HD patient population.

We have completed our initial preclinical studies intended to establish the safety and distribution of our stereopure antisense oligonucleotides. The Phase 1b/2a clinical trials are designed to conduct two simultaneous multi-ascending-dose ("MAD") trials targeting SNP-1 and SNP-2, respectively, to establish the safety and tolerability, pharmacokinetics, pharmacodynamic effects, and potentially preliminary evidence of therapeutic effect in patients with early manifest HD. Key inclusion criteria is expected to be stage I or II patients between the ages of 25-65. The route of administration will be intrathecal by lumbar puncture. We expect to dose on a monthly basis or potentially less frequently. We believe that the ability to selectively reduce mutant *huntingtin*, as demonstrated in our preclinical studies, may enable us to proceed rapidly to clinical proof-of-concept studies to assess target engagement in SNP-1 and SNP-2 positive patients. cGMP-manufactured supplies of WVE-120101 and WVE-120102 have been completed to conduct the Phase 1b/2a clinical trials. As part of our HD global development strategy, we expect to initiate clinical development of both allele-specific HD programs in mid-2017.

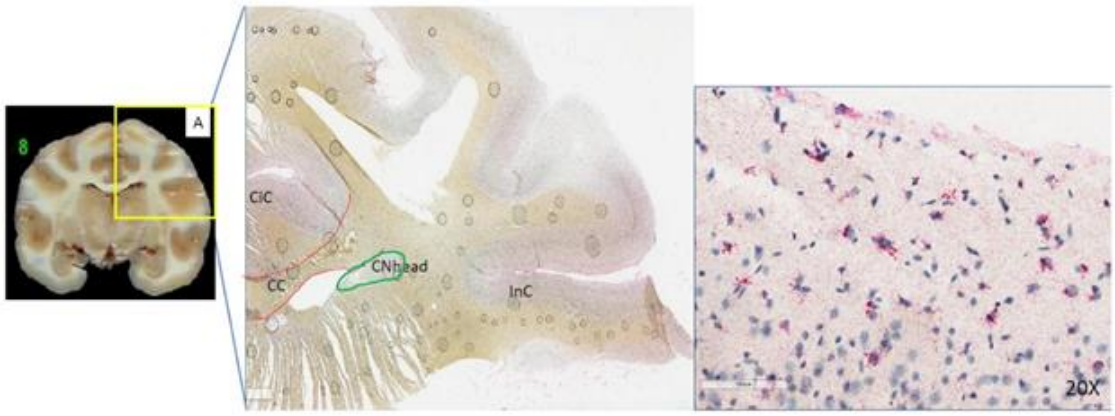
In our preclinical studies, as shown below, *huntingtin* targeted stereoisomer 1 (circles) or stereomixture (triangles) drugs were bound to healthy and mutant *huntingtin* mRNA and incubated with human RNase H (left figure). Catalysis mediated by the stereopure drug increased the degree of knockdown while also discriminating between healthy versus mutant *huntingtin*, compared with the stereomixture.



Using non-human primate serum, we analyzed the activation of the complement system following exposure to a panel of *huntingtin* targeted stereoisomers and the parent stereomixture. Each isomer and parent stereomixture was incubated at physiological temperature in non-human primate serum from three individual animals. Samples were removed at the indicated times and complement activation was measured by the increase in C3a levels using the ELISA analytical method. As shown above (right figure), certain stereoisomers and the stereomixture demonstrated increased production of C3a, notably stereoisomer 3, however there was no production of C3a following exposure to stereoisomer 1, which showed discrimination between heathy and mutant *huntingtin.*



Our HD SNP-1 candidate, WVE-120101, was tested for potency and selectivity of knocking down U-variant HTT/mutant HTT (mHTT), or the mutant disease-causing allele. As shown in above, WVE-120101 potently reduced mutant huntingtin mRNA and protein, and exhibited great selectivity for mHTT at all the doses tested. WVE-120101 targeting U-variant HTT was co-transfected into HEK293 cells with two reporter plasmids: a plasmid with V5-tagged full-length HTT containing the U-variant SNP-1 and a plasmid with FLAG-tagged full-length HTT containing the C-variant SNP-1. The knockdown of mHTT mRNA and mHTT protein was determined by quantitative reverse transcription PCR (RT-qPCR) and western blot analysis, respectively. All results were normalized to a non-specific stereorandom control. The preclinical data demonstrate the ability to knock down the mutant allele while leaving the wild type, healthy allele intact.



Following promising preclinical data, we have also investigated distribution characteristics of our lead HD candidate. Based on our preclinical studies, we believe stereochemistry enables improved protein binding and distribution, as evidenced by the NHP distribution data seen above. The figure above demonstrates meaningful distribution in a non-human primate ("NHP") study of WVE-120101. In this preclinical study, we employed an in situ hybridization ("ISH") ViewRNA assay. The ViewRNA assay provides the ability to stain oligonucleotides, allowing increased visibility and understanding of distribution of WVE-120101 in the brain. As shown above, our lead HD SNP-1 candidate, WVE-120101, is stained in red. Results demonstrated perinuclear and nuclear distribution of WVE-120101 (red) in NHP gray matter structures following intrathecal administration. The NHP viewRNA assay demonstrated broad tissue distribution, including the cortex and striatum. These findings are encouraging as we believe distribution and penetration into several areas of the brain will be beneficial for the treatment of HD.

Duchenne Muscular Dystrophy

Background and Market Opportunity

Duchenne Muscular Dystrophy ("DMD"), is a genetic disorder caused by mutations in the *dystrophin* gene on the X chromosome that affects approximately one in 3,500 newborn boys around the world. In skeletal and cardiac muscles, the dystrophin protein is part of a protein complex called the dystrophin-associated protein complex that acts as an anchor, connecting each muscle cell's structural framework with the lattice of proteins and other molecules outside the cell through the muscle cell membrane. The dystrophin-associated protein complex protects the muscle from injury during contraction and relaxation. DMD patients typically develop muscle weakness in the early years of life and become wheelchair-bound in their early teens. As the disease progresses, DMD patients typically develop respiratory, orthopedic and cardiac complications. Cardiomyopathy and breathing difficulties usually begin by the age of 20 and few individuals with DMD live beyond their 30's.

Current Treatments

There is currently one FDA-approved exon skipping nucleic acid therapeutic in the United States, Sarepta Therapeutics' Exondys 51 *(*eteplirsen), which was approved in September 2016. Exon skipping allows for the production of shortened, but functional, dystrophin protein instead of dysfunctional dystrophin. In September 2016, the FDA concluded that the data submitted demonstrated an increase in dystrophin production that is reasonably likely to predict clinical benefit in some patients with DMD who have a confirmed mutation of the dystrophin gene amenable to exon 51 skipping. According to U.S. accelerated approval guidelines, no clinical benefit needs to be established at the time of FDA approval, and no clinical benefit of eteplirsen has yet been established. Thus, consistent with the FDA's accelerated approval regulations, eteplirsen is the subject of a post-marketing approval clinical trial to verify and describe the drug's clinical benefit. The required clinical trial is designed to assess whether eteplirsen improves motor function of DMD patients with a confirmed mutation of the dystrophin gene amenable to exon 51 skipping.

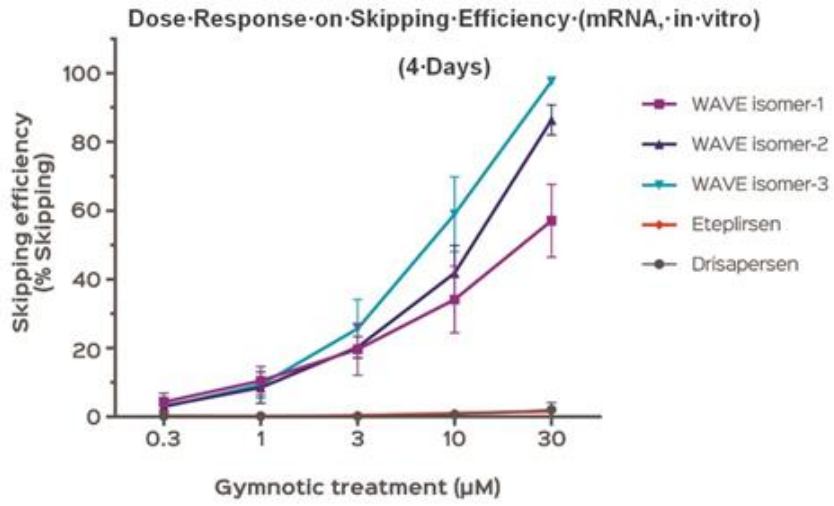
In Europe, conditional market authorization has been granted to PTC Therapeutics' TRANSLARNA (ataluren) for the treatment of nonsense mutation DMD for ambulatory patients who are 5 years or older. The FDA has also granted a standard review and has assigned a Prescription Drug User Fee Act ("PDUFA") date of October, 24, 2017. Another exon-skipping nucleic acid therapeutic candidate for DMD is BioMarin Pharmaceutical's drisapersen, for which the FDA issued a complete response letter in January 2016 indicating that the review cycle was complete and that the application was not ready for approval in its present form. In addition, treatments aimed to address the symptoms of DMD include corticosteroids and physical and respiratory therapy to slow the decline in muscle strength and to prolong ambulation and respiratory function. In addition, in February 2017, the FDA approved Emflaza (deflazacort), the first corticosteroid approved as a treatment in the United States for DMD patients older than 5 years of age.

Our Program

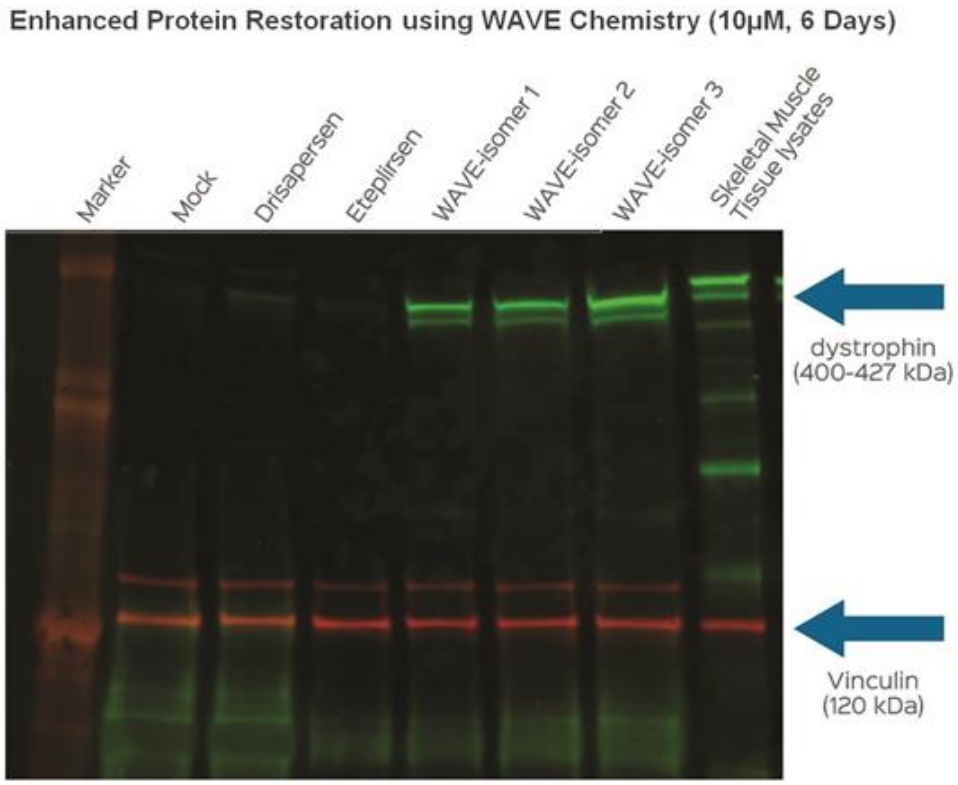
Based on our interactions with the DMD patient community and DMD patient advocacy groups, despite the availability of eteplirsen in the U.S. and ataluren in the EU, we believe that there continues to be a significant unmet medical need in DMD patients. We are developing stereochemically optimized oligonucleotides that we believe have superior pharmacology attributes as compared to stereomixtures. Using a variety of preclinical *in vitro* assays, we will advance WVE-210201, our stereopure exon skipping candidate that targets exon 51, to clinical trials because we believe it has the potential to benefit the estimated 13% of the DMD patient population that are amenable to exon 51 skipping.

As described below, preclinical quantitative western blot studies of WVE-210201 demonstrated 52% dystrophin protein restoration as compared with normal skeletal muscle tissue lysates, versus approximately 1% when testing other exon skipping therapies *in vitro*. We are developing our clinical trial protocol for our clinical trial for WVE-210201 and intend to include both ambulatory and non-ambulatory patients in our clinical trial, as well as patients previously treated with other exon skipping therapies after appropriate washout. Preclinical toxicology studies are currently underway. Our internal cGMP manufacturing is ongoing to support our planned clinical trials. We plan to initiate our global clinical development program for WVE-210201 in the second half of 2017.

WVE-210201 was selected for further development, in part, based on its ability to demonstrate efficient restoration of dystrophin production in patient-derived muscle cells. Efficiency at skipping exon 51 was determined by quantitative RT-PCR following exposure to equal concentrations of oligonucleotides. As shown below, our stereoisomers demonstrated a dose-dependent increase in exon skipping efficiency compared to eteplirsen and drisapersen.



Using patient-derived muscle cells, we analyzed protein restoration by western blot with gymnotic uptake, meaning delivery of drug candidate to the cell in the absence of any carriers or conjugation, at 10µM concentration of each compound. The extent of dystrophin protein restoration *in vitro* was quantified to be between 50% - 100% of normal skeletal lysates, as compared to about 1% by drisapersen or eteplirsen at this concentration.



We believe that the use of a stereochemically-optimized compound (in contrast to a stereomixture) has the potential to reduce the frequency and severity of significant adverse events incident to stereomixtures, such as injection site reactions, renal toxicity and thrombocytopenia. Our Phase 1b/2a clinical trials in WVE-210201 will seek to establish safety, tolerability, pharmacokinetics and efficiency of exon skipping. The efficiency of exon skipping will be determined through measurement of restored production of shortened dystrophin protein in muscle biopsies. Such a positive effect over time would be expected to lead to improvement in muscle function, which is an anticipated clinical endpoint of our clinical trials.

We have selected WAVE isomer-1 as our lead DMD candidate, WVE-210201. Preclinical quantitative Western blot studies of WAVE's DMD exon 51 candidate demonstrated 52% dystrophin protein restoration as compared with normal skeletal muscle tissue lysates, versus approximately 1% when testing other exon skipping therapies, as shown above. WAVE isomer-1 was selected due to its more favorable profile, including potency, stability and safety.

Licensing Arrangements and Research Collaborations

Our business strategy is to develop and commercialize a broad pipeline of nucleic acid therapies. As part of this strategy, we have entered into, and expect to enter into additional, license and research collaboration agreements as a means of seeking to advance our own nucleic acid therapeutic programs in neurology, investing in third party technologies to further strengthen our drug development platform and leveraging external partnerships to extend the reach of our drug development platform in therapeutic areas outside of neurology where our technology demonstrates a competitive advantage.

Our Partnerships

Pfizer

In May 2016, we entered into a research, license and option agreement with Pfizer Inc. (the "Collaboration Agreement"). Pursuant to the terms of the Collaboration Agreement, we and Pfizer agreed to collaborate on the discovery, development and commercialization of stereopure oligonucleotide therapeutics for up to five programs ("the Pfizer Programs"), each directed at a genetically-defined hepatic target selected by Pfizer (the "Collaboration"). Under the terms of the agreements we entered into with Pfizer and its affiliate, Pfizer paid us $40.0 million upfront, $30.0 million of which took the form of an equity investment in our ordinary shares, as described below. Subject to option exercises by Pfizer, assuming five potential products are successfully developed and commercialized, we may earn up to $871.0 million in potential research, development and commercial milestone payments, plus royalties, tiered up to low double-digits, on sales of any products that may result from the Collaboration.

Under the Collaboration Agreement, the parties agreed to collaborate during the four-year research term. During the research term, we are responsible to use our commercially reasonable efforts to advance up to five programs through to the selection of clinical candidates. At that stage, Pfizer may elect to license any of these programs exclusively and to have exclusive rights to undertake the clinical development of the clinical candidates into products and the potential commercialization of any such products thereafter. In addition, under the Collaboration, we receive a non-exclusive, royalty-bearing sublicenseable license to use Pfizer's hepatic targeting technology in any of our own hepatic programs that are outside the scope of the collaboration (the "WAVE Programs"). If we use Pfizer's technology on our programs, Pfizer is eligible to receive potential development and commercial milestone payments from us. Pfizer is also eligible to receive tiered royalties on sales of any products that include Pfizer's hepatic targeting technology.

As of the date of the filing of this Annual Report on Form 10-K for the fiscal year ended December 31, 2016 with the Securities and Exchange Commission ("SEC"), Pfizer had declared three hepatic targets, including our Apolipoprotein C-III program and two undisclosed programs, with the remaining two hepatic targets to be declared by November 2017. Also in connection with the Collaboration, Pfizer agreed that it will be subject to a standstill such that, for a certain period of time, neither Pfizer nor its controlled affiliates, except as we expressly approve in writing, will, subject to certain conditions, directly or indirectly, acquire our outstanding ordinary shares, seek to call any meeting of our shareholders, solicit proxies or consents in opposition to the recommendation of a majority of our board of directors with respect to any matter or undertake other specified actions related to the potential acquisition of additional equity interests in the Company. The term of the Collaboration Agreement runs from the effective date until the date of the last to expire payment obligations with respect to each Pfizer Program and with respect to each WAVE Program, and expires on a program-by-program basis accordingly.

Simultaneously with the entry into the Collaboration Agreement with Pfizer, we entered into a share purchase agreement with C.P. Pharmaceuticals International C.V., an affiliate of Pfizer (the "Pfizer affiliate"). Pursuant to the terms of the share purchase agreement, the Pfizer affiliate purchased 1,875,000 of our ordinary shares at a purchase price of $16.00 per share, for an aggregate purchase price of $30.0 million. The shares purchased by the Pfizer affiliate are subject to lock-up restrictions and carry certain registration rights outlined in the share purchase agreement.

Our Technology Licenses

Max-Planck-Innovation GmbH

In June 2015, we entered into an agreement with Max-Planck-Innovation GmbH ("MI"), pursuant to which we obtained a co-exclusive royalty-bearing, worldwide license, with the right to sublicense, to research, develop, manufacture and commercialize products in all fields of use under certain patent rights owned by Max-Planck-Gesellschaft ("MPG"), and patent rights owned by University of Massachusetts Medical School ("UMMS"), which has been granted to us by MI, a wholly-owned subsidiary of MPG, acting as MPG's technology transfer agency and UMMS's authorized licensing agency for such patents. MPG and MI are collectively referred to herein as Max-Planck.

Our patent rights under this license are to patent filings that relate to certain sequence and structural features of single-stranded RNA molecules that mediate target-specific RNA interference, and include both filings that are owned by Max-Planck and arose from research conducted by Thomas Tuschl, Ph.D. and his colleagues at the Max-Planck-Institute for Biophysical Chemistry, and also an issued U.S. patent owned by the University of Massachusetts ("UMASS"), that prevailed in an interference with one of the Max-Planck filings and was subsequently included, through a separate agreement between Max-Planck and UMASS, within the portfolio that Max-Planck is authorized to license. The Max-Planck licensed patent portfolio includes issued U.S. and Canadian patents, and pending U.S. and European patent applications, each of which has a projected 20-year term that extends into 2023. We intend to develop and commercialize diagnostic and therapeutic products based on our patent rights under this license, although currently we do not rely on the patent rights under this license for any of our drug candidates under development in our therapeutic or discovery programs. Max-Planck retains the right to practice the intellectual property licensed under the agreement for non-commercial purposes.

Our license is one of two maximum allowable co-exclusive licenses for these patents, the other of which is currently held by Ionis Pharmaceuticals, Inc. ("Ionis"). If either we terminate our or Ionis terminates its respective co-exclusive portion of the license, Max-Planck is obligated to grant the other party an exclusive license on substantially the same terms and conditions previously applicable to the terminated co-exclusive licensee.

Under certain conditions, we are permitted to sublicense our rights under the license. The license requires that we use commercially reasonable efforts to develop and commercialize products under the agreement, whether solely or through our affiliates and sublicensees. In order to secure the license, we made an upfront payment of less than $0.1 million to Max-Planck. Additionally, starting on the first anniversary of the agreement, we are required to pay annual license maintenance fees of less than $0.1 million to Max-Planck which are to be credited against any royalties payable for the applicable calendar year. We will be required to make payments based upon regulatory milestones, including the initiation of clinical trials, and product approval milestones totaling up to $1.6 million for each licensed product reaching such clinical stage, provided that such milestone payments will only be payable once per target irrespective of the number of licensed products targeting such target to achieve such milestones. In addition to milestone payments, we will be required to pay royalties of a percentage of cumulative annual net sales of a licensed product commercialized by us, our affiliates and sublicensees. The percentage is in the low single digits. The royalties payable to Max-Planck are subject to reduction for any third party payments required to be made, with a minimum floor in the low single digits. If we grant a sublicense of our rights under this license, we will be obligated to pay Max-Planck a percentage of specified sublicensing consideration received from such sublicensee attributable to the sublicense granted under the licensed patents, ranging from the mid-single digits to the low thirties depending on the stage of development at the time the sublicense is executed.

We may unilaterally terminate the license agreement upon 90 days' prior written notice and payment of all accrued amounts owing to Max-Planck. Max-Planck may terminate the agreement upon 30 days' prior written notice if we challenge the validity of its patents, upon 30 days' prior written notice if we undergo a change of control and cannot demonstrate that we will maintain a development and commercialization program that is substantially similar or greater in scope than the program prior to the change of control event, or in the event of our material breach which remains uncured after 60 days of receiving written notice of such breach (or 45 days in the case of nonpayment). Absent early termination, the agreement will automatically terminate upon the later of the expiration or abandonment of all issued patents and filed patent applications with the patent rights covered by the agreement or April 28, 2019.

Our Research Collaborations

University of Oxford; Professor Matthew Wood's Laboratory

Since April 2015, we have been collaborating with Dr. Matthew J.A. Wood, Professor of Neuroscience at the University of Oxford and Co-Director of the Oxford Centre for Neuromuscular Science under a translational research collaboration agreement with The Chancellor, Masters, and Scholars of the University of Oxford ("Oxford"). Dr. Wood's research is in the field of degenerative disorders of the nervous system and muscle. His laboratory's main focus is the investigation of novel therapeutic approaches using short nucleic acids to target messenger RNA ("mRNA"). His team has been investigating the potential of single-stranded antisense oligonucleotides for the modification of mRNA splicing, for example in Duchenne Muscular Dystrophy. In addition, his laboratory's work includes the potential of double-stranded RNA for gene silencing ("RNAi"), for the silencing of target genes and mutant alleles both in muscle and in the nervous system. In October 2016, we extended our research collaboration for an additional 18 months in order for Oxford to characterize our proprietary isomers in murine models to further improve the pharmacology of oligonucleotides using our novel chemistries, and to discover biomarkers associated with disease progression and pharmacological activity for the treatment of DMD. Under this collaboration, we are exploring additional exon targets, including exon 45, exon 53 and exon 44 beyond our lead DMD program, which targets exon 51.

University of Dundee

Since September 2015, we have been conducting research in collaboration with the University of Dundee ("Dundee") that involves characterizing our proprietary isomers in order to improve the pharmacology of oligonucleotides for the treatment of keratin disorders. We and Dundee recently submitted a collaborative proposal for funding to the Medical Research Council ("MRC"), to support the project entitled 'Delivering gene silencing therapy to the epidermic and ocular surface'. MRC has accepted the proposal and has issued an offer of a five-year grant to support this proposed research.

University of Massachusetts Medical School

In January 2017, we entered into a research collaboration agreement with University of Massachusetts Medical School ("UMMS"), to deepen our knowledge and experience in neurodegenerative and neuromuscular diseases, including amyotrophic lateral sclerosis ("ALS"). Research under this collaboration is being conducted by Dr. Robert H. Brown, Jr., the Leo P. and Theresa M. LaChance Chair in Medical Research and Chair of the Department of Neurology at UMMS, an internationally known researcher and physician in

the field. Our research collaboration with UMMS is initially focused on characterizing our proprietary isomers in order to improve the pharmacology of oligonucleotides for the treatment of ALS.

nLife Therapeutics S.L.

In October 2016, we entered into a research collaboration and option agreement with nLife Therapeutics S.L., an early-stage biopharmaceutical company developing chemical conjugates technologies, aimed at exploring cell-specific targeting of nucleic acid therapeutics in the CNS. For the two-year term that commenced in October 2016, nLife and WAVE are collaborating to assess the ability of several chemical moieties to direct distribution and uptake of nucleic acid cargo to specific cell-types within the central nervous system, including neurons, glia and astrocytes. As part of the collaboration, nLife is developing conjugates of small molecules and oligonucleotides that direct the delivery to specific cells in a selective manner. Under the terms of the agreement, we have agreed to fund certain research activities being conducted by nLife and have the option to license nLife's technology for development and commercialization across our portfolio.

Manufacturing

To provide internal cGMP manufacturing capabilities and increase control and visibility of our drug product supply chain, we signed a lease in September 2016 for a manufacturing facility of approximately 90,000 square feet in Lexington, MA. This new facility supplements our existing Cambridge, MA headquarters, secures availability of drug product for current and future development activities, and potentially provides commercial-scale manufacturing capabilities. The new facility will also provide additional laboratory and office space to support our anticipated growth. We plan to occupy the facility by the end of the second quarter in 2017.

We believe we have sufficient manufacturing capacity through our third-party contract manufacturers and our internal GLP manufacturing facility to meet our current research, clinical and early-stage commercial needs. We believe that the addition of our internal cGMP manufacturing capabilities, together with the supply capacity we have established externally will be sufficient to meet our anticipated manufacturing needs for the next several years. We monitor the capacity availability for the manufacture of drug substance and drug product and believe that our supply agreements with our contract manufactures and the lead times for new supply agreements would allow us to access additional capacity should the need arise. We also believe that our products can be manufactured at a scale and with production and procurement efficiencies that will result in commercially competitive costs.

Research and Development

Since commencing operations, we have dedicated a significant portion of our resources to research and development activities, including the development of our core platform technology and our therapeutic programs. We incurred research and development expenses of $40.8 million, $9.1 million and $2.4 million during the fiscal years ended December 31, 2016, 2015 and 2014, respectively.

We anticipate that a significant portion of our operating expenses will continue to be related to research and development as we continue to advance our therapeutic programs.

Intellectual Property

We own or have rights to worldwide patent filings that protect our proprietary technologies for making stereochemically pure oligonucleotide compositions, and that also protect the compositions themselves, as well as methods of using them, including in the treatment of diseases. As of March 1, 2017, our portfolio includes at least six issued U.S. patents, at least 21 issued foreign patents, and pending applications in at least 22 jurisdictions. The information contained below in this "Business — Intellectual Property" subsection is current as of March 1, 2017.

Synthetic Methodologies

Our patent portfolio includes multiple families that protect synthetic methodologies and/or key reagents for generating stereochemically pure oligonucleotide compositions. Certain synthetic methodologies and/or key reagents are covered by families originally filed by the University of Tokyo. We have obtained exclusive rights to these families, which include two issued Japanese patents that have terms that extend to 2022 to 2025.

Additional synthetic methodologies and/or reagents are protected by families that we own, including one with issued patents in the United States, Australia, Europe, Japan, Russia, and Singapore and pending applications in Brazil, Canada, China, Europe, India, Russia, Singapore, South Korea, and the United States that has a 20-year expiration date in 2029, one with pending applications in Australia, Brazil, Canada, Chile, China, Europe, Hong Kong, India, Indonesia, Israel, Japan, Mexico, Russia, Singapore, South Africa, South Korea, and the United States that has a 20-year expiration date in 2033, and one with an issued patent in China and pending

applications in Australia, Brazil, Canada, China, Europe, India, Japan, Russia, Singapore, South Korea, and the United States that has a 20-year expiration date in 2033.

Certain synthetic methods and/or reagents are protected by families that we own, which have issued patents in Australia, China, Europe, Japan, Mexico, and Singapore and pending applications in Australia, Brazil, Canada, Chile, China, Europe, India, Indonesia, Israel, Japan, Mexico, Russia, Singapore, South Africa, South Korea and the United States, and have 20-year expiration dates in 2030 and 2032, respectively.

We also own or co-own with either the University of Tokyo or Shin Nippon Biomedical Laboratories, Ltd. certain filings that are directed to certain methods and/or reagents for synthesizing oligonucleotides. These include issued patents in the United States, Europe and Japan, and pending applications in Europe, Hong Kong, Japan and/or the United States; their 20-year expiration dates fall in 2030 and 2031.

Stereochemically Pure Oligonucleotide Compositions

Certain of our patent filings protect stereochemically pure compositions, particularly of therapeutically relevant oligonucleotides. Some such filings are directed to compositions whose oligonucleotides are characterized by particular patterns of chemical modification (including modifications of bases, sugars and/or internucleotidic linkages) and/or of internucleotidic linkage stereochemistry. Specific compositions designed for use in the treatment of particular diseases (e.g., HD, etc.) were also described. One such family that we own is pending in Australia, Brazil, Canada, Chile, China, Europe, Hong Kong, India, Indonesia, Israel, Japan, Mexico, Russia, Singapore, South Africa, South Korea, and the United States, and has a 20-year term extending into 2033; another that we own is pending in Australia, Brazil, Canada, Chile, China, Europe, India, Indonesia, Israel, Japan, Malaysia, Mexico, New Zealand, Russia, Singapore, South Africa, South Korea, and the United States, and has a 20-year term extending into 2035. This latter family includes data demonstrating key valuable attributes of particular stereochemically pure oligonucleotide compositions that act as antisense agents.

We also own or co-own with Shin Nippon Biomedical Laboratories, Ltd. various patent families that relate to stereochemically pure oligonucleotide adjuvant compositions. These include pending filings in Australia, Brazil, Canada, China, Europe, India, Israel, Japan, Mexico, Russia, Singapore, South Korea, the United Arab Emirates, and the United States, and have 20-year terms extending to 2033 to 2035.

Filings that protect compositions are also directed to methods of using such compositions, for example, in the treatment of particular diseases. We also own patent families that relate to stereochemically pure oligonucleotide compositions for treating certain diseases, including HD.

Future Filings

We maintain a thoughtful and ambitious program for developing and protecting additional intellectual property, including new synthetic methodologies and reagents. We also intend to prepare and submit patent filings specifically directed to protecting individual product candidates and their uses as we finalize leads and collect relevant data, which is expected to include comparison data confirming novel and/or beneficial attributes of our product candidates.

Singapore Intellectual Property Law

Section 34 of the Singapore Patents Act provides that a person residing in Singapore is required to obtain written authorization from the Singapore Registrar of Patents before filing an application for a patent for an invention outside of Singapore, unless all of the following conditions have been satisfied: (a) the person has filed an application for a patent for the same invention in the Singapore Registry of Patents at least two months before the filing of the patent application outside Singapore, and (b) the Singapore Registrar of Patents has not, in respect of this patent application, given directions to prohibit or restrict the publication of information contained in the patent application or its communication to any persons or description of persons pursuant to Section 33 of the Singapore Patents Act, or if the Singapore Registrar of Patents has given any such directions, all such directions have been revoked. A violation of Section 34 is a criminal offense punishable by a fine not exceeding S$5,000, or imprisonment for a term not exceeding two years, or both. There have been some instances where we have undertaken filings outside of Singapore without first obtaining written authorization from the Singapore Registrar of Patents. When this has happened in the past, we have notified the Registrar and the Registrar has offered a compound of the offences against payment of a sum of S$50 in each of these cases. Under Singapore law, the Registrar has discretion to offer a compound of such offences against payment of a sum of money of up to S$2,000.

Competition

The pharmaceutical marketplace is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our expertise in nucleic acid therapeutics, scientific knowledge and intellectual property estate 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. Not only must we compete with other companies that are focused on nucleic acid therapeutics, but any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

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

Huntington's Disease

There are no approved treatments available to slow the progression of Huntington's disease. We believe, based on publicly available information, that Ionis Pharmaceuticals and Roche (Phase 1/2) and Sangamo Biosciences (preclinical) are developing therapies that directly target the *huntingtin* RNA and that uniQure (preclinical) and Voyager (preclinical) are developing an AAV-delivered gene therapy. A number of other companies are developing drugs to treat symptoms associated with Huntington's disease, including Auspex Pharmaceuticals and Teva Pharmaceutical Industries (which have submitted a New Drug Application ("NDA"), to the FDA), Prana Biotechnology (Phase 2), Siena Biotech (Phase 2), Raptor Pharmaceuticals (Phase 2), Omeros Corporation (Phase 2), Pfizer (Phase 2) and Ipsen (Phase 2), among others.

Duchenne Muscular Dystrophy

Sarepta Therapeutics' Exondys 51 (eteplirsen), an exon skipping nucleic acid therapeutic, was approved by the FDA for the treatment of DMD in the United States in September 2016. The FDA concluded that the data submitted demonstrated an increase in dystrophin production that is reasonably likely to predict clinical benefit in some patients with DMD who have a confirmed mutation of the dystrophin gene amenable to exon 51 skipping. No clinical benefit of Exondys 51 has been established. Thus, in accordance with the U.S. accelerated approval regulations, the FDA is requiring Sarepta to conduct a clinical trial to verify and describe the drug's clinical benefit. The required study is designed to assess whether Exondys 51 improves motor function of DMD patients with a confirmed mutation of the dystrophin gene amenable to exon 51 skipping. If the trial fails to verify clinical benefit, the FDA could initiate proceedings to withdraw approval of the drug.

In addition, we believe, based on publicly available information, that a number of other companies, including Summit Therapeutics (Phase 2) and Catabasis (Phase 2), are developing drugs that can alter the progression of the disease in patients. For PTC Therapeutics, conditional market authorization has been granted in Europe for TRANSLARNA (ataluren) for the treatment of nonsense mutation DMD for ambulatory patients who are 5 years or older. In March 2017, the FDA acknowledged the filing over protest of PTC's NDA for TRANSLARNA. FDA granted standard review and assigned a PDUFA date of October 24, 2017. BioMarin Pharmaceutical's drisapersen is an exon skipping nucleic acid therapeutic candidate for DMD for which the FDA issued a complete response letter in January 2016 indicating that the review cycle was complete and that the NDA was not ready for approval in its present form.

In addition, symptomatic treatments for DMD include corticosteroids and physical and respiratory therapy in DMD patients to slow the decline in muscle strength and to prolong ambulation and respiratory function. In February 2017, the FDA approved Emflaza (deflazacort), the first coticosteriod for the treatment of DMD, in the United States.

Government Regulation

FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Food Drug and Cosmetic Act ("FDCA"), and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable FDA or other requirements may subject a company to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications,

a clinical hold, warning letters, recall or seizure of products, partial or total suspension of production, withdrawal of the product from the market, injunctions, fines, civil penalties or criminal prosecution.

FDA approval is required before any new drug, such as a new molecular or chemical entity, or a new dosage form, new use or new route of administration of a previously approved product, can be marketed in the United States. The process required by the FDA before a new drug product may be marketed in the United States generally involves:

- completion of preclinical laboratory and animal testing in compliance with applicable FDA good laboratory practice regulations and other requirements ("GLPs");
- submission to the FDA of an Investigational New Drug ("IND") for human clinical testing which must become effective before human clinical trials may begin in the United States;
- approval by an independent institutional review board ("IRB"), at each site where a clinical trial will be performed before the trial may be initiated at that site;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices ("GCPs"), to establish safety and substantial evidence of effectiveness of the proposed product candidate for each intended use;
- thorough characterization of the product candidate and establishment of acceptable standards to assure its purity, identity, strength, quality, and stability in compliance with current good manufacturing practices ("cGMPs");
- satisfactory completion of an FDA pre-approval inspection of the facility or facilities at which the product is manufactured to assess compliance with cGMPs;
- satisfactory completion of an FDA pre-approval inspection of a clinical trial site(s) or contract research organization responsible for conduct of key clinical trials in accordance with GCP;
- submission to the FDA of a new drug application ("NDA"), which must be accepted for filing by the FDA;
- completion of an FDA advisory committee review, if applicable;
- payment of user fees, if applicable; and
- FDA review and approval of the NDA.

The manufacturing development, preclinical and clinical testing, and review process requires substantial time, effort and financial resources. Manufacturing development includes laboratory evaluation of product chemistry, formulation, development of manufacturing and control procedures, evaluation of stability, and the establishment of procedures to ensure continued product quality.

Preclinical tests include animal studies to assess the toxicity and other safety characteristics of the product candidate, as well as other important aspects of drug pharmacology. The results of preclinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol and other information, are submitted as part of an IND to the FDA. Preclinical testing will often continue after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold. In such a case, the IND sponsor must resolve all outstanding concerns before the clinical trial can begin. As a result, our submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development, or if changes are made in trial design. Even if the IND becomes effective and the trial proceeds without initial FDA objection, the FDA may stop the trial at a later time if it has concerns, such as if unacceptable safety risks arise.

Further, an independent IRB at each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and informed consent information for subjects before the trial commences at that site and it must perform an ongoing review of the research on an annual basis until the trial is completed. The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk or that the trials are not being conducted in accordance with GCPs, and an IRB may also suspend a clinical trial at its site for similar reasons.

Clinical trials involve the administration of the product candidate to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Sponsors of clinical trials generally must register and report, at the NIH-maintained website clinicaltrials.gov, key parameters of a clinical trial. For purposes of an NDA submission, human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

- ***Phase 1.*** The product is initially introduced into healthy human subjects or patients and tested for safety, dose tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early indication of its effectiveness.
- ***Phase 2.*** The product is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted indications and to determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more extensive clinical trials.
- ***Phase 3.*** These are commonly referred to as pivotal studies. When Phase 2 evaluations demonstrate that a dose range of the product appears to be effective and has an acceptable safety profile, trials are undertaken in larger patient populations to further evaluate dosage, to obtain substantial evidence of clinical efficacy and safety, generally at multiple, geographically-dispersed clinical trial sites, to establish the overall risk-benefit relationship of the product and to provide adequate information for approval of the product.
- ***Phase 4.*** In some cases, the FDA may condition approval of an NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials to further assess the product's safety and effectiveness after NDA approval. Such post-approval trials are typically referred to as Phase 4 studies.

The results of product development, preclinical studies and clinical trials are submitted to the FDA as part of an NDA. NDAs must also contain extensive information relating to the product's pharmacology, chemistry, manufacturing and controls and proposed labeling, among other things.

For some products, the FDA may require a risk evaluation and mitigation strategy ("REMS"), which could include measures imposed by the FDA such as programs to communicate risk outside of labeling, prescribing restrictions, or certain restrictions on distribution and use.

Under federal law, the submission of most NDAs is subject to a substantial application user fee, and the manufacturer and/or sponsor under an approved NDA are also subject to annual product and establishment user fees. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. Any resubmitted application is also subject to 60-day review before the FDA accepts it for filing.

Once the submission has been accepted for filing, the FDA begins an in-depth review. Under the PDUFA the FDA agrees to specific performance goals for NDA review time through a two-tiered classification system, Standard Review and Priority Review. Standard Review for an NDA for a new molecular entity ("NME") has a goal of being completed within a ten-month timeframe from FDA filing of the application. A Priority Review designation is given to products intended for serious conditions that provide a significant improvement in safety or effectiveness, such as providing a treatment where no adequate therapy exists. The goal for completing a Priority Review for an NME NDA is six months from filing.

The review process may be extended by the FDA by 3 months from the goal date to consider certain information or obtain clarification regarding information already provided in the submission. The FDA may refer applications for novel products or products which present difficult questions of safety or efficacy to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA may inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP. The FDA may also inspect one or more of the clinical sites where pivotal trials were conducted in order to ensure compliance with GCP and the integrity of the study data.

After the FDA evaluates the NDA it may issue an approval letter or a Complete Response Letter ("CRL"), to indicate that the review cycle for an application is complete and that the application is not ready for approval. CRLs outline the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when the deficiencies have been addressed to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications.

The FDA may withdraw product approval if ongoing regulatory requirements are not met or if safety problems are identified after the product reaches the market. In addition, the FDA may require post-approval testing, including Phase 4 studies, and surveillance programs to monitor the effect of approved products which have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. Products may be marketed only for the approved indications and in accordance with the provisions of the approved label, and, even if the FDA approves a product, the FDA may limit the approved indications for use for the product or impose other conditions, including labeling or distribution restrictions or other risk- management mechanisms, such as a Boxed Warning, which highlights a serious safety concern that should be mitigated under a REMS program. Further, if there are any modifications to the product, including changes in indications, labeling, or manufacturing processes or facilities, a company is generally required to submit and obtain FDA approval of a supplemental NDA, which may require the company to develop additional data or conduct additional preclinical studies and clinical trials.

Post-Approval Requirements

Once an NDA is approved, a product will be subject to continuing regulation by the FDA, including, among other things, requirements relating to safety surveillance and adverse event reporting, periodic reporting, continued cGMP compliance and quality oversight, compliance with post-marketing commitments, recordkeeping, advertising and promotion, and reporting manufacturing and labeling changes, as applicable.

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 some state agencies, and are subject to periodic unannounced inspections by the FDA for assessment of compliance with cGMPs. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction, and sometimes notification of, any deviations from cGMP. These regulations impose reporting and documentation requirements on the sponsor and any third-party manufacturers that we 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. Discovery of previously unknown problems with a product, including adverse events of unlisted severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements such as noncompliance with cGMP or failure to correct previously identified inspection findings, may result in, among other things:

- issuance of field alerts, restrictions on the marketing or manufacturing of the product, product recalls, or complete withdrawal of the product from the market;
- fines, warning letters or holds on clinical trials using the product or other products manufactured at the same facility;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions, consent decrees, 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. While physicians may generally prescribe a drug for off label uses, manufacturers may only promote the drug in accordance with the data provided in the approved product 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 promoted false and misleading information about the product may be subject to significant liability, both at the federal and state levels.

The FDA has authority to require a Risk Evaluation and Mitigation Strategy (“REMS”), from manufacturers to ensure that the benefits of a drug or biological product outweigh its risks. In determining whether a REMS is necessary, the FDA may consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, the seriousness of known or potential adverse events, and whether the drug is a new molecular entity. If the FDA determines a REMS is necessary, the drug sponsor must agree to the REMS plan at the time of approval, or at a later date should significant new risk information come to light. A REMS may be required to include various elements, such as a medication guide, a communication plan to educate healthcare providers of the drug’s risks, limitations on who may prescribe or dispense the drug, or other elements to assure safe use that the FDA deems necessary to assure the benefits of use of the drug outweigh its risks. In addition, the REMS must include a timetable to assess the strategy, often at 18 months, three years, and seven years after the strategy’s approval. The FDA may also impose a REMS requirement on a drug already on the market if the FDA determines, based on new safety information, that a REMS is necessary to ensure that the drug’s benefits outweigh its risks.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition which is defined as one affecting fewer than 200,000 individuals in the United States or more than 200,000 individuals where there is no reasonable expectation that the product development cost will be recovered from product sales in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the drug and its potential orphan use will be disclosed publicly by the FDA; the posting will also indicate whether a drug is no longer designated as an orphan drug. More than one product candidate may receive an orphan drug designation for the same indication. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If an orphan drug-designated product subsequently receives FDA approval for the disease for which it was designed, the product will have an orphan-exclusive approval and be entitled to seven years of product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years. If a competitor obtains approval of the same drug, as defined by the FDA, or if our product candidate is determined to be the same drug as a competitor's product for the same indication or disease, the competitor's exclusivity could block the approval of our product candidate in the designated orphan indication for seven years, unless our product is demonstrated to be clinically superior to the competitor's drug.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our therapeutic candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for extension must be made prior to the expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application ("ANDA"), or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Other Healthcare Laws

Although we currently do not have any products on the market, we may be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and other countries in which we conduct our business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations, many of which may become more applicable to us if our product candidates are approved and we begin commercialization. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Healthcare Reform

Political, economic and regulatory influences are subjecting the healthcare industry in the United States to fundamental changes. There have been, and we expect there will continue to be, legislative and regulatory proposals to change the healthcare system in ways that could significantly affect our future business. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively the "ACA"), substantially changed the way healthcare is financed by both governmental and private insurers. The ACA was designed to expand coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, ACA expanded and increased industry rebates for drugs covered under Medicaid programs and made changes to the coverage requirements under the Medicare prescription drug benefit. We continue to evaluate the effect that ACA has or any potential changes to the ACA could have on our business. We expect that healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that may be charged for any of our product candidates, if approved. These and other potential legislative and regulatory changes could be made to governmental health programs that could significantly impact pharmaceutical companies and the success of our product candidates. ACA, as well as other federal, state and foreign healthcare reform measures that have been and may be adopted in the future, could harm our future revenues.

Pharmaceutical Coverage, Pricing, and Reimbursement

Sales of our products, when and if approved for marketing, will depend, in part, on the extent to which our products will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly reducing reimbursements for medical products, drugs and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Limited third-party reimbursement for our product candidates or a decision by a third-party payor not to cover our product candidates could reduce physician usage of our products once approved and have a material adverse effect on our sales, results of operations and financial condition.

Manufacturing Requirements

We and our third-party manufacturers must comply with applicable cGMP requirements. The cGMP requirements include requirements relating to, among other things, organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. The manufacturing facilities for our products must meet cGMP requirements to the satisfaction of the FDA pursuant to a pre-approval inspection before we can use them to manufacture commercial products. We and our third-party manufacturers are also subject to periodic unannounced inspections of facilities by the FDA and other authorities, including procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations. Failure to comply with statutory and regulatory requirements subjects a manufacturer to possible legal or regulatory action, including, among other things, warning letters, voluntary corrective action, the seizure of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations, disgorgement of profits, and other civil and criminal penalties.

Other Regulatory Requirements

We are also subject to various laws and regulations regarding laboratory practices, the experimental use of animals, and the use and disposal of hazardous or potentially hazardous substances in connection with our research. In each of these areas, as above, the FDA has broad regulatory and enforcement powers, including, among other things, the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products, and withdraw approvals, any one or more of which could have an adverse effect on our ability to operate our business and generate revenues. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, operating results and financial condition.

Employees

As of December 31, 2016, we employed 96 full-time employees. A significant number of our management and professional employees have had prior experience with pharmaceutical, biotechnology or medical product companies. Management considers relations with our employees to be good.

Corporate Information

WAVE Life Sciences Pte. Ltd. (Registration No.: 201218209G) was incorporated under the laws of Singapore on July 23, 2012. On November 16, 2015, we closed our initial public offering. In connection with our initial public offering, on November 5, 2015, WAVE Life Sciences Pte. Ltd. converted from a private limited company to a public limited company known as WAVE Life Sciences Ltd. ("WAVE"). WAVE has three wholly-owned subsidiaries: WAVE Life Sciences USA, Inc. ("WAVE USA"), a Delaware corporation (formerly Ontorii, Inc.); WAVE Life Sciences Japan, Inc. ("WAVE Japan"), a company organized under the laws of Japan (formerly Chiralgen., Ltd.); and WAVE Life Sciences Ireland Limited ("WAVE Ireland"), a company organized under the laws of Ireland. Our therapeutic development research and development activities are conducted in WAVE USA's facilities and our process development research and development activities are conducted in WAVE Japan's facilities.

Our registered office is located at 8 Cross Street #10-00, PWC Building, Singapore 048424, and our telephone number at that address is +65 6236 3388. Our principal offices for WAVE USA are located at 733 Concord Avenue, Cambridge, MA 02138, and our telephone number at that address is +1-617-949-2900. WAVE Japan's office is located at OHBIC 108, 12-75 Suzaki Uruma-shi, Okinawa, 904-2234, Japan. Our registered office for WAVE Ireland is located at One Spencer Dock, North Wall Quay, Dublin 1, Ireland.

Information Available on the Internet

Our Internet website address is http://www.wavelifesciences.com. The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference. We make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through the "Investors & Media—Financial Information" section of our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the Securities and Exchange Commission, or SEC. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% shareholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. You can find, copy and inspect information we file at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's public reference room. You can review our electronically filed reports and other information that we file with the SEC on the SEC's website at http://www.sec.gov.

In addition, we regularly use our website to post information regarding our business and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors & Media," as a source of information about us.

Item 1A. Risk Factors.

You should carefully consider the following risk factors, in addition to the other information contained in this Annual Report on Form 10-K, including the section of this report titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and related notes. If any of the events described in the following risk factors and the risks described elsewhere in this Annual Report on Form 10-K occurs, our business, operating results and financial condition could be seriously harmed and the trading price of our ordinary shares could decline. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this Annual Report on Form 10-K.

Risks Related to Our Financial Results and Capital Requirements

We are a preclinical genetic medicines company with a history of losses, and we expect to continue to incur losses for the foreseeable future, and we may never achieve or maintain profitability.

We are a preclinical genetic medicines company and have incurred significant operating losses since our incorporation in 2012. Our net loss was $55.4 million, $19.2 million and $5.2 million for the fiscal years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016 and December 31, 2015, we had an accumulated deficit of $90.5 million and $35.1 million, respectively. To date, we have not generated any product revenue. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We have no products on the market, we have not initiated clinical development of any product candidates and expect that it will be many years, if ever, before we have a product candidate ready for commercialization.

We have not generated, and do not expect to generate, any product revenue for the foreseeable future, and we expect to continue to incur significant operating losses for the foreseeable future due to the cost of research and development, developing manufacturing

capabilities, preclinical studies and clinical trials and the regulatory review process for product candidates. The amount of future losses is uncertain. To achieve profitability, we must successfully develop product candidates, obtain regulatory approvals to market and commercialize product candidates, manufacture any approved product candidates on commercially reasonable terms, establish a sales and marketing organization or suitable third-party alternatives for any approved product and raise sufficient funds to finance our business activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause our shareholders to lose all or part of their investment.

We will require substantial additional funding, which may not be available on acceptable terms, or at all.

We have used substantial funds to develop our programs and proprietary drug development platform and will require substantial funds to conduct further research and development, including preclinical studies and clinical trials of our product candidates, seek regulatory approvals for our product candidates and manufacture and market any products that are approved for commercial sale. We expect that the capital resources available to us as of December 31, 2016, along with anticipated milestone payments under our existing collaboration, will fund our operating expenses and capital expenditure requirements into 2019. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. Our monthly spending levels vary based on new and ongoing development and corporate activities. Because we cannot be certain of the length of time or activities associated with successful development and commercialization of our product candidates, we are unable to estimate the actual funds we will require to develop and commercialize them.

We do not expect to realize any appreciable revenue from product sales or royalties in the foreseeable future, if at all. Our revenue sources will remain extremely limited unless and until our product candidates complete clinical development and are approved for commercialization and successfully marketed. To date, we have primarily financed our operations through sales of our securities and third party collaborations. We intend to seek additional funding in the future through collaborations, public or private equity offerings or debt financings, credit or loan facilities or a combination of one or more of these financing sources. On January 4, 2017, we filed a universal shelf registration statement on Form S-3, which was declared effective by the SEC on February 6, 2017, on which we registered for sale up to $500.0 million of any combination of our ordinary shares, debt securities, warrants, rights, purchase contracts and/or units from time to time and at prices and on terms that we may determine. This registration statement will remain in effect for up to three years from the date it was declared effective. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all. If we raise additional funds by issuing equity or convertible debt securities, our shareholders will suffer dilution and the terms of any financing may adversely affect the rights of our shareholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing shareholders. Debt financing, if available, may involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of equity securities received any distribution of corporate assets.

If we are unable to obtain funding on a timely basis or on acceptable terms, we may have to delay, limit or terminate our research and development programs and preclinical studies or clinical trials, if any, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our product candidates or technologies that we would otherwise pursue on our own.

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

We are a preclinical genetic medicines company with limited operating history. We commenced active operations in 2012. Our operations to date have been limited to organizing and staffing our company, research and development activities, business planning and raising capital. All of our therapeutic programs are still in the preclinical development stage. We expect to initiate six development programs by the end of 2018. These programs include our three most advanced programs, which are in HD and DMD, and we expect to select three additional development candidates by the end of 2017. We have not yet demonstrated our ability to initiate or successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Typically, it takes many years to develop one new medicine from the time it is discovered to when it is available for treating patients. Further, drug development is a capital-intensive and highly speculative undertaking that involves a substantial degree of risk. You should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development, especially preclinical biotechnology companies such as ours. Any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

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

Our management has broad discretion over the use of the net proceeds from equity offerings and the proceeds may not be used effectively.

Our management has broad discretion as to the use of the net proceeds from our equity offerings and could use them for purposes other than those contemplated at the time of such offerings. It is also possible that the proceeds from any of our equity offerings will be invested in a way that does not yield a favorable, or any, return for us.

Risks Related to the Discovery, Manufacturing, Development and Commercialization of Our Product Candidates

The approach we are taking to discover and develop nucleic acid therapeutics is novel and may never lead to marketable products.

We have concentrated our efforts and research and development activities on nucleic acid therapeutics and our synthetic chemistry drug development platform. Our future success depends on the successful development of such therapeutics and the effectiveness of our platform. The scientific discoveries that form the basis for our efforts to discover and develop new drugs, including our discoveries about the relationships between oligonucleotide stereochemistry and pharmacology, are relatively new. The scientific evidence to support the feasibility of developing drugs based on these discoveries is limited. Skepticism as to the feasibility of developing nucleic acid therapeutics generally has been, and may continue to be, expressed in scientific literature. In addition, decisions by other companies with respect to their oligonucleotides development efforts may increase skepticism in the marketplace regarding the potential for oligonucleotides.

Relatively few nucleic acid therapeutic product candidates have been tested on humans, and a number of clinical trials for such therapeutics conducted by other companies have not been successful. Only four nucleic acid therapeutics have received regulatory approval. The drugs we are studying may not demonstrate in patients the pharmacological properties ascribed to them in laboratory studies, and they may interact with human biological systems in unforeseen, ineffective or harmful ways. If our nucleic acid product candidates prove to be ineffective, unsafe or commercially unviable, our entire platform and pipeline would have little, if any, value, which would substantially harm our business, financial condition, results of operations and prospects.

Because we are developing nucleic acid therapeutics, which are considered a relatively new class of drugs, there is increased risk that the outcome of our future clinical trials will not be sufficient to obtain regulatory approval.

The U.S. Food and Drug Administration ("FDA"), has relatively limited experience with nucleic acid therapeutics, which may increase the complexity, uncertainty and length of the regulatory review process for our product candidates. To date, the FDA has approved only four nucleic acid therapeutics for marketing and commercialization, and the FDA and its foreign counterparts have not yet established any definitive policies, practices or guidelines specifically in relation to these drugs. The lack of policies, practices or guidelines specific to nucleic acid therapeutics may hinder or slow review by the FDA of any regulatory filings that we may submit. Moreover, the FDA may respond to these submissions by defining requirements we may not have anticipated. Such responses could lead to significant delays in the development of our product candidates. In addition, because there may be approved treatments for some of the diseases for which we may seek approval, in order to receive regulatory approval, we may need to demonstrate through clinical trials that the product candidates we develop to treat these diseases, if any, are not only safe and effective, but safer or more effective than existing products. Furthermore, in recent years, there has been increased public and political pressure on the FDA with respect to the approval process for new drugs, and the FDA's standards, especially regarding drug safety, appear to have become more stringent. As a result of the foregoing factors, we may never receive regulatory approval to market and commercialize any product candidate.

Even if we obtain regulatory approval, the approval may be for disease indications or patient populations that are not as broad as we intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We may be required to perform additional or unanticipated clinical trials to obtain regulatory approval or be subject to additional post-marketing studies or other requirements to maintain such approval. As a result, we may never succeed in developing a marketable product, we may not become profitable and the value of our ordinary shares could decline.

All of our therapeutic programs are in the preclinical development stage. Our preclinical studies and clinical trials may not be successful. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We are very early in our development efforts, and all of our drug candidates are still in preclinical development. We have identified lead product candidates for three of our programs. We have no products on the market or in clinical development. We have invested a significant portion of our efforts and financial resources in the identification and preclinical development of oligonucleotides and the

development of our platform. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates. Our success will depend on several factors, including the following:

- successfully completing preclinical studies and clinical trials;
- successful process development and manufacturing campaigns conducted in accordance with cGMP;
- receiving regulatory approvals from applicable regulatory authorities to market our product candidates;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;
- acceptance of the products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies; and
- a continued acceptable safety profile of the products following approval.

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

We may not be able to conduct clinical trials successfully due to various process-related factors that could negatively impact our business plans.

A successful start and completion of any of our clinical trials, within timeframes consistent with our business plans, is dependent on various factors, which include, but are not limited to, our ability to retain and recruit employees, contractors or consultants with the required level of knowledge and experience; retain and recruit a sufficient number of patients necessary to conduct a clinical trial, which is a function of many factors, including the proximity of participants to clinical sites, the size of the relevant population, the eligibility criteria for the trial, side effects from treatments, the existence of competing clinical trials, the involvement of patient advocacy groups, the availability of new or alternative treatments, lack of efficacy, personal issues and ease of participation; ensure adherence to trial designs and protocols agreed upon and approved by regulatory authorities and applicable regulatory and legal guidelines; manage or resolve unforeseen adverse side effects during a clinical trial; execute clinical trial designs and protocols approved by regulatory authorities without deficiencies; timely and effectively contract with (under reasonable terms), manage and work with investigators, institutions, hospitals and the contract research organizations ("CROs") involved in the clinical trial; negotiate contracts and other related documents with clinical trial parties and institutional review boards ("IRBs"), such as informed consents, CRO agreements and site agreements, which can be subject to extensive negotiations that could cause significant delays in the clinical trial process, with terms possibly varying significantly among different trial sites and CROs and possibly subjecting us to various risks; and conduct the clinical trials in a cost-effective manner, including management of foreign currency risk in clinical trials conducted in foreign jurisdictions and cost increases due to unforeseen or unexpected complications such as enrollment delays, or needing to outsource certain functions during the clinical trial. If we are not able to manage the clinical trial process sufficiently, our business plans could be delayed or be rendered unfeasible for us to execute within our planned or required time frames, or at all.

If we cannot successfully manufacture our product candidates for our research and development and preclinical activities, or manufacture sufficient amounts of our product candidates to meet our anticipated clinical requirements, our business may be materially harmed.

In order to develop our product candidates, apply for regulatory approvals and commercialize our product candidates, we will need to develop, contract for, or otherwise arrange for the necessary manufacturing capabilities. In September 2016, we entered into a lease for a manufacturing facility of approximately 90,000 square feet in Lexington, Massachusetts, primarily to build out and conduct certain of our cGMP manufacturing activities, as well as to provide additional laboratory and office space to support our growth. However, we have never built a manufacturing facility, have limited manufacturing experience and resources and must incur significant costs to develop this expertise internally. There can be no assurance that our internal manufacturing capabilities will be available in time to support our clinical development or produce sufficient quantities to meet clinical trial demands.

We manufacture limited quantities of preclinical trial materials ourselves, but otherwise we currently rely on third party contract manufacturing organizations ("CMOs") to manufacture the oligonucleotides required for many preclinical studies and any clinical trials that we initiate. There are a limited number of manufacturers that supply oligonucleotides. There are risks inherent in pharmaceutical manufacturing that could affect the ability of our CMOs to meet our delivery time requirements or provide adequate amounts of material to meet our needs. Included in these risks are potential synthesis and purification failures and/or contamination during the manufacturing process, as well as other issues with the CMOs facility and ability to comply with the applicable

manufacturing requirements, which could result in unusable product and cause delays in our manufacturing timelines and ultimately delay our clinical trials, as well as result in additional expense to us. To manufacture our oligonucleotides, we rely on third parties to supply the required raw materials. We will likely need to secure alternative suppliers for these starting materials, and such alternative suppliers are limited and may not be readily available, or we may be unable to enter into agreements with them on reasonable terms and in a timely manner. Additionally, our cost of goods development is at an early stage. The actual cost to manufacture and process our product candidates could be greater than we expect and could materially and adversely affect the commercial viability of our product candidates.

Our product candidates and the manufacture of our product candidates is complex and we may encounter difficulties in production, particularly with respect to process development or scaling-up of our manufacturing capabilities.

Our product candidates are nucleic acids and the process of manufacturing our product candidates is complex, highly-regulated and subject to multiple risks. The manufacture of our product candidates involves complex processes. We also may make changes to our manufacturing process at various points during development, and even after commercialization, for various reasons, such as controlling costs, achieving scale, decreasing processing time, increasing manufacturing success rate, or other reasons. Such changes carry the risk that they will not achieve their intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of future clinical trials, or the performance of the product, once commercialized. In some circumstances, changes in the manufacturing process may require us to perform *ex vivo* comparability studies and to collect additional data from patients prior to undertaking more advanced clinical trials. For instance, changes in our process during the course of clinical development may require us to show the comparability of the product used in earlier clinical phases or at earlier portions of a trial to the product used in later clinical phases or later portions of the trial. We may also make further changes to our manufacturing process before or after commercialization, and such changes may require us to show the comparability of the resulting product to the product used in the clinical trials using earlier processes. We may be required to collect additional clinical data from any modified process prior to obtaining marketing approval for the product candidate produced with such modified process. If clinical data are not ultimately comparable to that seen in the earlier trials in terms of safety or efficacy, we may be required to make further changes to our process and/or undertake additional clinical testing, either of which could significantly delay the clinical development or commercialization of the associated product candidate.

Although we have hired, and are continuing to hire, employees with experience in manufacturing nucleic acid therapeutics, we have no experience as a company manufacturing product candidates for use in clinical trials and no experience as a company manufacturing product candidates for commercial supply. We may never be successful in manufacturing product candidates in sufficient quantities or with sufficient quality for clinical or commercial use. Even if we are successful in developing our manufacturing capabilities sufficient for clinical and commercial supply, our manufacturing capabilities could be affected by cost-overruns, unexpected delays, equipment failures, labor shortages, operator error, natural disasters, availability of qualified personnel, difficulties with logistics and shipping, problems regarding yields or stability of product, contamination or other quality control issues, power failures, and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

Furthermore, if contaminants are discovered in our supply of our product candidates or in our manufacturing facilities or those of our CMOs, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that any stability failures or other issues relating to the manufacture of our product candidates will not occur in the future. Additionally, we and our CMOs may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If we or our CMOs were to encounter any of these difficulties, our ability to provide our product candidate to patients in clinical trials, or to provide product for treatment of patients once approved, would be jeopardized.

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

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both regulatory approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may 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.

Any product candidates we develop may fail in development or be delayed to a point where they do not become commercially viable.

Before obtaining regulatory approval for the commercial distribution of any of our product candidates, we must conduct, at our own expense, extensive preclinical studies and clinical trials to demonstrate the safety and efficacy in humans of our product candidates. Preclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome, and the historical failure rate for drugs in preclinical and clinical development is high. We currently have a number of therapeutic programs in the preclinical development stage. However, we may not be able to further advance any product candidates through clinical trials. In addition, we, the FDA or comparable foreign regulatory authorities, or an IRB, or similar foreign review board or ethics committee, may suspend clinical trials of a product candidate at any time for various reasons, including if we or they believe the healthy volunteer subjects or patients participating in such trials are being exposed to unacceptable health risks. Among other reasons, unacceptable side effects or other more serious adverse effects of a product candidate in healthy volunteer subjects or patients in a clinical trial could result in the FDA or comparable foreign regulatory authorities suspending or terminating the trial and refusing to approve a particular product candidate for any or all indications of use.

Clinical trials also require the review, oversight and approval of IRBs, which review the clinical protocols for investigations that will be conducted at their institutions in order to protect the rights and welfare of human subjects. Inability to obtain or delay in obtaining IRB approval can prevent or any delay the initiation and completion of clinical trials at particular sites. Furthermore, failure to provide information to the IRB as required throughout the study, such as emergent safety reports and annual updates, may result in suspension of the IRB's approval of the trial. Our product candidates may encounter problems during clinical trials that will cause us or regulatory authorities to delay, suspend or terminate these trials, or that will delay or confound the analysis of data from these trials. If we experience any such problems, we may not have the financial resources to continue development of the product candidate that is affected, or development of any of our other product candidates. We may also lose, or be unable to enter into, collaborative arrangements for the affected product candidate and for other product candidates we are developing.

The development of one or more of our product candidates can fail at any stage of testing. We may experience numerous unforeseen events during, or as a result of, preclinical studies and clinical trials that could delay or prevent regulatory approval or our ability to commercialize our product candidates, including:

- our preclinical studies or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials, or we may abandon projects that we had expected to be promising;
- delays in filing clinical trial applications or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators or IRBs in order to commence a clinical trial at a prospective trial site, or their suspension or termination of a clinical trial once commenced;
- conditions imposed on us by the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- problems in obtaining or maintaining IRB approval of trials;
- delays in enrolling patients or volunteers into clinical trials, and variability in the number and types of patients available for clinical trials;
- high drop-out rates for patients in clinical trials;
- negative or inconclusive results from our clinical trials or the clinical trials of others for product candidates similar to ours;
- inability to consistently manufacture, inadequate supply, or unacceptable quality of product candidate materials or other materials necessary for the conduct of our clinical trials;
- greater than anticipated clinical trial costs;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- poor or disappointing effectiveness of our product candidates during clinical trials;
- unfavorable FDA or other regulatory agency inspection and review of a manufacturing or clinical trial site or other records relating to the clinical investigation;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- governmental or regulatory delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our product candidates in particular;

or

- varying interpretations of data by the FDA and similar foreign regulatory agencies.

If the development of any of our product candidates fails or is delayed to a point where such product candidate is no longer commercially viable, our business may be materially harmed.

Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials.

If we enter into clinical trials, the results from preclinical studies or early clinical trials of a product candidate may not predict the results that will be obtained in subsequent subjects or in subsequent clinical trials of that product candidate or any other product candidate. The design of a clinical trial can determine whether its results will support approval of a product candidate and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have no experience in designing clinical trials and we may be unable to design and execute a clinical trial to support regulatory approval of our product candidates. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Product candidates that seemingly perform satisfactorily in preclinical studies may nonetheless fail to obtain regulatory approval. There is a high failure rate for drugs proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could negatively affect our business and operating results.

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

Clinical trials of a new product candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the product candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the patient population, the age and condition of the patients, the stage and severity of disease, the nature and requirements of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, and the eligibility criteria for the clinical trial. Delays or difficulties in patient enrollment or difficulties retaining trial participants, including as a result of the availability of existing or other investigational treatments, can result in increased costs, longer development times or termination of a clinical trial.

In addition, our success may depend, in part, on our ability to identify patients who qualify for our clinical trials, or are likely to benefit from any medicines that we may develop, which will require those potential patients to undergo a screening assay for the presence or absence of a particular genetic sequence. For example, in HD, we are advancing WVE-120101 and WVE-120102, targeting SNPs associated with the mutant alleles of the huntingtin gene. Each SNP has a particular demographic distribution, and defines a subpopulation of patients suited for allele-specific interventions. More than two-thirds of the HD patient population possess one of the two most common SNPs. We have developed a novel screening assay that is intended to identify whether a patient has the particular SNP that our product candidate is targeting, however, we have limited experience in developing screening assays to support patient identification for clinical trials. If we, or any third parties that we engage to assist us, are unable to successfully identify patients with the appropriate SNPs that we are targeting, or experience delays in doing so, then we may not realize the full commercial potential of any product candidates we develop.

We may be unable to obtain regulatory approval in the United States or foreign jurisdictions and, as a result, be unable to commercialize our product candidates and our ability to generate revenue will be materially impaired.

Our product candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, quality, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing and distribution of drugs. Rigorous preclinical studies and clinical trials and an extensive regulatory approval process are required to be successfully completed in the United States and in many foreign jurisdictions before a new drug can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the product candidates we may develop will obtain the regulatory approvals necessary for us or our collaborators to begin selling them.

We have no experience in conducting and managing the human clinical trials necessary to obtain regulatory approvals, including approval by the FDA or other foreign agencies, or otherwise advancing product candidates through the regulatory approval process. The time required to obtain FDA and other approvals is unpredictable but typically takes many years following the commencement of clinical trials, depending upon the type, complexity and novelty of the product candidate. The standards that the FDA and its foreign counterparts use when regulating companies such as ours are not always applied predictably or uniformly and can change. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

Any delay or failure in obtaining required approvals could adversely affect our ability to generate revenues from the particular product candidate for which we are seeking approval. Furthermore, any regulatory approval to market a product may be subject to limitations on the approved uses for which we may market the product or the labeling or other restrictions. In addition, the FDA has the authority to require a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval, which may impose further requirements or restrictions on the distribution or safe use of an approved drug, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients as specially defined by the indication statement or who meet certain safe-use criteria, and requiring treated patients to enroll in a registry, among other requirements. These limitations and restrictions may limit the size of the market for the product and affect reimbursement by third-party payors.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and payment. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Approval by the FDA does not ensure approval by comparable regulatory authorities outside the United States and vice versa.

We have been granted orphan drug designation in the United States for WVE-120101, but there can be no guarantee that we will maintain orphan status for this product candidate or receive orphan drug approval.

In 2016, we were granted orphan drug designation under the Orphan Drug Act by the FDA for our product candidate, WVE-120101 for the treatment of Huntington's disease. Subject to receiving approval from the FDA of an NDA, products granted orphan drug status are generally provided with seven years of marketing exclusivity in the U.S., meaning the FDA generally will not approve applications for other product candidates for the same orphan indication that contain the same active ingredient. Even if we are the first to obtain approval of an orphan product and are granted exclusivity in the United States, there are limited circumstances under which a later competitor product may be approved for the same indication during the seven-year period of marketing exclusivity, such as if the later product is shown to be clinically superior to our product or if we are not able to provide a sufficient quantity of the orphan drug.

We are not guaranteed to receive or maintain orphan status for our current or future product candidates, and if our product candidate that was granted orphan status were to lose its status as an orphan drug or the marketing exclusivity provided for it in the United States, our business and results of operations could be materially adversely affected. While orphan status for any of our products, if granted or maintained, would provide market exclusivity in the United States for the time period specified above, we would not be able to exclude other companies from manufacturing and/or selling products using the same active ingredient for the same indication beyond the exclusivity period applicable to our product on the basis of orphan drug status.

Even if we obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory oversight. If we fail to comply with continuing U.S. and foreign requirements, our approvals could be limited or withdrawn, we could be subject to other penalties, and our business would be seriously harmed.

Following any initial regulatory approval of any drugs we may develop, we will also be subject to continuing regulatory oversight, including the review of adverse drug experiences and safety data that are reported after our drug products are made commercially available. This would include results from any post-marketing studies or surveillance to monitor the safety and efficacy of the drug product required as a condition of approval or agreed to by us. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved uses for which the product may be marketed. Other ongoing regulatory requirements include, among other things, submissions of safety and other post-marketing information and reports, registration and listing, as well as continued maintenance of our marketing application, compliance with cGMP requirements and quality oversight, compliance with post-marketing commitments, and compliance with good clinical practice for any clinical trials that we conduct post-approval. Failure to comply with these requirements could result in criminal or civil penalties, recalls, or product withdrawals. In addition, we intend to conduct clinical trials for our product candidates and we intend to seek approval to market our product candidates in jurisdictions outside of the United States, and therefore will be subject to, and must comply with, regulatory requirements in those jurisdictions.

The FDA has significant post-market authority, including, for example, the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials for a variety of reasons. The FDA also has the authority to require a REMS plan after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug.

The manufacturer and manufacturing facilities we use to make our product candidates will also be subject to ongoing assessment of product quality, compliance with cGMP, and periodic inspection by the FDA and potentially other regulatory agencies. The discovery of any new or previously unknown problems with us or our third-party manufacturers, or our or their manufacturing processes or facilities, may result in the need for field alerts, product recalls, restrictions on the drug or manufacturer or facility, including withdrawal of the drug from the market. We may not have the ability or capacity to manufacture material at a broader commercial scale in the future. We may manufacture clinical trial materials or we may contract with a third party to manufacture these materials for us. Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured products ourselves, including reliance on the third-party manufacturer for regulatory compliance. Our product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review.

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

Even if we receive regulatory approval to market our product candidates, the market may not be receptive to our product candidates upon their commercial introduction, which will prevent us from becoming profitable.

Our product candidates are based upon new discoveries, technologies and therapeutic approaches. Key participants in pharmaceutical marketplaces, such as physicians, third-party payors and consumers, may not adopt a product intended to improve therapeutic results that is based on the technology employed by nucleic acid therapeutics. As a result, it may be more difficult for us to convince the medical community and third-party payors to accept and use our product, or to provide favorable reimbursement.

Other factors that we believe will materially affect market acceptance of our product candidates include:

- the timing of our receipt of any regulatory approvals, the terms of any approvals and the countries in which approvals are obtained;
- the ability to consistently manufacture our products within acceptable quality standards;
- the safety and efficacy of our product candidates, as demonstrated in clinical trials and as compared with alternative treatments, if any;
- the incidence, seriousness and severity of any side effects;
- relative convenience and ease of administration of our product candidates;
- the willingness of patients to accept potentially new routes of administration and their risk tolerance as it relates to potentially serious side effects;
- the success of our physician education programs;

- the availability of government and third-party payer coverage and adequate reimbursement;
- the pricing of our products, particularly as compared to alternative treatments; and
- availability of alternative effective treatments for the diseases that product candidates we develop are intended to treat and the relative risks, benefits and costs of those treatments.

In addition, our estimates regarding the potential market size may be materially different from what we currently expect at the time we commence commercialization, which could result in significant changes in our business plan and may significantly harm our results of operations and financial condition.

The pharmaceutical market is intensely competitive. If we are unable to compete effectively with existing drugs, new treatment methods and new technologies, we may be unable to commercialize successfully any drugs that we develop.

The pharmaceutical market is intensely competitive and rapidly changing. Many large pharmaceutical and biotechnology companies, academic institutions, governmental agencies and other public and private research organizations are pursuing the development of novel drugs for the same diseases that we are targeting or expect to target. Many of our competitors have:

- much greater financial, technical and human resources than we have at every stage of the discovery, development, manufacture and commercialization of products;
- more extensive experience in designing and conducting preclinical studies and clinical trials, obtaining regulatory approvals, and in manufacturing, marketing and selling pharmaceutical products;
- product candidates that are based on previously tested or accepted technologies;
- products that have been approved or are in late stages of development; and
- collaborative arrangements in our target markets with leading companies and research institutions.

We will face intense competition from drugs that have already been approved and accepted by the medical community for the treatment of the conditions for which we may develop drugs. We also expect to face competition from new drugs that enter the market. We believe a significant number of drugs are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop drugs. These drugs may be more effective, safer, less expensive, or marketed and sold more effectively, than any products we develop.

Our competitors may develop or commercialize products with significant advantages over any products we are able to develop and commercialize based on many different factors, including:

- the safety and effectiveness of our products relative to alternative therapies, if any;
- the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration;
- the timing and scope of regulatory approvals for these products;
- the availability and cost of manufacturing, marketing and sales capabilities;
- price;
- reimbursement coverage; and
- patent position.

Our competitors may therefore be more successful in commercializing their products than we are, which could adversely affect our competitive position and business. Competitive products may make any products we develop obsolete or noncompetitive before we can recover the expenses of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute on our business plan.

If we or our collaborators, manufacturers or service providers fail to comply with applicable healthcare laws and regulations, we or they could be subject to enforcement actions, which could affect our ability to develop, market and sell our products and may harm our reputation.

As a manufacturer of pharmaceuticals, we are currently or may in the future be subject to federal, state, local, and comparable foreign healthcare laws and regulations pertaining to such topics as fraud and abuse and patients' rights. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our products for which we obtain marketing approval. These laws and regulations include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and

willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for a healthcare item or service, or the purchasing, recommending, or ordering of an item or service, for which payment may be made under a federal healthcare program such as Medicare or Medicaid;

- the U.S. federal false claims and civil monetary penalties laws, including the civil False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting or causing to be presented, claims for payment by government-funded programs such as Medicare or Medicaid that are false or fraudulent, or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government;
- the U.S. federal Health Insurance Portability and Accountability Act ("HIPAA"), which imposes criminal and civil liability for, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA as amended by the Health Information Technology for Economic and Clinical Health ("HITECH"), Act, and its implementing regulations, which impose requirements relating to the privacy, security, and transmission of individually identifiable health information; and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;
- the U.S. federal Physician Payments Sunshine Act, which requires certain manufacturers of medical devices, biological products, medical supplies, and drugs for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare and Medicaid Services ("CMS"), all transfers of value, including consulting fees, travel reimbursements, research grants, and other payments or gifts with values over $10 made to physicians and teaching hospitals, and teaching hospitals, applicable manufacturers, and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members. Disclosure of such information is made by CMS on a publicly available website; and
- state and foreign laws comparable to each of the above federal laws, such as, for example: state anti-kickback and false claims laws applicable to commercial insurers and other non-federal payors; state laws that require pharmaceutical manufacturers to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws relating governing the privacy and security of health information, some which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, criminal prosecution, monetary damages, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, exclusion from participation in federal healthcare programs including Medicare and Medicaid, the imposition of a corporate integrity agreement with the Office of Inspector General of the Department of Health and Human Services, disgorgement, individual imprisonment, contractual damages, reputational harm, and diminished profits and future earnings, any of which could adversely affect our financial results and adversely affect our ability to operate our business. We intend to develop and implement a comprehensive corporate compliance program prior to the commercialization of our product candidates. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

If we or our collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our products successfully and could harm our reputation and lead to reduced acceptance of our products by the market. These enforcement actions include, among others:

- adverse regulatory inspection findings;
- warning and/or untitled letters;
- voluntary or mandatory product recalls or public notification or medical product safety alerts to healthcare professionals;
- restrictions on, or prohibitions against, marketing our products;
- restrictions on, or prohibitions against, importation or exportation of our products;
- suspension of review or refusal to approve pending applications or supplements to approved applications;
- exclusion from participation in government-funded healthcare programs;

- exclusion from eligibility for the award of government contracts for our products;
- suspension or withdrawal of product approvals;
- product seizures;
- injunctions;
- consent decrees; and
- civil and criminal penalties, up to and including criminal prosecution resulting in fines, exclusion from healthcare reimbursement programs and imprisonment.

Moreover, federal, state or foreign laws or regulations are subject to change, and while we, our collaborators, manufacturers and/or service providers currently may be compliant, that could change due to changes in interpretation, prevailing industry standards or other reasons.

Any drugs we develop may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, thereby harming our business.

Because our product candidates represent new approaches to the treatment of genetic-based diseases, we cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop. The regulations that govern marketing approvals, pricing and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. We are monitoring these regulations as several of our programs move into later stages of development, however, many of our programs are currently in the earlier stages of development and we will not be able to assess the impact of price regulations for a number of years. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product and negatively impact the revenues we are able to generate from the sale of the product in that country and potentially in other countries due to reference pricing.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement/payment for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Even if we succeed in bringing one or more products to the market, these products may not be considered medically necessary and/or cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis. We are unable at this time to determine their cost effectiveness or the likely level or method of reimbursement for our product candidates. Increasingly, third-party payors , such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts paid for pharmaceutical products. If the price we are able to charge for any products we develop, or the payments provided for such products, is inadequate in light of our development and other costs, our return on investment could be adversely affected.

We currently expect that any drugs we develop may need to be administered under the supervision of a physician on an outpatient basis. Under currently applicable U.S. law, certain drugs that are not usually self-administered (including injectable drugs) may be eligible for coverage under the Medicare Part B program if:

- they are incident to a physician’s services;
- they are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standards of medical practice; and
- they have been approved by the FDA and meet other requirements of the statute.

There may be significant delays in obtaining coverage for newly-approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to pay all or part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided and payment is adequate to cover all or a significant portion of the cost of our products. Therefore, coverage and adequate payment is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Moreover, eligibility for coverage does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement may be based on payments allowed for lower-cost drugs that are already reimbursed,

may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. However, no uniform policy requirement for coverage and reimbursement for drug products exists among third-party payors in the United States. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for new drugs that we develop and for which we obtain regulatory approval could adversely affect our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare and legislative and regulatory proposals to broaden the availability of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory changes in the healthcare system in the United States and other major healthcare markets have been proposed and/or adopted in recent years, and such efforts have expanded substantially in recent years. These developments have included prescription drug benefit legislation that was enacted in 2003 and took effect in January 2006, healthcare reform legislation enacted by certain states, and major healthcare reform legislation that was passed by Congress and enacted into law in the United States in 2010. These developments could, directly or indirectly, affect our ability to sell our products, if approved, at a favorable price.

In particular, in March 2010, the Patient Protection and Affordable Care Act (“ACA”), was signed into law. This legislation changed the system of healthcare insurance and benefits and was intended to broaden access to healthcare coverage, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose taxes and fees on the healthcare industry, impose health policy reforms, and control costs. This law also contains provisions that would affect companies in the pharmaceutical industry and other healthcare related industries by imposing additional costs and changes to business practices. Provisions affecting pharmaceutical companies included the following:

- Minimum rebates for drugs sold under the Medicaid Drug Rebate Program have increased, and the rebate requirement has been extended to drugs used in risk-based Medicaid managed care plans.
- The 340B Drug Pricing Program under the Public Health Service Act has been extended to require mandatory discounts for drug products sold to certain critical access hospitals, cancer hospitals and other covered entities.
- Pharmaceutical manufacturers are required to offer discounts off negotiated prices on applicable brand-name drugs to eligible beneficiaries who fall within the Medicare Part D coverage gap, commonly referred to as the “Donut Hole.”
- Pharmaceutical manufacturers are required to pay an annual non-tax deductible fee to the federal government based on each company’s market share of prior year total sales of branded products to certain federal healthcare programs, such as Medicare and Medicaid, and programs administered by the Department of Veterans Affairs or the Department of Defense. Since we expect our branded pharmaceutical sales to constitute a small portion of the total federal health program pharmaceutical market, we do not expect this annual assessment to have a material impact on our financial condition.
- 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.
- Expansion of eligibility criteria for Medicaid programs.
- A new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

At the time of filing this Annual Report on Form 10-K, Congress is trying to repeal most, if not all, of the ACA, and we cannot predict whether that effort will be successful or what healthcare reform initiatives may be adopted in the future. Additional federal and state legislative and regulatory developments are likely, and we expect ongoing initiatives in the United States to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop drug candidates.

Our ability to obtain services, reimbursement or funding from the federal government may be impacted by possible reductions in federal spending.

Other legislative changes have been proposed and adopted since ACA was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction

(Joint Select Committee) to recommend to Congress proposals in spending reductions. The failure of Congress to enact deficit reduction measures of at least $1.2 trillion for the years 2013 through 2021 triggered the legislation's automatic reduction to several government programs. These cuts included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect beginning on April 1, 2013, and will stay in effect through 2024 unless additional Congressional action is taken. Additionally, under the American Taxpayer Relief Act of 2012, which was enacted on January 1, 2013, the imposition of these automatic cuts was delayed until March 1, 2013. As required by law, President Obama issued a sequestration order on March 1, 2013. Certain of these automatic cuts have been implemented resulting in reductions in Medicare payments to physicians, hospitals, and other healthcare providers, among other things. The full impact on our business of these automatic cuts is uncertain.

If other federal spending is reduced, any budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or National Institutes of Health to continue to function. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve drug research and development, manufacturing, and marketing activities, which may delay our ability to develop, market and sell any products we may develop.

Changes in laws and regulations affecting the healthcare industry could adversely affect our business.

All aspects of our business, including research and development, manufacturing, marketing, pricing, sales, litigation, and intellectual property rights, are subject to extensive legislation and regulation. Changes in applicable federal and state laws and agency regulation could have a materially negative impact on our business. These include changes in the FDA and foreign regulatory processes for new therapeutics that may delay or prevent the approval of any of our current or future product candidates; new laws, regulations, or judicial decisions related to healthcare availability or the payment for healthcare products and services, including prescription drugs, that would make it more difficult for us to market and sell products once they are approved by the FDA or foreign regulatory agencies; changes in FDA and foreign regulations that may require additional safety monitoring prior to or after the introduction of new products to market, which could materially increase our costs of doing business; and changes in FDA and foreign cGMPs that may make it more difficult and costly for us to maintain regulatory compliance and/or manufacture our marketed product and product candidates in accordance with cGMPs.

The current U.S. administration and Congress could carry out significant changes in legislation, regulation, and government policy (including with respect to the possible repeal of all or portions of ACA, possible changes in the existing treaty and trade relationships with other countries, and tax reform), as evidenced by statements and recent actions of the current president. While it is not possible to predict whether and when any such changes will occur, changes in the laws, regulations, and policies governing the development and approval of our product candidates and the commercialization, importation, and reimbursement of our products could adversely affect our business. The full effects of any U.S. healthcare reform legislation cannot be known until the law is fully implemented through regulations or guidance issued by the CMS and other federal and state healthcare agencies. The financial impact of the U.S. healthcare reform legislation over the next few years will depend on several factors, including, but not limited, to the policies reflected in implementing regulations and guidance, and changes in sales volumes for products affected by the new system of rebates, discounts and fees.

Risks associated with our operations outside of the United States could adversely affect our business.

We have operations and conduct business outside the United States and we plan to expand these operations, particularly as we commence our global development plans in 2017. Therefore, we are subject to risks related to operating in foreign countries, which include unfamiliar foreign laws or regulatory requirements or unexpected changes to those laws or requirements; other laws and regulatory requirements to which our business activities abroad are subject, such as the Foreign Corrupt Practices Act and the U.K. Bribery Act; changes in the political or economic condition of a specific country or region; fluctuations in the value of foreign currency versus the U.S. dollar; our ability to deploy overseas funds in an efficient manner; tariffs, trade protection measures, import or export licensing requirements, trade embargoes, and sanctions (including those administered by the Office of Foreign Assets Control of the U.S. Department of the Treasury), and other trade barriers; difficulties in attracting and retaining qualified personnel; and cultural differences in the conduct of business.

Further complicating potential uncertainties caused by conducting business outside the United States are recent political movements that are changing decades-old institutions, including, for example, on June 23, 2016, the United Kingdom held a referendum in which voters approved an exit from the EU, commonly referred to as "Brexit." As a result of the referendum, it is expected that the British government will begin negotiating the terms of the United Kingdom's future relationship with the EU. We do not know to what extent Brexit will impact the business and regulatory environment in the United Kingdom, the rest of the EU, or other countries. Changes impacting our ability to conduct business in the United Kingdom or other EU countries, or changes to the regulatory regime applicable to our operations in those countries (such as with respect to the approval of our product candidates), may materially and adversely impact our business, prospects, operating results, and financial condition.

There is a substantial risk of product liability claims in our business. If we are unable to obtain sufficient insurance, a product liability claim against us could adversely affect our business.

Our business exposes us to significant potential product liability risks that are inherent in the development, testing, manufacturing and marketing of human therapeutic products. Product liability claims could delay or prevent completion of our clinical development programs. If we succeed in marketing products, such claims could result in an FDA investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs, and potentially a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used, or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our products, injury to our reputation, costs to defend the related litigation, a diversion of management's time and our resources, substantial monetary awards to trial participants or patients and a decline in our share price. Any insurance we obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could adversely affect our business.

If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our research, development and manufacturing processes involve the use of hazardous materials, chemicals and various radioactive compounds. We maintain quantities of various flammable and toxic chemicals in our facilities that are required for our research, development and manufacturing activities. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. We believe our procedures for storing, handling and disposing of these materials comply with the relevant guidelines and laws of the jurisdictions in which our facilities are located. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards mandated by applicable regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of biohazardous materials. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of these materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate any of these laws or regulations.

Risks Related to Our Dependence on Third Parties

We expect to depend on collaborations with third parties for the development and commercialization of product candidates outside our core focus area of neurology.

We expect to depend on third-party collaborators for the development and commercialization of product candidates in therapeutic areas outside of our core focus of neurology. We face significant competition in seeking appropriate collaborators. Our likely collaborators include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

In May 2016, we entered into a collaboration with Pfizer focused on the advancement of genetically defined targets for the treatment of metabolic diseases, bringing together our proprietary drug development platform, across antisense and single-stranded RNAi modalities, along with GalNAc and Pfizer's hepatic targeting technology for delivery to the liver. The collaboration seeks to leverage our stereochemistry platform across antisense and RNAi modalities and incorporates GalNAc and Pfizer's hepatic targeting technology. Under the terms of the agreement, Pfizer will select, and we will advance, up to five targets from discovery through to the selection of clinical candidates, at which point Pfizer may elect to exclusively license the programs and undertake further development and potential commercialization. Two targets were declared upon initiation of the agreement, including Apolipoprotein C-III. In the third quarter of 2016, Pfizer nominated its third target. Per the terms of the agreement, Pfizer is entitled to nominate the remaining two targets by November 2017.

Collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. We may also be restricted under existing license agreements from entering into agreements on certain terms with potential collaborators. If we are unable to enter into collaborations with respect to a product candidate, we may have to curtail the development of such product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures

to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Even if we are able to enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates would pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. Further, if a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

We rely, and expect to continue to rely, on third parties to conduct some aspects of our compound formulation, research and preclinical studies, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such formulation, research or testing.

We do not independently conduct all aspects of our drug discovery activities, compound formulation research or preclinical studies of product candidates. We currently rely, and expect to continue to rely, on third parties to conduct some aspects of our research and development and preclinical studies. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our studies that support our clinical trial applications and our clinical trials are conducted in accordance with the study plan and protocols for the trial. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the necessary preclinical studies to enable us or our strategic alliance partners to select viable product candidates for clinical trial application submissions and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize such product candidates.

If any of our research collaborators terminates or fails to perform its obligations under agreements with us, the development and commercialization of our product candidates could be delayed or our business could be otherwise adversely affected.

We are party to research collaboration agreements with certain academic partners, including Matthew Woods' laboratory at the University of Oxford, the University of Dundee and Robert Brown's laboratory at the University of Massachusetts Medical School, among others. Our dependence on these research collaborators for select research capabilities means that our business could be adversely affected if any collaborator terminates its collaboration agreement with us or fails to perform its obligations under that agreement. Our current or future research collaborations, if any, may not be scientifically successful. Disputes may arise in the future with respect to the ownership of rights to technology or products developed with collaborators, which could have an adverse effect on our ability to develop and commercialize any affected product candidate.

Our current research collaborations allow, and we expect that any future research collaborations will allow, either party to terminate the collaboration for a material breach by the other party. In addition, our collaborators may have additional termination rights for convenience under certain circumstances. If we were to lose a collaborator, we would have to attract a new collaborator or develop internal research capabilities, which would require us to invest significant amounts of financial and management resources.

In addition, if we have a dispute with a collaborator over the ownership of technology or other matters, or if a collaborator terminates its collaboration with us, for breach or otherwise, or determines not to pursue the research that is the subject of the collaboration, it could delay or prevent the development of our product candidates, result in the need for additional company resources to develop product candidates, make it more difficult for us to attract new collaborators and could adversely affect how we are perceived in the business and financial communities.

We intend to rely on third parties to design, conduct, supervise and monitor our preclinical studies and clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We rely on third party clinical investigators, contract research organizations ("CROs"), clinical data management organizations and consultants to design, conduct, supervise and monitor preclinical studies of our product candidates and will do the same for any clinical trials. Because we rely on third parties and do not have the ability to conduct preclinical studies or clinical trials independently, we have less control over the timing, quality and other aspects of preclinical studies and clinical trials than we would if we conducted them on our own. These investigators, CROs and consultants are not our employees and we have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our programs. Further, these third parties may not be diligent, careful or timely in conducting our preclinical studies or clinical trials, resulting in the preclinical studies or clinical trials being delayed or unsuccessful.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. The FDA requires clinical trials to be conducted in accordance with good clinical practices, including for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. If we or our CROs fail to comply with these requirements, the data generated in our clinical trials may be deemed unreliable or uninterpretable and the FDA may require us to perform additional clinical trials. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Any such event could adversely affect our business, financial condition, results of operations and prospects.

We rely on third parties to supply and manufacture our product candidates for our research, preclinical and clinical activities, and may do the same for commercial supplies of our product candidates.

While we are in the process of developing our own internal manufacturing capabilities, we have not yet manufactured our product candidates on a clinical or commercial scale, and may be unable to do so for any of our product candidates. We currently rely on third parties to supply and manufacture the materials for our research, preclinical and clinical activities and may continue to do so for the foreseeable future. We may do the same for the commercial supply of our drug product. We use third parties to perform additional steps in the manufacturing process, such as the filling, finishing and labeling of vials and storage of our product candidates and we expect to do so for the foreseeable future. There can be no assurance that our supply of research and development, preclinical and clinical development drugs and other materials will not be limited, interrupted or restricted or will be of satisfactory quality or continue to be available at acceptable prices. Replacement of any of the third parties we may engage could require significant effort and expertise because there may be a limited number of qualified replacements. In addition, raw materials, reagents, and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available, may not be

suitable or acceptable for use due to material or component defects, or may introduce variability into the supply of our product candidates.

We may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA and foreign regulatory authorities must approve any manufacturers that we elect to engage. Suppliers and manufacturers, including us, must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards. In the event that any of our suppliers or manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, some of which may be out of their or our control, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to increase the manufacturing of the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. Any interruption of the development or operation of the manufacturing of our product candidates, such as order delays for equipment or materials, equipment malfunction, quality control and quality assurance issues, regulatory delays and possible negative effects of such delays on supply chains and expected timelines for product availability, production yield issues, shortages of qualified personnel, discontinuation of a facility or business or failure or damage to a facility resulting from natural disasters, could result in the cancellation of shipments, loss of product in the manufacturing process or a shortfall in available product candidates or materials. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We may rely on third party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. We may also be required to enter into long-term manufacturing agreements that contain exclusivity provisions and/or substantial termination penalties which could have a material adverse effect on our business prior to or after commercialization of any of our product candidates. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Failure to execute on our manufacturing requirements, either by us or by one of our third-party vendors, could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of a collaborator;
- additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

If any of our product candidates are approved for marketing and commercialization and we are unable to develop sales, marketing and distribution capabilities on our own or enter into agreements with third parties to perform these functions on acceptable terms, we will be unable to commercialize successfully any such future products.

Although we are in the process of hiring employees with commercial experience, we currently have no sales, marketing or distribution capabilities. If any of our product candidates is approved, we will need to develop internal sales, marketing and distribution capabilities to commercialize such products, which would be expensive and time-consuming, or enter into collaborations with third parties to perform these services. If we decide to market our products directly, we will need to commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and supporting distribution, administration and compliance capabilities. If we rely on third parties with such capabilities to market our products or decide to co-promote products with collaborators, we will need to establish and maintain marketing and distribution arrangements with third parties, and there can be no assurance that we will be able to enter into such arrangements on acceptable terms or at all. In entering into third-party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of the third parties and there can be no assurance that such third parties will establish adequate sales and distribution capabilities or be successful in gaining market acceptance of any approved product. If we are not successful in commercializing any product approved in the future, either on our own or through third parties, our business, financial condition, results of operations and prospects would be adversely affected.

Risks Related to Managing Our Operations

If we are unable to attract and retain qualified key management and scientists, staff, consultants and advisors, our ability to implement our business plan may be adversely affected.

We are highly dependent upon our senior management and our scientific, clinical and medical staff and advisors. The loss of the service of any of the members of our senior management could delay our research and development programs and materially harm our business, financial condition, results of operations and prospects. We are dependent on the continued service of our technical personnel because of the highly technical and novel nature of our product candidates, platform and technologies and the specialized nature of the regulatory approval process. Replacing such personnel may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully execute our business strategy. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty. We do not maintain key person life insurance policies on any of our management team members or key employees. Our future success will depend in large part on our continued ability to attract and retain additional highly qualified scientific, technical and management personnel, as well as personnel with expertise in preclinical and clinical testing, manufacturing, governmental regulation and commercialization. We face competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations. If we are unable to attract and retain qualified personnel, the rate and success at which we may be able to discover and develop our product candidates and implement our business plan will be limited.

As we continue with our preclinical studies and advance to any clinical trials, we may experience difficulties in managing our growth and expanding our operations.

Although we have assembled a team of employees with experience developing drugs and obtaining regulatory approval to market those drugs, we have limited experience in drug development and have not begun clinical trials for any of our product candidates. As we advance product candidates through preclinical studies and any clinical trials, we will need to expand our development, regulatory and manufacturing capabilities or contract with other organizations to provide these capabilities for us. In the future, we expect to have to manage additional relationships with collaborators or partners, suppliers and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. In addition, our future growth may require significant capital expenditures and may divert financial resources from other projects, such as the development of our product candidates. If we are unable to effectively manage our future growth, our expenses may increase and our ability to generate revenue could be reduced.

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

We are exposed to the risk of fraud or other misconduct by our employees, consultants and collaborators. Such misconduct could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards required by the FDA or that we may establish, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter such misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

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

Despite the implementation of security measures, our internal computer systems and those of our contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. Such events could cause interruption of our operations. For example, the loss of preclinical trial data or data from completed or ongoing clinical trials for our product candidates could result in delays in our regulatory filings and development efforts and significantly increase our costs. To the extent that any disruption or security breach were to result in a loss of or damage to our data, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the development of our product candidates could be delayed.

Foreign currency exchange rates may adversely affect our results.

We are exposed to the effects of changes in foreign currency exchange rates, and we have not historically hedged our foreign currency exposure. Our Japanese subsidiary conducts its business in Japanese yen. As of December 31, 2016, and December 31, 2015, 0.2% and 0.5% of our assets, respectively, were located in Japan. Additionally, 1.7% and 6.4% of our research and development expenses were transacted in Japanese yen during the years ended December 31, 2016 and 2015, respectively. And finally, 1.4% and 2.6% of our general and administrative expenses were transacted in Japanese yen for the years ended December 31, 2016 and 2015, respectively. Therefore, when the U.S. dollar strengthens relative to the yen, as it has in recent periods, our U.S. dollar reported revenue from non-U.S. dollar denominated income will decrease. Conversely, when the U.S. dollar weakens relative to the yen, our U.S. dollar reported expenses from non-U.S. dollar denominated operating costs will increase. Changes in the relative values of currencies occur regularly and, in some instances, could materially adversely affect our business, results of operations, financial condition or cash flows.

Risks Related to Our Intellectual Property

If we are not able to obtain and enforce patent protection for our technologies or product candidates, development and commercialization of our product candidates may be adversely affected.

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including trademarks, trade secrets and in-licenses of intellectual property rights of others, for our product candidates and platform technologies, methods used to manufacture our product candidates, methods of patient stratification and methods for treating patients using our product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. We may not be able to apply for patents on certain aspects of our product candidates or our platform in a timely fashion or at all. Our existing issued and granted patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable, or that any issued or granted patents will not include claims that are sufficiently broad to cover our product candidates, our platform technologies, or any methods relating to them, or to provide meaningful protection from our competitors. Moreover, the patent position of biotechnology and pharmaceutical companies can be highly uncertain and involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and product candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely impact our position in the market.

Legal issues related to the patentability of biopharmaceuticals, and methods of their manufacture and use, are complex and uncertain in some countries. In some countries, applicants are not able to protect methods of treating human beings or medical treatment processes. Intellectual property protection varies throughout the world and is subject to change over time. Jurisdictions such as India, Mexico, China, Europe and others have enacted various rules and laws precluding issuance of patents encompassing any methods a doctor may practice on a human being or any other animal to treat a disease or condition. Further, many countries have enacted laws and regulatory regimes that do not provide patent protection for methods of use of known compounds. Particularly given that some of our product candidates may represent stereopure versions of previously described oligonucleotides, it may be difficult or impossible to obtain patent protection for them in relevant jurisdictions. Thus, in some countries and jurisdictions, it may not be possible to patent some of our product candidates at all. In some countries and jurisdictions, only composition claims may be obtained, and only when those compositions are or contain compounds that are new and/or novel. Also, patents issued with composition claims (*i.e.,* covering product candidates) cannot always be enforced to protect methods of using those compositions to treat or diagnose diseases or medical conditions. In such countries or jurisdictions, enforcement of patents to protect our product candidates, or their uses, may be difficult or impossible. Lack of patent protection in such cases may have a materially adverse effect on our business and financial condition.

Furthermore, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates, their manufacture or their use might expire before or shortly after those candidates receive regulatory approval and 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. We expect to seek extensions of patent terms where these are available upon regulatory approval in those countries where we are prosecuting patents. This includes in the United States under the Drug Price Competition and Patent Term Restoration Act of 1984, which permits a patent term extension of up to five years beyond the expiration of the patent. However, the applicable authorities, including the FDA in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be possible.

The U.S. Patent and Trademark Office, or USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent prosecution process. There are situations in

which noncompliance can result in abandonment or lapse of a patent or patent application, or loss of right to enforce patent claims, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. The standards applied by the USPTO and foreign patent offices in granting patents are not uniform, can vary substantially from country to country, and are not always applied predictably, requiring country-specific patent expertise in each jurisdiction in which patent protection is sought. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. As such, we do not know the degree of future protection that we will have on our proprietary products and technologies. While we will endeavor to try to protect our product candidates and platform technology with intellectual property rights such as patents, as appropriate, the process of filing and prosecuting patent applications, and obtaining, maintaining and defending patents is time-consuming, expensive and sometimes unpredictable.

In addition, there are numerous recent changes to the patent laws and proposed changes to the rules of the USPTO which may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the America Invents Act, enacted within the last several years, involves significant changes in patent legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, some of which cases either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. The recent decision by the U.S. Supreme Court in *Association for Molecular Pathology v. Myriad Genetics, Inc.* precludes a claim to a nucleic acid having a stated nucleotide sequence which is identical to a sequence found in nature and unmodified. We currently are not aware of an immediate impact of this decision on our patents or patent applications because we are developing nucleic acid products which contain modifications that we believe are not found in nature. However, this decision has yet to be clearly interpreted by courts and by the USPTO. We cannot make assurances that the interpretations of this decision or subsequent rulings will not adversely impact our patents or patent applications. 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 decisions 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.

Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, *inter partes* review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such initial grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked, or may lose the allowed or granted claims altogether. In addition, there can be no assurance that:

- Others will not or may not be able to make, use or sell compounds that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or license.
- We or our licensors, collaborators or any future collaborators are the first to make the inventions covered by each of our issued patents and pending patent applications that we own or license.
- We or our licensors, collaborators or any future collaborators are the first to file patent applications covering certain aspects of our inventions.
- Others will not independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- A third party may not challenge, invalidate, circumvent or weaken our patents; nor can there be any assurance if any of these events should occur, that a court would hold that our patents are valid, enforceable and infringed.
- Any issued patents that we own or have licensed will provide us with any competitive advantages, or will not be challenged, invalidated, circumvented or weakened by third parties.
- We may develop additional proprietary technologies that are patentable.
- The patents of others will not have an adverse effect on our business.
- Our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.

We license patent rights from third-party owners or licensees. If such owners or licensees do not properly or successfully obtain, maintain or enforce the patents underlying such licenses, or if they retain or license to others any competing rights, our competitive position and business prospects may be adversely affected.

We do, and will continue to, rely on intellectual property rights licensed from third parties to protect certain aspects of our technology and programs. Specifically, we are a party to a license agreement with Max-Planck-Innovation GmbH, or Max Planck, pursuant to

which Max Planck has licensed to us certain patent rights that provide intellectual property for research and development of single-stranded RNAi oligonucleotides. Under this agreement, we have a worldwide co-exclusive license from Max Planck for the exploitation of key intellectual property rights in this respect, and Max Planck retains ownership of the patents and patent applications to which we are licensed under the agreement. We also intend to license additional third-party intellectual property in the future. Our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property, in particular, those patents to which we have secured exclusive rights. Our licensors may not successfully prosecute the patent applications licensed to us. Even if patents issue or are granted, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue litigation less aggressively than we would. Further, we may not obtain exclusive rights, which would allow for third parties to develop competing products. Without protection for, or exclusive right to, the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects. In addition, we may sublicense our rights under our third-party licenses to current or future collaborators or any future strategic partners. Any impairment of these sublicensed rights could result in reduced revenue under any future collaboration agreements we may enter into or result in termination of an agreement by one or more of our collaborators or any future strategic partners.

Certain third parties have rights in the patents related to single-stranded oligonucleotides included in the license granted to us by Max Planck, which could allow them to develop, market and sell product candidates in competition with ours.

Our license from Max Planck is one of two maximum allowable co-exclusive licenses for the patents that are the subject of the license, the other of which is currently held by Ionis Pharmaceuticals, Inc. (formerly Isis Pharmaceuticals), or Ionis. We therefore do not have rights under this license to prevent Ionis from developing product candidates in competition with ours. In addition, the German and U.S. governments have certain rights to the inventions covered by the patent rights and Max Planck, as an academic research and medical center, has the right to practice the licensed patent rights for educational, research and clinical uses. If a third party develops, manufactures, markets and sells any product covered by the same patent rights and technologies that compete with ours, it could significantly undercut the value of any of our product candidates that rely on the patent rights under that license, which would materially adversely affect our revenue, financial condition and results of operations.

Other companies or organizations may challenge our or our licensors' patent rights or may assert patent rights that prevent us from developing and commercializing our products.

Nucleic acid therapeutics is a relatively new scientific field, the commercial exploitation of which has resulted in many different patents and patent applications from organizations and individuals seeking to obtain patent protection in the field. We have obtained grants and issuances of patents in this field, and also have licensed from Max Planck certain such patents on a co-exclusive basis. The issued patents and pending patent applications in the U.S. and in key markets around the world that we own or license claim certain methods, compositions and processes relating to the discovery, development, manufacture and/or commercialization of nucleic acid therapeutics and/or our platform.

As the field of nucleic acid therapeutics matures, patent applications are being processed by national patent offices around the world. There is uncertainty about which patents will issue, and, if they do, as to when, to whom, and with what claims. It is likely that there will be significant litigation in the courts and other proceedings, such as interference, reexamination and opposition proceedings, in various patent offices relating to patent rights in the nucleic acid therapeutics field. In many cases, the possibility of appeal or opposition exists for either us or our opponents, and it may be years before final, unappealable rulings are made with respect to these patents in certain jurisdictions. The timing and outcome of these and other proceedings is uncertain and may adversely affect our business, particularly if we are not successful in defending the patentability and scope of our pending and issued patent claims or if third parties are successful in obtaining claims that cover any of our product candidates or our platform. In addition, third parties may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, invalidated or circumvented, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to challenge, invalidate, circumvent or weaken our intellectual property rights could be costly to us, could require significant time and attention of our management and could adversely affect our business and our ability to successfully compete in the field of nucleic acid therapeutics.

There are many issued patents and/or pending patent applications that claim aspects of oligonucleotide chemistry and/or modifications that we may want or need to apply to our product candidates. There are also many issued patents and/or pending patent applications that claim targeted genes or portions of genes that may be relevant for nucleic acid drugs we wish to develop. Thus, it is possible that one or more organizations will hold patent rights to which we will need or want a license. If those organizations refuse to grant us a license to such patent rights on reasonable terms, we may not be able to market products or perform research and development or other activities covered by these patents.

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

Obtaining a valid and enforceable issued or granted patent covering our technology in the United States and worldwide can be extremely costly. In jurisdictions where we have not obtained patent protection, competitors may use our technology to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but where it is more difficult to enforce a patent as compared to the United States. Competitor products may compete with our future products in jurisdictions where we do not have issued or granted patents or where our issued or granted patent claims or other intellectual property rights are not sufficient to prevent competitor activities in these jurisdictions. The legal systems of certain countries, particularly certain developing countries, make it difficult to enforce patents and such countries may not recognize other types of intellectual property protection, particularly that relating to biopharmaceuticals. This could make it difficult for us to prevent the infringement of our patents or marketing of competing products in violation of our proprietary rights generally in certain jurisdictions. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

We generally file a provisional patent application first (a priority filing) at the USPTO. A Patent Cooperation Treaty, or PCT, application is usually filed within twelve months after the priority filing. Regional and/or national patent applications may be pursued outside of the United States, either based on a PCT application or as a direct filing, in some cases claiming priority to a prior U.S. or PCT filing. Some of our cases have been filed in, for example, Argentina, Australia, Brazil, Canada, Chile, China, Europe, Hong Kong, Indonesia, Israel, India, Japan, Malaysia, New Zealand, South Korea, Mexico, Russia, Singapore, South Africa, Taiwan, United Arab Emirates, and Venezuela. We also commonly enter the national stage in the United States through a PCT filing. We have so far not filed for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before grant. Finally, the grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant registration authorities, while granted by others. It is also quite common that depending on the country, various scopes of patent protection may be granted on the same product or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws in the United States, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties, allowing competitors to manufacture and sell their own versions of our product, thereby reducing our sales. In addition, many countries do not permit enforcement of patents, or limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such a patent. If we or any of our licensors, collaborators or present or future partners are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position in the relevant jurisdiction may be impaired and our business and results of operations may be adversely affected.

The requirements for patentability may differ in certain countries, particularly developing countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval of a drug and its patent status. Furthermore, generic or biosimilar drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' or collaborators' patents, requiring us or our licensors or collaborators to engage in complex, lengthy and costly litigation or other proceedings. Generic or biosimilar drug manufacturers may develop, seek approval for, and launch generic versions of our products. In addition to India, certain countries in Europe and developing countries, including China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors or collaborators may have limited remedies if patents are infringed or if we or our licensors or collaborators are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our and our licensors' and collaborators' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

We or our licensors, collaborators or any future strategic partners may become subject to third party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights, and we may need to resort to litigation to protect or enforce our patents or other proprietary rights, all of which could be costly and time consuming, or delay or prevent the development and commercialization of our product candidates, or put our patents and other proprietary rights at risk.

We or our licensors, collaborators or any future strategic partners may be subject to third-party claims for infringement or misappropriation of patent or other proprietary rights. We are generally obligated under our license or collaboration agreements to indemnify and hold harmless our licensors or collaborators for damages arising from intellectual property infringement by us. If we or

our licensors, collaborators or any future strategic partners are found to infringe a third party patent or other intellectual property rights, we could be required to pay damages, potentially including treble damages, if we are found to have willfully infringed. In addition, we or our licensors, collaborators or any future strategic partners may choose to seek, or be required to seek, a license from a third party, which may not be available on acceptable terms, if at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we or our collaborator, or any future collaborator, may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our products or our technology, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, lack of written disclosure, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal allegations of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our products or certain aspects of our platform technology. Such a loss of patent protection could negatively impact our business. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights.

Intellectual property rights of third parties could adversely affect our ability to commercialize our product candidates, and we might be required to litigate or obtain licenses from third parties in order to develop or market our product candidates. Such litigation or licenses could be costly or not available on commercially reasonable terms.

Because the nucleic acid therapeutics intellectual property landscape is still evolving, it is difficult to conclusively assess our freedom to operate without infringing third party rights. There are numerous companies that have pending patent applications and issued patents directed to certain aspects of nucleic acid therapeutics. Our competitive position may suffer if patents issued to third parties or other third party intellectual property rights cover, or may be alleged to cover, our products or elements thereof, or methods of manufacture or use relevant to our development plans. In such cases, we may not be in a position to develop or commercialize product candidates unless we successfully pursue litigation to nullify or invalidate the third party intellectual property right concerned, or enter into a license agreement with the intellectual property right holder, if available on commercially reasonable terms.

It is also possible that we have failed to identify relevant third party patents or applications. For example, U.S. applications filed before November 29, 2000, and certain U.S. applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing date for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our products or platform technology could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technologies, our products or the use of our products. Third party intellectual property right holders may also actively bring infringement claims against us. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage in or continue costly, unpredictable and time-consuming litigation and may be prevented from or experience substantial delays in marketing our products. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing any of our product candidates that are held to be infringing. We might, if possible, also be forced to redesign product candidates so that we no longer infringe the third party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

If we fail to comply with our obligations under any license, collaboration or other agreement, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our product candidates, or we could lose certain rights to grant sublicenses.

Our technology licenses and any future licenses we enter into are likely to impose various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, and/or other obligations on us. If we breach any of these imposed obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

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

In addition to seeking patent protection for certain aspects of our product candidates, we also consider trade secrets, including confidential and unpatented know-how, improvements and technological innovation important to the maintenance of our competitive position. We protect trade secrets and confidential and unpatented know-how, improvements and technological innovation, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants that obligate them to maintain confidentiality and assign their inventions to us. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts in the United States and certain foreign jurisdictions are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We may be subject to claims that we or our employees or consultants have wrongfully used or disclosed alleged trade secrets of our employees' or consultants' former employers or their clients. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and may lose valuable intellectual property rights or personnel.

Many of our employees were previously employed at universities or biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper our ability to commercialize, or prevent us from commercializing, our product candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our trademarks or trade names may be infringed, challenged, invalidated, circumvented, weakened or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Our Being a Singapore Company

We are a Singapore incorporated company and it may be difficult to enforce a judgment of U.S. courts for civil liabilities under U.S. federal securities laws against us, our directors or officers in Singapore.

We are incorporated under the laws of the Republic of Singapore, and certain of our officers and directors are residents outside the United States. Moreover, a majority of our consolidated assets are located outside the United States. Although we are incorporated

outside the United States, we have agreed to accept service of process in the United States through our agent designated for that purpose. Nevertheless, because a majority of the consolidated assets owned by us are located outside the United States, any judgment obtained in the United States against us may not be enforceable within the United States.

There is no treaty between the United States and Singapore providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters and a final judgment for the payment of money rendered by any federal or state court in the United States based on civil liability, whether or not predicated solely upon the federal securities laws, would, therefore, not be automatically enforceable in Singapore. There is uncertainty as to whether judgments of courts in the United States based upon the civil liability provisions of the federal securities laws of the United States would be recognized or enforceable in Singapore. In addition, holders of book-entry interests in our shares will be required to be registered shareholders as reflected in our shareholder register in order to have standing to bring a shareholder action and, if successful, to enforce a foreign judgment against us, our directors or our executive officers in the Singapore courts. The administrative process of becoming a registered holder could result in delays prejudicial to any legal proceedings or enforcement action. Consequently, it may be difficult for investors to enforce against us, our directors or our officers in Singapore judgments obtained in the United States which are predicated upon the civil liability provisions of the federal securities laws of the United States.

We are incorporated in Singapore and our shareholders may have more difficulty in protecting their interests than they would as shareholders of a corporation incorporated in the United States.

Our corporate affairs are governed by our constitution and by the laws governing corporations incorporated in Singapore. The rights of our shareholders and the responsibilities of the members of our board of directors under Singapore law are different from those applicable to a corporation incorporated in the United States. Principal shareholders of Singapore companies do not owe fiduciary duties to minority shareholders, as compared, for example, to controlling shareholders in corporations incorporated in Delaware. Our public shareholders may have more difficulty in protecting their interests in connection with actions taken by our management, members of our board of directors or our principal shareholders than they would as shareholders of a corporation incorporated in the United States.

In addition, only persons who are registered as shareholders in our shareholder register are recognized under Singapore law as shareholders of our company. Only registered shareholders have legal standing to institute shareholder actions against us or otherwise seek to enforce their rights as shareholders. Investors in our shares who are not specifically registered as shareholders in our shareholder register (for example, where such shareholders hold shares indirectly through the Depository Trust Company) are required to become registered as shareholders in our shareholder register in order to institute or enforce any legal proceedings or claims against us, our directors or our executive officers relating to shareholder rights. Holders of book-entry interests in our shares may become registered shareholders by exchanging their book-entry interests in our shares for certificated shares and being registered in our shareholder register. Such process could result in administrative delays which may be prejudicial to any legal proceeding or enforcement action.

We are subject to the laws of Singapore, which differ in certain material respects from the laws of the United States.

As a company incorporated under the laws of the Republic of Singapore, we are required to comply with the laws of Singapore, certain of which are capable of extra-territorial application, as well as our constitution. In particular, we are required to comply with certain provisions of the Securities and Futures Act of Singapore (Cap 289) (the "SFA"), which prohibit certain forms of market conduct and information disclosures, and impose criminal and civil penalties on corporations, directors and officers in respect of any breach of such provisions. We are also required to comply with the Singapore Code on Take-Overs and Mergers (the "Singapore Takeover Code"), which specifies, among other things, certain circumstances in which a general offer is to be made upon a change in effective control, and further specifies the manner and price at which voluntary and mandatory general offers are to be made.

The laws of Singapore and of the United States differ in certain significant respects. The rights of our shareholders and the obligations of our directors and officers under Singapore law (including under the Companies Act of Singapore (Cap 50) (the "Singapore Companies Act")) are different from those applicable to a company incorporated in the State of Delaware in material respects, and our shareholders may have more difficulty and less clarity in protecting their interests in connection with actions taken by our management, members of our board of directors or our controlling shareholders than would otherwise apply to a company incorporated in the State of Delaware.

The application of Singapore law, in particular, the Singapore Companies Act may, in certain circumstances, impose more restrictions on us and our shareholders, directors and officers than would otherwise be applicable to a company incorporated in the State of Delaware. For example, the Singapore Companies Act requires directors to act with a reasonable degree of diligence and, in certain circumstances, imposes criminal liability for specified contraventions of particular statutory requirements or prohibitions. In addition, pursuant to the provisions of the Singapore Companies Act, shareholders holding 10% or more of the total number of paid-up shares

carrying the right of voting in general meetings may require the convening of an extraordinary general meeting of shareholders by our directors. If our directors fail to comply with such request within 21 days of the receipt thereof, the original requisitioning shareholders, or any of them holding more than 50% of the voting rights represented by the original requisitioning shareholders may proceed to convene such meeting, and we will be liable for the reasonable expenses incurred by such requisitioning shareholders. We are also required by the Singapore Companies Act to deduct such corresponding amounts from fees or other remuneration payable by us to such non-complying directors.

We are subject to the Singapore Takeover Code, which requires a person acquiring 30% or more of our voting shares to conduct a takeover offer for all of our voting shares. This could have the effect of discouraging, delaying or preventing a merger or acquisition and limit the market price of our ordinary shares.

We are subject to the Singapore Takeover Code. The Singapore Takeover Code contains provisions that may delay, deter or prevent a future takeover or change in control of our company and limit the market price of our ordinary shares for so long as we remain a public company with more than 50 shareholders and net tangible assets of S$5 million (Singapore dollars) or more. For example, under the Singapore Takeover Code, any person acquiring, whether by a series of transactions over a period of time or not, either on his own or together with parties acting in concert with him, 30% or more of our voting shares, or if such person holds, either on his own or together with parties acting in concert with him, between 30% and 50% (both inclusive) of our voting shares, and if he (or parties acting in concert with him) acquires additional voting shares representing more than 1% of our voting shares in any six-month period, must, except with the consent of Securities Industry Council in Singapore, extend a takeover offer for our remaining voting shares in accordance with the Singapore Takeover Code. Therefore, any investor seeking to acquire a significant stake in our company may be deterred from doing so if, as a result, such investor would be required to conduct a takeover offer for all of our voting shares.

These same provisions could discourage potential investors from acquiring a stake or making a significant investment in our company and may substantially impede the ability of our shareholders to benefit from a change of effective control and, as a result, may adversely affect the market price of our ordinary shares and the ability to realize any benefits from a potential change of control.

For a limited period of time, our directors have general authority to allot and issue new ordinary shares on terms and conditions and for such purposes as may be determined by our board of directors in its sole discretion.

Under Singapore law, we may only allot and issue new shares with the prior approval of our shareholders in a general meeting. At our 2016 annual general meeting of shareholders, our shareholders provided our directors with a general authority, subject to the provisions of the Singapore Companies Act and our constitution, to allot and issue any number of new ordinary shares and/or make or grant offers, agreements, options or other instruments (including the grant of awards or options pursuant to our equity-based incentive plans and agreements in effect from time to time) that might or would require ordinary shares to be allotted and issued (collectively, the "Instruments"); and unless revoked or varied by the Company in a general meeting, such authority will continue in force until the earlier of (i) the conclusion of our 2017 annual general meeting of shareholders, or (ii) the expiration of the period within which our 2017 annual general meeting of shareholders is required by law to be held. Subject to the general requirements of the Singapore Companies Act and our constitution, the general authority given to our directors by our shareholders to allot and issue ordinary shares and/or make or grant the Instruments may be exercised by our directors on such terms and conditions, for such purposes and for consideration as they may in their sole discretion deem fit, and with such rights or restrictions as they may think fit to impose. Any additional issuances of new ordinary shares and/or any grant of the Instruments by our directors may dilute our shareholders' interests in our ordinary shares and/or adversely impact the market price of our ordinary shares.

We may be or become a passive foreign investment company, or a PFIC, which could result in adverse U.S. federal income tax consequences to U.S. Holders.

The rules governing passive foreign investment companies ("PFICs"), can have adverse effects for U.S. federal income tax purposes. The tests for determining PFIC status for a taxable year depend upon the relative values of certain categories of assets and the relative amounts of certain kinds of income. The determination of whether we are a PFIC depends on the particular facts and circumstances (such as the valuation of our assets, including goodwill and other intangible assets) and may also be affected by the application of the PFIC rules, which are subject to differing interpretations. The fair market value of our assets is expected to relate, in part, to (a) the market price of our ordinary shares and (b) the composition of our income and assets, which will be affected by how, and how quickly, we spend any cash that is raised in any financing transaction. Moreover, our ability to earn specific types of income that we currently treat as non-passive for purposes of the PFIC rules is uncertain with respect to future years. Based on the current and anticipated value of our assets and the composition of our income and assets, we do not expect to be treated as a PFIC for our current taxable year ending December 31, 2017; however, there can be no assurance that we will not be considered a PFIC for any future taxable year.

If we are a PFIC, a U.S. Holder (defined below) would be subject to adverse U.S. federal income tax consequences, such as ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as

deferred, and additional reporting requirements under U.S. federal income tax laws and regulations. A U.S. Holder may in certain circumstances mitigate adverse tax consequences of the PFIC rules by filing an election to treat the PFIC as a qualified electing fund ("QEF") or, if shares of the PFIC are "marketable stock" for purposes of the PFIC rules, by making a mark-to-market election with respect to the shares of the PFIC. We do not intend to comply with the reporting requirements necessary to permit U.S. Holders to elect to treat us as a QEF. If a U.S. Holder makes a mark-to-market election with respect to its ordinary shares, the U.S. Holder is required to include annually in its U.S. federal taxable income an amount reflecting any year end increase in the value of its ordinary shares. For purposes of this discussion, a "U.S. Holder" is a beneficial owner of ordinary shares that is for U.S. federal income tax purposes: (i) an individual who is a citizen or resident of the United States; (ii) a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the United States, any state thereof or the District of Columbia; (iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or (iv) a trust (a) if a court within the U.S. can exercise primary supervision over its administration, and one or more U.S. persons have the authority to control all of the substantial decisions of that trust, or (b) that was in existence on August 20, 1996, and validly elected under applicable Treasury Regulations to continue to be treated as a domestic trust.

Investors should consult their own tax advisors regarding all aspects of the application of the PFIC rules to the ordinary shares.

Singapore taxes may differ from the tax laws of other jurisdictions.

Prospective investors should consult their tax advisers concerning the overall tax consequences of purchasing, owning and disposing of our shares. Singapore tax law may differ from the tax laws of other jurisdictions, including the United States.

We may become subject to unanticipated tax liabilities.

We are incorporated under the laws of Singapore. We may, however, become subject to income, withholding or other taxes in certain jurisdictions by reason of our activities and operations, and it is also possible that taxing authorities in any such jurisdictions could assert that we are subject to greater taxation than we currently anticipate. Any such non-Singaporean tax liability could materially adversely affect our results of operations.

Taxing authorities could reallocate our taxable income among our subsidiaries, which could increase our overall tax liability.

We are organized in Singapore, and we currently have subsidiaries in the United States, Japan and Ireland. As we grow our business, we expect to conduct increased operations through our subsidiaries in various tax jurisdictions pursuant to transfer pricing arrangements between us and our subsidiaries. If two or more affiliated companies are located in different countries, the tax laws or regulations of each country generally will require that transfer prices be the same as those between unrelated companies dealing at arms' length and that appropriate documentation is maintained to support the transfer prices. We maintain our transfer pricing policies to be compliant with applicable transfer pricing laws, but our transfer pricing procedures are not binding on applicable tax authorities.

If tax authorities in any of these countries were to successfully challenge our transfer prices as not reflecting arms' length transactions, they could require us to adjust our transfer prices and thereby reallocate our income to reflect these revised transfer prices, which could result in a higher tax liability to us. In addition, if the country from which the income is reallocated does not agree with the reallocation, both countries could tax the same income, resulting in double taxation. If tax authorities were to allocate income to a higher tax jurisdiction, subject our income to double taxation or assess interest and penalties, it would increase our consolidated tax liability, which could adversely affect our financial condition, results of operations and cash flows.

Risks Related to Our Ordinary Shares

The public market for our ordinary shares may not be liquid enough for our shareholders to sell their ordinary shares quickly or at market price, or at all.

Prior to the completion of our initial public offering, there was no public market for our ordinary shares. An active trading market for our shares may not develop or be maintained and our shareholders may not be able to sell their ordinary shares quickly or at the market price, or at all. Further, an inactive market may also impair our ability to raise capital by selling our ordinary shares and may impair our ability to enter into strategic partnerships or acquire companies or products by using our ordinary shares as consideration.

The market price of our ordinary shares is likely to be highly volatile, and our shareholders may lose some or all of their investment.

The market price of our ordinary shares is likely to be highly volatile, including in response to factors that are beyond our control. The stock market in general has recently experienced extreme price and volume fluctuations. In particular, the market prices of securities of pharmaceutical and biotechnology companies have been extremely volatile, and have experienced fluctuations that often have been unrelated or disproportionate to the operating performance of these companies. These broad market fluctuations could result in extreme fluctuations in the price of our ordinary shares, regardless of our operating performance, and could cause our shareholders to lose some or all of their investment in the Company.

We incur significant costs due to operating as a public company, and our management is required to devote substantial time to compliance initiatives.

As a public company, we incur significant legal, accounting and other expenses. We are subject to the reporting and other requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and the Dodd-Frank Wall Street Reform and Protection Act, as well as rules subsequently adopted by the SEC and the NASDAQ Stock Market. These rules and regulations require, among other things, that we file annual, quarterly and current reports with respect to our business and financial condition and establish and maintain effective disclosure and financial controls and corporate governance practices. We expect that compliance with these rules and regulations will substantially increase our legal and financial compliance costs and will make some activities more time-consuming and costly, particularly after we are no longer an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012 ("the JOBS Act"). Our management and other personnel will devote a substantial amount of time to these compliance requirements.

We may take advantage of specified reduced disclosure requirements applicable to an "emerging growth company" under the JOBS Act, and the information that we provide to shareholders may be different than they might receive from other public companies.

We are an "emerging growth company," as defined under the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- Reduced disclosure about our executive compensation arrangements.
- No non-binding advisory votes on executive compensation or golden parachute arrangements.
- Exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We intend to take advantage of certain of the exemptions provided under the JOBS Act. We may continue to take advantage of exemptions under the JOBS Act for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1 billion in annual revenues, we have more than $700 million in market value of our shares held by non-affiliates, or we issue more than $1 billion of non-convertible debt over a three-year period. We may choose to take advantage of some but not all of these reduced burdens. Therefore, the information that we provide shareholders may be different than one might get from other public companies. Further, if some investors find our ordinary shares less attractive as result, there may be a less active trading market for our ordinary shares and the market price of our ordinary shares may be more volatile.

We previously identified a material weakness in our internal control over financial reporting. Although we believe this material weakness has since been remediated, we may identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal control over financial reporting, which may result in material misstatements of our financial statements or cause us to fail to meet our reporting obligations.

Prior to the completion of our initial public offering, we were a private company and had limited accounting and financial reporting personnel and other resources with which to address our internal controls and procedures. In connection with the audit of our consolidated financial statements for the years ended December 31, 2015 and 2014, we and our independent registered public accounting firm identified a material weakness in our internal control over financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. Our lack of adequate accounting personnel resulted in the identification of a material weakness in our internal control over financial reporting. Specifically, we did not appropriately design and implement controls over the review and approval of manual journal entries and the related supporting journal entry calculations.

Beginning in late 2015 and continuing into 2016, we hired additional finance and accounting personnel with appropriate training to build our financial management and reporting infrastructure and provide a segregation of duties. We also hired a full-time Chief Financial Officer who provides oversight for the finance and accounting team as well as the design and implementation of our internal controls. With the added personnel, we were able to able to implement appropriate segregation of duties with respect to journal entries. We have formalized and implemented our accounting policies and internal controls and the related documentation. As a result, we have remediated the material weakness as of December 31, 2016. However, we cannot assure that the measures we have taken to date, or any measures we may take in the future, will be sufficient to identify or prevent future material weaknesses or other deficiencies. If other material weaknesses or other deficiencies occur, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Our principal shareholders and management own a significant percentage of our ordinary shares and will be able to exert significant control over matters subject to shareholder approval.

As of December 31, 2016, our executive officers and directors, together with holders of 5% or more of our outstanding ordinary shares (assuming the conversion of all of our outstanding preferred shares into ordinary shares) and their respective affiliates, beneficially owned approximately 86% of our outstanding ordinary shares. As a result, these shareholders, if acting together, will continue to have significant influence over the outcome of corporate actions requiring shareholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. The interests of these shareholders may not be the same as or may even conflict with the interests of our other shareholders. For example, these shareholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other shareholders, which could deprive shareholders of an opportunity to receive a premium for their ordinary shares as part of a sale of our company or our assets and might affect the prevailing market price of our ordinary shares. The significant concentration of share ownership may adversely affect the trading price of our ordinary shares due to investors' perception that conflicts of interest may exist or arise.

We do not anticipate paying any cash dividends on our ordinary shares in the foreseeable future.

We have never declared or paid cash dividends on our ordinary shares. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business, and we do not anticipate paying any cash dividends on our ordinary shares in the foreseeable future. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our ordinary shares will be our shareholders' sole source of gain for the foreseeable future.

We may incur significant costs from class action litigation due to share volatility.

Our share price may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development efforts or the development efforts of our collaborators and/or competitors, the addition or departure of our key personnel, variations in our quarterly operating results and changes in market valuations of pharmaceutical and biotechnology companies. Holders of stock which has experienced significant price and trading volatility have occasionally brought securities class action litigation against the companies that issued the stocks. If any of our shareholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management, which could harm our business.

Sales of additional ordinary shares could cause the price of our ordinary shares to decline.

Sales of substantial amounts of our ordinary shares in the public market, or the availability of such shares for sale, by us or others, including the issuance of ordinary shares upon exercise of outstanding options, or the perception that such sales could occur, could adversely affect the price of our ordinary shares. Certain of our shareholders have the right to require us to register the sales of their shares under the Securities Act of 1933, as amended (the "Securities Act"), under agreements between us and such shareholders.

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

The trading market for our ordinary shares may depend 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 cover our company, the trading price for our ordinary shares would likely be negatively impacted. If one or more of the analysts who cover us downgrade our ordinary shares or publish inaccurate or unfavorable research about our business, our share price 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 our share price and trading volume to decline.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We maintain our U.S. corporate offices and research and development facilities in Cambridge, Massachusetts, where we occupy approximately 33,750 square feet of office and laboratory space under a lease that expires in March 2023.

In 2016, we entered into a lease for approximately 90,000 square feet of space in Lexington, Massachusetts, which we intend to use primarily for our cGMP manufacturing, as well as for additional laboratory and office space. In addition, we maintain research and development facilities in Okinawa, Japan. We believe our existing facilities are adequate to meet our current needs.

Item 3. Legal Proceedings.

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

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Price Range of Ordinary Shares

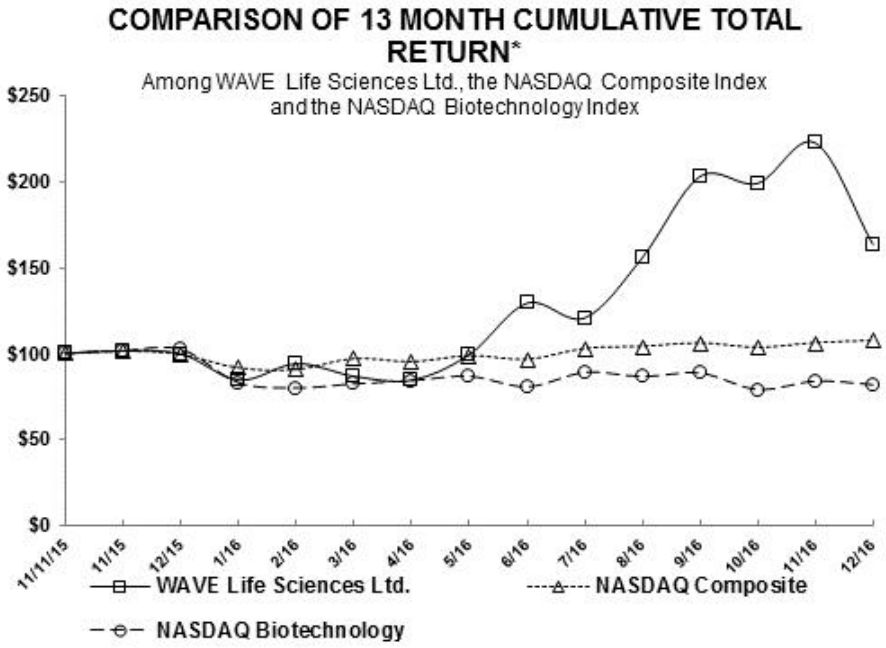
Our ordinary shares commenced trading on the NASDAQ Global Market under the symbol "WVE" on November 11, 2015. Prior to that date, there was no public trading market for our ordinary shares. The following table sets forth, for the periods indicated, the high and low reported sales prices of our ordinary shares as reported on the NASDAQ Global Market:

	High	Low
2015		
Fourth Quarter 2015	$20.999	$11.52
2016		
First Quarter 2016	$21.4899	$8.95
Second Quarter 2016	$23.059	$11.99
Third Quarter 2016	$37.30	$17.41
Fourth Quarter 2016	$40.15	$25.65

As of March 1, 2017, there were 13 shareholders of record of our ordinary shares.

Share Price Performance Graph

The following share performance graph compares our total share return with the total return for (i) the NASDAQ Composite Index and the (ii) the NASDAQ Biotechnology Index for the period from November 11, 2015 (the date our ordinary shares commenced trading on the NASDAQ Global Market) through December 31, 2016. The figures represented below assume an investment of $100.00 in our ordinary shares at the closing price of $16.00 on November 11, 2015 and in the NASDAQ Composite Index and the NASDAQ Biotechnology Index on November 11, 2015 and the reinvestment of dividends, if any, into ordinary shares.



This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liabilities under that Section and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

Dividend Policy

We have never declared or paid any dividends on our ordinary shares. We currently anticipate that we will retain any future earnings for the operation and expansion of our business. Accordingly, we do not currently anticipate declaring or paying any cash dividends on our ordinary shares for the foreseeable future. Any future determination relating to our dividend policy will be made at the discretion of our board of directors and will depend on then existing conditions, including our financial condition, results of operations, contractual restrictions (including in the agreements governing our credit facilities), capital requirements, business prospects and other factors our board of directors may deem relevant. We may, by ordinary resolution, declare dividends at a general meeting of shareholders, but we are restricted from paying dividends in excess of the amount recommended by our board of directors. In addition, pursuant to Singapore law and our constitution, no dividends may be paid except out of our profits.

Unregistered Sales of Securities

Not applicable.

Use of Proceeds from Initial Public Offering

On November 16, 2015, we closed our initial public offering, in which we issued and sold 6,375,000 ordinary shares at a public offering price of $16.00 per share. On December 4, 2015, we issued an additional 618,126 ordinary shares at a price of $16.00 per share pursuant to a partial exercise of the underwriters' over-allotment option. The aggregate gross proceeds to us from our initial public offering, inclusive of the over-allotment exercise, were approximately $111.9 million. All of the ordinary shares issued and sold in our initial public offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (Registration No. 333-207379), which was declared effective by the SEC on November 10, 2015. Jefferies LLC and Leerink Partners LLC were joint book-running managers for the initial public offering and JMP Securities LLC and SunTrust Robinson Humphrey, Inc. were co-managers. The aggregate net proceeds to us, inclusive of the over-allotment exercise, were approximately $100.4 million, after deducting underwriting discounts and commissions and offering expenses payable by us of approximately $11.5 million.

No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC on November 12, 2015 pursuant to Rule 424(b). We have been using and will continue to use the net offering proceeds to advance our product candidates through clinical trial programs and for working capital and general corporate purposes. As of December 31, 2016, we have used approximately $53.5 million of the net offering proceeds.

Issuer Purchases of Equity Securities

None.

Item 6. Selected Financial Data.

The following tables set forth our selected consolidated financial data for the periods, and as of the dates, indicated. The statement of operations data for the years ended December 31, 2016, 2015 and 2014 and the balance sheet data as of December 31, 2016 and 2015 are derived from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. The statement of operations data for the fiscal year ended December 31, 2013 and the balance sheet data as of December 31, 2014 and 2013 are derived from our audited consolidated financial statements that are not included in this Annual Report on Form 10-K, which financial statements have been audited by KPMG LLP, our independent registered accounting firm.

Our historical results are not necessarily indicative of the results to be expected in the future. You should read the selected financial data below in conjunction with the section of this report entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes thereto included elsewhere in this Annual Report on Form 10-K.

	Year Ended December 31,			
	2016	2015	2014	2013
	(in thousands except share and per share data)			
Revenue	$ 1,485	$ 152	$ —	$ —
Operating Expenses				
Research and development	40,818	9,057	2,395	1,920
General and administrative	15,994	10,393	2,999	1,654
Total operating expenses	56,812	19,450	5,394	3,574
Loss from operations	(55,327)	(19,298)	(5,394)	(3,574)
Other income (expense), net:				
Dividend income	255	—	—	—
Interest income (expense), net	337	86	(12)	(111)
Other income (expense), net	(50)	56	261	37
Total other income (expense), net	542	142	249	(74)
Loss before income taxes	(54,785)	(19,156)	(5,145)	(3,648)
Income tax provision	(616)	(44)	(84)	330
Net loss	$ (55,401)	$ (19,200)	$ (5,229)	$ (3,318)
Net loss per share attributable to ordinary shareholders–basic and diluted[1]	$ (2.43)	$ (1.83)	$ (1.34)	$ (1.90)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders– basic and diluted[1]	22,800,628	10,501,455	3,911,556	1,743,014

(1) See Note 9 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for further details on the calculation of net loss per share attributable to ordinary shareholders, basic and diluted.

	December 31,			
	2016	2015	2014	2013
	(in thousands)			
Cash and cash equivalents	$ 150,293	$ 161,220	$ 1,048	$ 439
Working capital (deficit)	139,835	157,566	605	(9,270)
Total assets	164,811	165,424	2,938	2,323
Total liabilities	22,074	4,059	911	10,085
Capital lease obligation	78	140	—	—
Series A preferred shares (temporary equity)	7,874	7,874	—	—
Accumulated deficit	(90,477)	(35,076)	(15,876)	(10,647)
Total shareholders' equity	134,863	153,491	2,027	(7,762)

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described, in or implied, by these forward-looking statements.

Overview

We are a genetic medicines company with an innovative and proprietary synthetic chemistry drug development platform that we are using to design, develop and commercialize a broad pipeline of first-in-class or best-in-class nucleic acid therapeutic candidates for genetically defined diseases. Nucleic acid therapeutics are a growing and innovative class of drugs that have the potential to address diseases that have historically been difficult to treat with small molecule drugs or biologics. Oligonucleotides are comprised of a sequence of nucleotides that are linked together by a backbone of chemical bonds. We are initially developing oligonucleotides that target genetic defects to either reduce the expression of disease-promoting proteins or transform the production of dysfunctional mutant proteins into the production of functional proteins.

The nucleic acid therapeutics we are developing are stereopure. A stereopure oligonucleotide is comprised of molecules with atoms precisely arranged in three-dimensional orientations at each linkage. We believe controlling the position of the sulfur atom following PS modification will optimize the pharmacological profile of our therapeutics by maximizing therapeutic effect, while minimizing the potential for side effects and safety risks. The stereopure therapies we are developing differ from the mixture-based nucleic acid therapeutics currently on the market and in development by others.

Our goal is to develop disease-modifying drugs for indications with a high degree of unmet medical need in genetically defined diseases. We are focused on designing single-stranded nucleic acid therapeutics that can distribute broadly within the human body, allowing us to target diseases across multiple organ systems and tissues, through both systemic and local administration. In addition to our current programs in development, we are also leveraging our platform to explore the next generation of stereopure nucleic acid therapeutics that have the potential to selectively target certain cell types.

Our core focus for our wholly-owned proprietary programs is neurology, which we broadly define as genetic diseases within the central nervous system (the "CNS") and neuromuscular system. We expect to initiate six development programs by the end of 2018. These programs include our three most advanced programs, which are in Huntington's disease ("HD"), and Duchenne Muscular Dystrophy ("DMD"), and three additional development candidates which we expect to select by the end of 2017.

Since our inception in 2012, we have devoted substantially all of our resources to developing an innovative and proprietary synthetic chemistry drug development platform that we are using to design, develop and commercialize nucleic acid therapeutic candidates, building our intellectual property portfolio, developing our supply chain, business planning, raising capital and providing general and administrative support for these operations. To date, we have not generated any product revenue and we have primarily financed our operations through sales of our securities.

We have never been profitable, and since our inception, we have incurred significant operating losses. Our net losses were $55.4 million in 2016, $19.2 million in 2015, and $5.2 million in 2014. As of December 31, 2016 and 2015, we had an accumulated deficit of $90.5 million and $35.1 million, respectively. We expect to incur significant expenses and increasing operating losses for the foreseeable future.

Financial Operations Overview

Revenue

We have not generated any product revenue since our inception and do not expect to generate any revenue from the sale of products for the foreseeable future. Our revenue during the year ended December 31, 2016 represented revenue earned under the Pfizer Collaboration Agreement that we entered into in May 2016. Our revenue during the year ended December 31, 2015 consisted of a payment received for research and development services under an agreement that was terminated in May 2015. Except as described above, we are not a party to any other license or collaboration agreements that have generated revenue as of December 31, 2016.

Operating Expenses

Our operating expenses since inception have consisted primarily of research and development costs and general and administrative costs.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our product candidates, which include:

- employee salaries, benefits and other related costs, including share-based compensation expense, for personnel in our research and development organization;
- expenses incurred under agreements with third parties, including contract research organizations ("CROs") that conduct research and preclinical activities on our behalf, as well as contract manufacturing organizations ("CMOs") that manufacture drug products for use in our preclinical trials;
- costs of third-party consultants, including fees, share-based compensation and related travel expenses;
- the cost of sponsored research, which includes laboratory supplies and facility-related expenses, including rent, maintenance and other operating costs; and
- costs related to compliance with regulatory requirements.

We recognize research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as prepaid or accrued research and development expenses.

Our primary research and development focus since inception has been the development of our synthetic chemistry drug development platform. We are using our platform to design, develop and commercialize a broad pipeline of nucleic acid therapeutic candidates.

Our direct research and development expenses consist primarily of certain external costs, consultants and CROs in connection with our preclinical studies and regulatory fees. We do not allocate the cost of sponsored research, which includes laboratory supplies and facility-related expenses, including rent, maintenance and other operating costs, because these costs are deployed across multiple product programs under development and, as such, are classified as costs of our research.

The table below summarizes our research and development expenses incurred on our platform and by program.

	For the Year Ended December 31,	
	2016	2015
	(in thousands)	
HD programs	$ 6,190	$ 376
DMD program	2,087	410
Other discovery programs, platform development and identification of potential drug discovery candidates	32,541	8,271
Total research and development expenses	$ 40,818	$ 9,057

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase in the foreseeable future as we initiate clinical trials for certain product candidates, continue to discover and develop additional product candidates, and pursue later stages of clinical development of product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, bonuses and other related benefits costs, including share-based compensation, for personnel in our executive, finance, corporate, business development, legal and administrative functions. General and administrative expenses also include legal fees relating to intellectual property and general corporate matters; expenses associated with being a public company; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; other operating costs; and facility-related expenses.

We anticipate that our general and administrative expenses will increase in the future, primarily due to additional compensation, including salaries, benefits, incentive arrangements and share-based compensation awards, as we increase our employee headcount to support the expected growth in our research and development activities and the potential commercialization of our product candidates. Additionally, we expect our facility-related expenses to increase related to the lease we entered into in 2016 for space in Lexington, Massachusetts which we intend to use primarily for our cGMP manufacturing, as well as for additional laboratory and office space.

Other Income (Expense), net

Other income (expense), net consists primarily of dividend and interest income earned on cash and cash equivalents balances for the year ended December 31, 2016. For the year ended December 31, 2015, other income (expense) consisted primarily of reimbursement of research and development costs extent under a research and development grant awarded by the Japanese Ministry of Economy, Trade and Industry ("METI").

Income Taxes

We are a multi-national company subject to taxation in the United States, Japan, Ireland and Singapore.

In 2016, 2015, and 2014 our provision for income taxes was $0.6 million, less than $0.1 million and $0.1 million, respectively, on pre-tax loss of $54.8 million, $19.2 million and $5.1 million, respectively. As of December 31, 2016, we had zero net operating loss carryforwards in the U.S. As of December 31, 2016 and 2015, we had U.S. federal and state research and development tax credit carryforwards of $0.2 million and $0.3 million, respectively, available to offset future U.S. federal and state income taxes. The U.S. federal and state research and development tax credits will begin to expire in 2031 and 2028, respectively. As of December 31, 2016 and 2015, we had net operating loss carryforwards in Japan of $5.3 million and $4.3 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2017. As of December 31, 2016 and 2015, we also had net operating loss carryforwards in Singapore of $84.0 million and $31.8 million, respectively, which may be available to offset future income tax liabilities and can be carried forward indefinitely.

Comparison of the Year Ended December 31, 2016 to the Year Ended December 31, 2015

The following table summarizes our results of operations for 2016 and 2015:

	For the Year Ended December 31,		Increase (Decrease)
	2016	2015	
	(in thousands)		
Revenues	$ 1,485	$ 152	$ 1,333
Operating expenses			
Research and development	40,818	9,057	31,761
General and administrative	15,994	10,393	5,601
Total operating expense	56,812	19,450	37,362
Loss from operations	(55,327)	(19,298)	(36,029)
Other income (expense), net	542	142	400
Loss before income taxes	(54,785)	(19,156)	(35,629)
Income tax benefit (provision)	(616)	(44)	(572)
Net loss	$ (55,401)	$ (19,200)	$ (36,201)

Revenue

Revenue was $1.5 million for the year ended December 31, 2016, which related to revenue earned in 2016 under the Pfizer Collaboration Agreement, which was entered into in May 2016, compared to revenue of $0.2 million for the year ended December 31, 2015. Revenue earned for the year ended December 31, 2015 was earned for research and development performed under our collaboration agreement with a third party which was entered into in 2014 and terminated in May 2015.

Research and Development Expenses

The table below summarizes our research and development expenses incurred for the years ended December 31, 2016 and 2015:

	For the Year Ended December 31,		
	2016	2015	Increase
	(in thousands)		
HD programs	$ 6,190	$ 376	$ 5,814
DMD program	2,087	410	1,677
Other discovery programs, platform development and identification of potential drug discovery candidates	32,541	8,271	24,270
Total research and development expenses	$ 40,818	$ 9,057	$ 31,761

Research and development expenses were $40.8 million for the year ended December 31, 2016, compared to approximately $9.0 million for the year ended December 31, 2015. The increase of $31.8 million was due, in part, to the following:

- an increase of $5.8 million in preclinical research and development expenses related to our HD programs, WVE-120101 and WVE-120102;
- an increase of $1.7 million preclinical research and development expenses related to our DMD program, WVE-210201; and
- an increase of $24.3 million in research and development expenses related to other discovery programs, platform development and identification of potential drug discovery candidates, due to an increase of $7.8 million in salary, bonus and related benefits costs and an increase of $2.7 million in share-based compensation expense, both of which are the result of an increase in employee headcount, and an increase of approximately $13.8 million in research and development supplies and services expenses and facility-related expenses.

Research and development expenses incurred at our Japan facility in 2016 and 2015 represented 1.7% and 6.4% of the related consolidated expenses for the year ended December 31, 2016 and 2015, respectively. The impact of changes in foreign currency did not have a significant impact on changes in our consolidated research and development expenses for the year ended December 31, 2016 compared to the year ended December 31, 2015.

General and Administrative Expenses

General and administrative expenses were $16.0 million for the year ended December 31, 2016 compared to $10.4 million for the year ended December 31, 2015. The increase of $5.6 million was primarily due to a $2.6 million increase in salary and related benefits cost resulting from an increase in employee headcount. The increase also partly resulted from an increase in share-based compensation expense of $0.2 million. Increased travel expense and other general and administrative expenses account for the remaining $2.8 million increase.

General and administrative expenses incurred at our Japan facility in 2016 and 2015 represented 1.4% and 2.6% of the related consolidated expenses for the year ended December 31, 2016 and 2015, respectively. The impact of changes in foreign currency did not have a significant impact on changes in our consolidated general and administrative expenses for the year ended December 31, 2016 compared to the year ended December 31, 2015.

Other Income (Expense), net

Other income (expense), net for the years ended December 31, 2016 and 2015 was $0.5 and $0.1 million, respectively. The increase in other income (expense), net is primarily related to the dividend and interest income earned in 2016 on our cash and cash equivalents.

Income Tax Provision

During the year ended December 31, 2016 and 2015, we recorded a tax provision of $0.6 million and less than $0.1 million, respectively, which is a result of income taxed in the United States due to income earned under a contract research arrangement between our U.S. and Singapore entities. During the years ended December 31, 2016 and 2015, we recorded no income tax benefits for the net operating losses incurred in Japan and Singapore due to uncertainty regarding future taxable income in these jurisdictions. In May 2016, we established a wholly-owned subsidiary in Ireland, however no income tax expense or benefit has been recorded.

Comparison of the Year Ended December 31, 2015 to the Year Ended December 31, 2014

The following table summarizes our results of operations for 2015 and 2014:

	For the Year Ended December 31,		Increase (Decrease)
	2015	2014	
	(in thousands)		
Revenues	$ 152	—	$ 152
Operating expenses			
Research and development	9,057	2,395	6,662
General and administrative	10,393	2,999	7,394
Total operating expense	19,450	5,394	14,056
Loss from operations	(19,298)	(5,394)	(13,904)
Other income (expense), net	142	249	(107)
Loss before income taxes	(19,156)	(5,145)	(14,011)
Income tax provision	(44)	(84)	40
Net loss	$ (19,200)	$ (5,229)	$ (13,971)

Revenue

Revenue was $0.2 million for the year ended December 31, 2015 due to revenue earned for research and development performed under our collaboration agreement with a third party that was entered into in 2014 and which was terminated in May 2015. There was no revenue for the year ended December 31, 2014.

Research and Development Expenses

The table below summarizes our research and development expenses incurred on our platform and by program for 2015 and 2014:

	For the Year Ended December 31,		Increase
	2015	2014	
	(in thousands)		
HD programs	$ 376	$ —	$ 376
DMD program	410	—	410
Other discovery programs, platform development and identification of potential drug discovery candidates	8,271	2,395	5,876
Total research and development expenses	$ 9,057	$ 2,395	$ 6,662

Research and development expenses were $9.1 million for the year ended December 31, 2015, compared to $2.4 million for the year ended December 31, 2014. The increase of $6.7 million was due, in part, to the following:

- an increase of $0.4 million in research and development expenses related to our HD programs, WVE-120101 and WVE-120102, including costs related to the collaboration with Children's Hospital of Philadelphia for preclinical research studies;
- an increase of $0.4 million in research and development expenses related to our DMD program, WVE-210201, including costs related to the collaboration with the University of Oxford for preclinical research studies; and
- an increase of $5.9 million in research and development expenses related to other discovery programs, platform development and identification of potential drug discovery candidates, which includes salary and related benefits costs, as well as costs associated with overall research directed at the identification of additional potential drug candidates. The increase was primarily the result of an increase in salary and related benefits costs of $4.2 million, including $2.2 million of share-based compensation costs, due to increased employee headcount, and an increase of approximately $1.7 million in research and development supplies and services expenses.

Research and development expenses incurred at our Japan facility in 2015 and 2014 represented 6.4% and 12.8% of the related consolidated expenses for the year ended December 31, 2015 and 2014, respectively. The impact of changes in foreign currency did not have a significant impact on changes in our consolidated research and development expenses for the year ended December 31, 2015 compared to the year ended December 31, 2014.

General and Administrative Expenses

General and administrative expenses were $10.4 million for the year ended December 31, 2015 compared to $3.0 million for the year ended December 31, 2014. The increase of $7.4 million was primarily due to a $3.4 million increase in professional fees related to legal fees and accounting fees as we prepared for our initial public offering in November 2015. The increase also partly resulted from an increase in share-based compensation expense of $1.8 million and an increase in salary and related benefits costs of $1.1 million resulting from an increase in employee headcount. Increased depreciation expense and other general and administrative expenses account for the remaining $1.1 million increase.

General and administrative expenses incurred at our Japan facility in 2015 and 2014 represented 2.6% and 4.9% of the related consolidated expenses for the year ended December 31, 2015 and 2014, respectively. The impact of changes in foreign currency did not have a significant impact on changes in our consolidated general and administrative expenses for the year ended December 31, 2015 compared to the year ended December 31, 2014.

Other Income (Expense), net

Other income (expense), net for the years ended December 31, 2015 and 2014 was $0.1 and $0.2 million, respectively.

Income Tax Provision

During the year ended December 31, 2015 and 2014, we recorded a tax provision of less than $0.1 million and $0.1 million, respectively, which is a result of income taxed in the United States due to income earned under a contract research arrangement between our U.S. and Singapore entities. During the years ended December 31, 2015 and 2014, we recorded no income tax benefits for the net operating losses incurred in Japan and Singapore due to uncertainty regarding future taxable income in these jurisdictions.

Liquidity and Capital Resources

On November 16, 2015, we closed an initial public offering of our ordinary shares, in which we issued and sold 6,375,000 ordinary shares at a price to the public of $16.00 per share. On December 4, 2015, we issued an additional 618,126 ordinary shares at a price of $16.00 per share pursuant to a partial exercise of the underwriters' over-allotment option. The aggregate net proceeds to us from our initial public offering, inclusive of the over-allotment exercise, were approximately $100.4 million after deducting underwriting discounts and commissions and offering expenses payable by us. Prior to the completion of our initial public offering, we financed our operations through private placements of our debt and equity securities, which resulted in net proceeds of $89.3 million from such transactions.

On May 5, 2016, we entered into a Research, License and Option Agreement (the "Pfizer Collaboration Agreement") with Pfizer Inc. ("Pfizer") and a Share Purchase Agreement (the "Pfizer Equity Agreement" and together with the Pfizer Collaboration Agreement, the "Pfizer Agreements") with an affiliate of Pfizer. Pursuant to the Pfizer Agreements, Pfizer paid us $40.0 million upfront, including $10.0 million as an upfront license fee and $30.0 million in the form of an equity investment in which we sold 1,875,000 of our ordinary shares to an affiliate of Pfizer.

Since our inception, we have not generated any product revenue and have incurred recurring net losses.

As of December 31, 2016, we had cash and cash equivalents totaling $150.3 million, restricted cash of $3.6 million related to letters of credit for office and laboratory space in Cambridge, Massachusetts and our newly leased facility in Lexington, Massachusetts and an accumulated deficit of $90.5 million.

We expect that the capital resources available to us as of December 31, 2016, along with anticipated milestone payments under our existing collaboration, will fund our operating expenses and capital expenditure requirements into 2019. We have based this estimate on assumptions that may prove to be incorrect, and we may use our available capital resources sooner than we currently expect. In addition, we may elect to raise additional funds before we need them if the conditions for raising capital are favorable due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Until we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public equity or debt financings or other sources, which may include collaborations with third parties. On January 4, 2017, we filed a universal shelf registration statement on Form S-3, which was declared effective by the SEC on February 6, 2017, on which we registered for sale up to $500.0 million of any combination of our ordinary shares, debt securities, warrants, rights, purchase contracts and/or units from time to time and at prices and on terms that we may determine. This registration statement will remain in effect for up to three years from the date it was declared effective. Adequate additional financing may not be available to us when we need it, on acceptable terms, or at all. Our inability to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We will need to generate significant revenue to achieve profitability, and we may never do so.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	For the Year Ended December 31,		
	2016	2015	2014
	(in thousands)		
Cash used in operating activities	$ (31,872)	$ (12,527)	$ (4,426)
Cash used in investing activities	(8,162)	(2,909)	(257)
Cash provided by financing activities	29,121	175,593	5,619
Effect of foreign exchange rates of cash	(14)	15	(327)
Net increase (decrease) in cash and cash equivalents	$ (10,927)	$ 160,172	$ 609

Operating Activities

During 2016, operating activities used $31.9 million of cash, primarily resulting from our net loss of $55.4 million offset by non-cash charges of $7.3 million and by cash provided by changes in our operating assets and liabilities of $16.2 million. The non-cash charges for 2016 related primarily to share-based compensation expense of $6.8 million. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2016 was due primarily to an increase in accounts payable due to higher research and development costs, as well as the timing of payments.

During 2015, operating activities used $12.5 million of cash, primarily resulting from our net loss of $19.2 million offset by non-cash charges of $4.7 million and by cash provided by changes in our operating assets and liabilities of $1.9 million. The non-cash charges for 2015 related primarily to share-based compensation expense of $4.0 million. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2015 was due primarily to an increase in accounts payable due to higher research and development costs, as well as the timing of payments.

During 2014, operating activities used $4.4 million of cash, primarily resulting from our net loss of $5.2 million offset by non-cash charges of $0.4 million and by cash provided by changes in our operating assets and liabilities of $0.4 million. The non-cash charges for 2014 related primarily to $0.3 million of depreciation and amortization associated with our property and equipment. Net cash provided by changes in our operating assets and liabilities during 2014 consisted primarily of a $0.4 million increase in accrued expenses due to higher accruals for research and development costs.

Investing Activities

During 2016, investing activities used $8.2 million of cash, consisting primarily of purchases of property and equipment of $5.6 million and an increase in restricted cash of $2.6 million related to a letter of credit for our new manufacturing space in Lexington, Massachusetts.

During 2015, investing activities used $2.9 million of cash, consisting of restricted cash of $1.0 million primarily placed in favor of a letter of credit for our office and laboratory space in Cambridge, Massachusetts along with purchases of property and equipment of $1.9 million.

During 2014, investing activities used $0.3 million of cash, primarily consisting of purchases of property and equipment of $0.6 million offset by reimbursements of $0.3 million from METI.

Financing Activities

During 2016, net cash provided by financing activities was $29.1 million, which was primarily due to the $30.0 million in proceeds from the issuance of 1,875,000 shares to an affiliate of Pfizer related to the Pfizer Equity Agreement. Additionally, during 2016 we made payments of $0.1 million related to our capital lease and $1.1 million related to initial public offering costs, which were included in accounts payable and accrued expenses as of December 31, 2015, and these payments were partially offset by the $0.3 million of proceeds from the exercise of share options.

During 2015, net cash provided by financing activities was $175.6 million, primarily from the issuance of ordinary shares in our initial public offering for net proceeds of $100.4 million in November 2015, the issuance of Series B preferred shares for $62.5 million in August 2015 and the issuance of ordinary shares for $11.6 million in January 2015.

During 2014, net cash provided by financing activities was $5.6 million, primarily from the issuance of ordinary shares to investors.

Effect of Foreign Exchange Rates on Cash

During 2016, the effect of changes in foreign exchange rates on cash was less than $0.1 million due to minimal changes in the Japanese yen in 2016.

During 2015, the effect of changes in foreign exchange rates on cash was less than $0.1 million due to minimal changes in the Japanese yen in 2015.

During 2014, the effect of changes in foreign exchange rates on cash was $0.3 million due to changes in the Japanese yen related primarily to the translation of intercompany accounts denominated in Japanese yen in 2014.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing research and development activities. We anticipate that our expenses will increase substantially if and as we:

- file clinical trial applications with global regulatory agencies and initiate clinical studies for our two programs in Huntington's disease and our program in Duchenne Muscular Dystrophy;
- conduct research and continue preclinical development of the discovery targets and advance additional programs into development;
- make strategic investments in manufacturing processes and formulations;
- develop manufacturing capabilities through outsourcing and a scalable manufacturing facility;
- maintain our intellectual property portfolio and consider the acquisition of complementary intellectual property;
- seek and obtain regulatory approvals for our product candidates; and
- establish and build capabilities to market, manufacture and distribute our product candidates.

We may experience delays or encounter issues with any of the above, including but not limited to failed studies, complex results, safety issues or other regulatory challenges.

Because of the numerous risks and uncertainties associated with the development of drug candidates or follow-on programs, and because the extent to which we may enter into collaborations with third parties for development of product candidates is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development for our therapeutic programs. Our future capital requirements for our therapeutic programs will depend on many factors, including:

- the progress and results of conducting research and preclinical and clinical development within our therapeutic programs and with respect to future potential pipeline candidates;
- the cost of manufacturing clinical supplies for our product candidates;
- the costs, timing and outcome of regulatory review for our product candidates;
- the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;

- the revenue, if any, received from commercial sales for our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the effect of competing technological and market developments; and
- the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our product revenue, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if ever. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives.

Adequate additional funds may not be available to us on acceptable terms when we need them, or at all. We do not currently have any committed external source of funds, except for possible future payments from Pfizer if milestones under the Pfizer Collaboration Agreement are achieved. On January 4, 2017, we filed a universal shelf registration statement on Form S-3, which was declared effective by the SEC on February 6, 2017, on which we registered for sale up to $500.0 million of any combination of our ordinary shares, debt securities, warrants, rights, purchase contracts and/or units from time to time and at prices and on terms that we may determine. This registration statement will remain in effect for up to three years from the date it was declared effective. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing shareholders will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our shareholders. Additional debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute our shareholders' ownership interests.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2016 and the effect such obligations are expected to have on our liquidity and cash flows in future periods:

	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
			(in thousands)		
Operating lease commitments	$ 57,953	$ 1,954	$ 16,430	$ 12,486	$ 27,083
Capital lease obligation	78	62	16	—	—
Total	$ 58,031	$ 2,016	$ 16,446	$ 12,486	$ 27,083

We enter into contracts in the normal course of business with CROs for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes. These contracts generally provide for termination upon notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

Off-Balance Sheet Arrangements

We have no off-balance sheet arrangements (as that term is defined in Item 303(a)(4)(ii) of Regulation S-K) as of December 31, 2016 that have or are reasonably likely to have a current or future effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources.

JOBS Act Accounting Election

In April 2012, the Jumpstart Our Business Startups Act of 2012 ("the JOBS Act"), was enacted. Section 107 of the JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

Recently Issued and Adopted Accounting Pronouncements

For detailed information regarding recently issued and adopted accounting pronouncements and the expected impact on our consolidated financial statements, see Note 2, "Significant Accounting Policies" in the notes to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Critical Accounting Policies and Significant Judgments and Estimates

Our financial statements are prepared in accordance with generally accepted accounting principles in the United States of America ("U.S. GAAP"). The preparation of our financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amount of assets, liabilities, revenue, costs and expenses and related disclosures. We believe that the estimates and assumptions involved in the accounting policies, particularly revenue recognition and income taxes, as described in Note 2, "Significant Accounting Policies" in the notes to the consolidated financial statements may have the greatest potential impact on our consolidated financial statements and, therefore, consider these to be our critical accounting policies. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions and conditions.

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

Market risk represents the risk of loss that may impact our financial position due to adverse changes in financial market prices and rates. Our market risk exposure is primarily the result of fluctuations in interest rates and foreign exchange rates as well as, to a lesser extent, inflation.

Interest Rate Risk

We are exposed to interest rate risk in the ordinary course of our business. Our cash and cash equivalents are held in readily available checking and money market accounts.

Foreign Currency Risk

We are exposed to market risk related to changes in the value of the Japanese yen, which is the currency our Japanese subsidiary conducts its business in. As of December 31, 2016 and 2015, 0.2% and 0.5% of our assets were located in Japan, respectively. During the years ended December 31, 2016 and 2015, 1.7% and 6.4% of our research and development expenses were transacted in Japanese yen during the years ended, respectively. And 1.4% and 2.6% of our general and administrative expenses were transacted in Japanese yen for the years ended December 31, 2016 and 2015, respectively. Therefore, when the U.S. dollar strengthens relative to the yen, our U.S. dollar reported expenses from non-U.S. dollar denominated operating costs will decrease. Conversely, when the U.S. dollar weakens relative to the yen, our U.S. dollar reported expenses from non-U.S. dollar denominated operating costs will increase. Changes in the relative values of currencies occur regularly and, in some instances, could materially adversely affect our business, results of operations, financial condition or cash flows. Our foreign currency sensitivity is affected by changes in the Japanese yen, which is impacted by economic factors both locally in Japan and worldwide. A hypothetical 10% change in foreign currency rates would not have a material impact on our historical financial position or results of operations.

Inflation Risk

We do not believe that inflation had a material effect on our business, financial condition or results of operations in the last three years.

Item 8. Financial Statements and Supplementary Data

The information required by this Item 8 is included at the end of this Annual Report on Form 10-K beginning on page F-1.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

Not applicable.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2016. 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 its management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2016, our principal executive officer and principal financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Remediation of Previously Disclosed Material Weakness

As previously discussed in our Form 10-K for the period ended December 31, 2015, and our Forms 10-Q for the periods ending March 31, 2016, June 30, 2016 and September 30, 2016, our management determined that a material weakness in internal control over financial reporting existed as of December 31, 2015 and continued to exist as of March 31, 2016, June 30, 2016 and September 30, 2016. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

A material weakness in internal control over financial reporting was identified as we did not appropriately design and implement controls over the review and approval of manual journal entries and the related supporting journal entry calculations.

As of December 31, 2016, we have designed and implemented controls over the review and approval of manual journal entries and the related supporting journal entry calculations. Specifically, these controls include the appropriate segregation of duties between the preparer and approver of the journal entries, the appropriate level of review of the supporting documentation for journal entry calculations and the appropriate level of competency of the reviewer based on the nature and complexity of the journal entry. Management has tested these additional controls and concluded that the material weakness previously identified has been remediated as of December 31, 2016.

Changes in Internal Control over Financial Reporting

Except as discussed under Remediation of Previously Disclosed Material Weakness above, there were no changes in our internal control over financial reporting identified in connection with the evaluation of such internal control required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the fiscal quarter ended December 31, 2016 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended, as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's 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:

- Pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company;
- 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 are being made only in accordance with authorizations of management and directors of the company; and
- 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.

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

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2016. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") in Internal Control-Integrated Framework (2013).

Based on our assessment, management believes that, as of December 31, 2016, our internal control over financial reporting is effective based on those criteria**.**

As an "emerging growth company" under the Jumpstart Our Business Startups Act, we are exempt from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002. As a result, KPMG LLP, our independent registered public accounting firm, has not audited or issued an attestation report with respect to the effectiveness of our internal control over financial reporting as of December 31, 2016.

Item 9B. Other Information

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission on Schedule 14A in connection with our 2017 Annual General Meeting of Shareholders, or the 2017 Proxy Statement, if the Proxy Statement is filed not later than 120 days after the end of our fiscal year ended December 31, 2016, in the sections titled "Management and Corporate Governance," "Section 16(a) Beneficial Ownership Reporting Compliance," and "Code of Business Conduct and Ethics," and is incorporated herein by reference. If the Proxy Statement is not filed within such 120-day period, the information required by this item will be contained in an amendment to this Annual Report on Form 10-K to be filed with the Securities and Exchange Commission, or the Form 10-K/A.

Item 11. Executive Compensation

The information required by this item regarding executive compensation is incorporated by reference to the information set forth in the section titled "Executive Officer and Director Compensation" in our Proxy Statement. If the Proxy Statement is not filed within 120 days after the end of our fiscal year ended December 31, 2016, the information required by this item will be contained in the Form 10-K/A.

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

The information required by this item regarding security ownership of certain beneficial owners and management is incorporated by reference to the information set forth in the sections titled "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" in our Proxy Statement. If the Proxy Statement is not filed within 120 days after the end of our fiscal year ended December 31, 2016, the information required by this item will be contained in the Form 10-K/A.

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

The information required by this item regarding certain relationships and related transactions and director independence is incorporated by reference to the information set forth in the sections titled "Certain Relationships and Related Person Transactions" and "Management and Corporate Governance – Board of Directors," respectively, in our Proxy Statement. If the Proxy Statement is not filed within 120 days after the end of our fiscal year ended December 31, 2016, the information required by this item will be contained in the Form 10-K/A.

Item 14. Principal Accounting Fees and Services

The information required by this item regarding principal accountant fees and services is incorporated by reference to the information set forth in the sections titled "Principal Accountant Fees and Services" and "Policy on Audit Committee Pre-Approval of Audit and Permissible Non-Audit Services of Independent Public Accountant and Independent Singapore Auditor" in our Proxy Statement. If the Proxy Statement is not filed within 120 days after the end of our fiscal year ended December 31, 2016, the information required by this item will be contained in the Form 10-K/A.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) The following documents are filed as part of this report:

1. Financial Statements

See Index to Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K.

2. Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
3.1	Constitution (formerly known as Memorandum of Association and Articles of Association)		Amendment No. 5 to Form S-1 (Exhibit 3.2)	11/10/2015	333-207379
4.1	Form of Specimen Ordinary Share Certificate		Amendment No. 3 to Form S-1 (Exhibit 4.1)	11/06/2015	333-207379
4.2	Investors' Rights Agreement by and among the Registrant and certain of its shareholders, dated as of August 14, 2015		Form S-1 (Exhibit 4.2)	10/09/2015	333-207379
4.3†	Share Purchase Agreement by and between the Registrant and C.P. Pharmaceuticals International C.V., dated as of May 5, 2016		Form10-Q (Exhibit 10.2)	08/15/2016	001-37627
Lease Agreements					
10.1	Lease Agreement by and among Harvard Real Estate—Allston, Inc., Shin Nippon Biomedical Laboratories Ltd., dated June 25, 2009		Form S-1 (Exhibit 10.2)	10/09/2015	333-207379
10.2	Commercial Lease Agreement by and among SNBL USA, Ltd. and Ontorii, Inc. (now WAVE Life Sciences USA, Inc.), dated as of January 1, 2010		Form S-1 (Exhibit 10.4)	10/09/2015	333-207379
10.3	Consent to Office Space Sublease by and among SNBL USA, Ltd, Ontorii, Inc. (now WAVE Life Sciences USA, Inc.) and Harvard Real Estate—Allston, Inc., dated as of January 1, 2010		Form S-1 (Exhibit 10.3)	10/09/2015	333-207379
10.4	Amendment 1 to the Commercial Lease Agreement by and between SNBL USA, Ltd. and Ontorii, Inc. (now WAVE Life Sciences USA, Inc.), dated as of July 1, 2011		Form S-1 (Exhibit 10.5)	10/09/2015	333-207379
10.5	Lease Agreement by and between the Registrant and King 733 Concord LLC, dated as of April 6, 2015		Form S-1 (Exhibit 10.7)	10/09/2015	333-207379
10.6	Lease Agreement by and between WAVE Life Sciences USA, Inc. and King 115 Hartwell LLC, dated as of September 26, 2016.		Form 8-K (Exhibit 10.1)	09/27/2016	001-37627

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
10.7	First Amendment (to Lease) by and between WAVE Life Sciences USA, Inc. and King 115 Hartwell LLC, dated as of December 31, 2016		Form 8-K (Exhibit 10.1)	01/06/2017	001-37627
Collaboration and License Agreements					
10.8†	Co-Exclusive License Agreement by and between the Registrant and Max-Planck-Innovation GmbH, dated as of June 8, 2015		Form S-1 (Exhibit 10.10)	10/09/2015	333-207379
10.9†	Research, License and Option Agreement by and between the Registrant and Pfizer Inc., dated as of May 5, 2016		Form10-Q (Exhibit 10.1)	08/15/2016	001-37627
Agreements with Executive Officers and Directors					
10.10+	Form of Deed of Indemnity by and between the Registrant and each of its directors and certain of its officers		Form S-1 (Exhibit 10.11)	10/09/2015	333-207379
10.11+	Employment Agreement by and between the Registrant and Paul B. Bolno, M.D., dated as of December 12, 2013		Form S-1 (Exhibit 10.12)	10/09/2015	333-207379
10.12+	Offer Letter by and between the Registrant and Chandra Vargeese, Ph.D., dated as of July 2, 2014		Form S-1 (Exhibit 10.14)	10/09/2015	333-207379
10.13+	Offer Letter by and between the Registrant and Christopher Francis, Ph.D., dated as of March 10, 2014		Form S-1 (Exhibit 10.15)	10/09/2015	333-207379
10.14+	Employment Agreement between the Registrant and Michael Panzara, M.D. dated as of July 11, 2016		Form 10-Q (Exhibit 10.4)	11/09/2016	001-37627
10.15+	Employment Agreement between the Registrant and Keith C. Regnante dated as of August 16, 2016		Form 10-Q (Exhibit 10.5)	11/09/2016	001-37627
10.16+	Non-Employee Director Compensation Policy effective as of November 10, 2016.		Form 8-K (Exhibit 10.1)	11/10/2016	001-37627
10.17+	Consulting Agreement by and between Ontorii, Inc. (now WAVE Life Sciences USA, Inc.) and Gregory Verdine, dated as of April 1, 2012		Form S-1 (Exhibit 10.16)	10/09/2015	333-207379
10.18+	Nominee Director Fee Agreement by and between the Registrant and Miura & Associates Management Consultants Pte. Ltd., dated as of October 23, 2012		Form S-1 (Exhibit 10.17)	10/09/2015	333-207379
Equity and Other Compensation Plans					
10.19+	WAVE Life Sciences Ltd. 2014 Equity Incentive Plan, as amended, and forms of agreement thereunder		Form S-8 (Exhibit 10.1)	12/17/2015	333-208598
10.20+	Form of Incentive Share Option Agreement (updated as of September 20, 2016) under the 2014 Equity Incentive Plan		Form 10-Q (Exhibit 10.1)	11/09/2016	001-37627
10.21+	Form Non-qualified Share Option Agreement (updated as of September 20, 2016) under the 2014 Equity Incentive Plan		Form 10-Q (Exhibit 10.2)	11/09/2016	001-37627
10.22+	Form of Restricted Share Unit Agreement under the 2014 Equity Incentive Plan		Form 10-Q (Exhibit 10.3)	11/09/2016	001-37627
21.1	List of Subsidiaries of the Registrant	X			
23.1	Consent of Independent Registered Public Accounting Firm	X			

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
24.1	Power of Attorney (included on signature page to this Annual Report on Form 10-K)	X			
31.1	Certifications of Principal Executive Officer pursuant to Rule 13a-14(a)	X			
31.2	Certifications of Principal Financial Officer pursuant to Rule 13a-14(a)	X			
32*	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, by Principal Executive Officer and Principal Financial Officer.	X			
101.INS	XBRL Instance Document	X			
101.SCH	XBRL Taxonomy Extension Schema Document	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	X			
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	X			

(*) The certification attached as Exhibit 32.1 that accompanies this Annual Report on Form 10-K is not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of WAVE Life Sciences Ltd. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

(+) Indicates management contract or compensatory plan or arrangement.

(†) Confidential treatment has been granted with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

WAVE Life Sciences Ltd.

Date: March 16, 2017

By: /s/ Paul B. Bolno, M.D.
Paul B. Bolno, M.D.
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Paul B. Bolno, M.D. with full power of substitution and resubstitution and full power to act, as his true and lawful attorney-in-fact and agent to act in his name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Report and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorney-in-fact and agent or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

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

Signature	Title	Date
/s/ Paul B. Bolno, M.D. Paul B. Bolno, M.D.	President, Chief Executive Officer and Director (*principal executive officer*)	March 16, 2017
/s/ Keith C. Regnante Keith C. Regnante	Chief Financial Officer (*principal financial officer and principal accounting officer*)	March 16, 2017
/s/ Gregory L. Verdine, Ph.D. Gregory L. Verdine, Ph.D.	Chairman of the Board	March 16, 2017
/s/ Christian Henry Christian Henry	Director	March 16, 2017
/s/ Peter Kolchinsky, Ph.D. Peter Kolchinsky, Ph.D.	Director	March 16, 2017
/s/ Koji Miura Koji Miura	Director	March 16, 2017
/s/ Adrian Rawcliffe Adrian Rawcliffe	Director	March 16, 2017
/s/ Ken Takanashi Ken Takanashi	Director	March 16, 2017
/s/ Masaharu Tanaka Masaharu Tanaka	Director	March 16, 2017

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Shareholders
WAVE Life Sciences Ltd.:

We have audited the accompanying consolidated balance sheets of WAVE Life Sciences Ltd. and subsidiaries as of December 31, 2016 and 2015, and the related consolidated statements of operations, comprehensive loss, Series A preferred shares and shareholders' equity, and cash flows for each of the years in the three year period ended December 31, 2016. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated 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. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of WAVE Life Sciences Ltd. and subsidiaries as of December 31, 2016 and 2015, and the results of their operations and their cash flows for each of the years in the three year period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

/s/ KPMG LLP

Cambridge, Massachusetts

March 16, 2017

WAVE LIFE SCIENCES LTD.
CONSOLIDATED BALANCE SHEETS

(In thousands, except share amounts)

	December 31, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 150,293	$ 161,220
Prepaid expenses and other current assets	1,483	146
Deferred tax assets	214	18
Total current assets	151,990	161,384
Property and equipment, net	8,607	2,789
Deferred tax assets	560	192
Restricted cash	3,601	1,055
Other assets	53	4
Total assets	$ 164,811	$ 165,424
Liabilities, Series A preferred shares and shareholders' equity		
Current liabilities:		
Accounts payable	$ 4,943	$ 2,811
Accrued expenses and other current liabilities	4,445	945
Current portion of capital lease obligation	62	62
Current portion of deferred revenue	2,705	—
Total current liabilities	12,155	3,818
Long-term liabilities:		
Capital lease obligation, net of current portion	16	78
Deferred revenue, net of current portion	8,311	—
Other liabilities	1,592	163
Total long-term liabilities	9,919	241
Total liabilities	$ 22,074	$ 4,059
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding	7,874	7,874
Shareholders' equity:		
Ordinary shares, no par value; 23,502,169 and 21,551,423 shares issued and outstanding at December 31, 2016 and 2015, respectively	215,602	185,344
Additional paid-in capital	10,029	3,182
Accumulated other comprehensive income (loss)	(291)	41
Accumulated deficit	(90,477)	(35,076)
Total shareholders' equity	134,863	153,491
Total liabilities, Series A preferred shares and shareholders' equity	$ 164,811	$ 165,424

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

WAVE LIFE SCIENCES LTD.
CONSOLIDATED STATEMENTS OF OPERATIONS

(In thousands, except share and per share amounts)

	For the Year Ended December 31,		
	2016	2015	2014
Revenue	$ 1,485	$ 152	$ —
Operating expenses:			
Research and development	40,818	9,057	2,395
General and administrative	15,994	10,393	2,999
Total operating expenses	56,812	19,450	5,394
Loss from operations	(55,327)	(19,298)	(5,394)
Other income (expense), net:			
Dividend income	255	—	—
Interest income (expense), net	337	86	(12)
Other income (expense), net	(50)	56	261
Total other income (expense), net	542	142	249
Loss before income tax provision	(54,785)	(19,156)	(5,145)
Income tax provision	(616)	(44)	(84)
Net loss	$ (55,401)	$ (19,200)	$ (5,229)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (2.43)	$ (1.83)	$ (1.34)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	22,800,628	10,501,455	3,911,556

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

WAVE LIFE SCIENCES LTD.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(In thousands, except share and per share amounts)

	For the Year Ended December 31,		
	2016	2015	2014
Net loss	$ (55,401)	$ (19,200)	$ (5,229)
Other comprehensive loss:			
Foreign currency translation	(332)	(15)	(169)
Comprehensive loss	$ (55,733)	$ (19,215)	$ (5,398)

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

WAVE LIFE SCIENCES LTD.
CONSOLIDATED STATEMENT OF SERIES A PREFERRED SHARES AND SHAREHOLDERS' EQUITY

(In thousands, except share amounts)

	Series A Preferred Shares		Series B Preferred Shares		Series A Preferred Shares		Ordinary Shares		Additional Paid-In-Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2013	—	$ —	—	$ —	1,536,209	$ 2,022	484,585	$ 638	$ —	$ 225	$ (10,647)	$ (7,762)
Conversion of related party notes payable to ordinary shares and Series A preferred shares	—	—	—	—	2,365,139	5,852	1,515,596	3,750	—	—	—	9,602
Issuance of ordinary shares, net of offering costs of $15	—	—	—	—	—	—	2,263,291	5,585	—	—	—	5,585
Other comprehensive loss	—	—	—	—	—	—	—	—	—	(169)		(169)
Net loss											(5,229)	(5,229)
Balance as of December 31, 2014	—	—	—	—	3,901,348	7,874	4,263,472	9,973	—	56	(15,876)	2,027
Issuance of ordinary shares, net of issuance costs of $169	—	—	—	—	—	—	4,769,077	11,631	—	—	—	11,631
Share-based compensation	—	—	—	—	—	—	190,856	842	3,182	—	—	4,024
Issuance of Series B preferred, net of issuance costs of $3,468	—	—	5,334,892	62,532	—	—	—	—	—	—	—	—
Reclassification of Series A preferred shares	3,901,348	7,874	—	—	(3,901,348)	(7,874)	—	—	—	—	—	(7,874)
Issuance of ordinary shares upon initial public offering, net of issuance costs of $3,702	—	—	—	—	—	—	6,993,126	100,366	—	—	—	100,366
Conversion of Series B preferred shares into ordinary shares upon initial public offering	—	—	(5,334,892)	(62,532)	—	—	5,334,892	62,532	—	—	—	62,532
Other comprehensive loss	—	—	—	—	—	—	—	—	—	(15)	—	(15)
Net loss	—	—	—	—	—	—	—	—	—	—	(19,200)	(19,200)
Balance at December 31, 2015	3,901,348	$ 7,874	—	$ —	—	$ —	21,551,423	$ 185,344	$ 3,182	$ 41	$ (35,076)	$ 153,491
Issuance of ordinary shares	—	—	—	—	—	—	1,875,000	30,000	—	—	—	30,000
Share-based compensation	—	—	—	—	—	—	—	—	6,847	—	—	6,847
Option exercises	—	—	—	—	—	—	75,746	258	—	—	—	258
Other comprehensive loss	—	—	—	—	—	—	—	—	—	(332)	—	(332)
Net loss	—	—	—	—	—	—	—	—	—	—	(55,401)	(55,401)
Balance at	3,901,348	$ 7,874	—	$ —	—	$ —	23,502,169	$ 215,602	$ 10,029	$ (291)	$ (90,477)	$ 134,863

December 31, 2016														

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

WAVE LIFE SCIENCES LTD.
CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	For the Year Ended December 31,		
	2016	2015	2014
Cash flows from operating activities			
Net loss	$ (55,401)	$ (19,200)	$ (5,229)
Adjustments to reconcile net loss to net cash flows used in operating activities:			
Depreciation and amortization	784	594	281
Share-based compensation expense	6,847	4,024	—
Deferred rent	565	88	(6)
Loss on disposal of property and equipment	—	—	14
Deferred income taxes	(564)	36	84
Tax benefit related to share-based compensation	(310)	—	—
Changes in operating assets and liabilities:			
Accounts receivable	-	193	(129)
Prepaid expenses and other current assets	(1,337)	(63)	(12)
Accounts payable	3,369	1,648	9
Accrued expenses and other current liabilities	2,296	267	410
Deferred revenue	11,015	(152)	152
Other non-current liabilities	864	38	—
Net cash used in operating activities	(31,872)	(12,527)	(4,426)
Cash flows from investing activities			
Increase in restricted cash	(2,599)	(1,055)	—
Proceeds from government grant reimbursements for property and equipment	—	3	319
Proceeds from the sale of property and equipment	4	—	14
Purchases of property and equipment	(5,567)	(1,857)	(590)
Net cash used in investing activities	(8,162)	(2,909)	(257)
Cash flows from financing activities			
Proceeds from initial public offering, net of offering costs and underwriter commissions	—	101,444	—
Costs associated with initial public offering	(1,075)	—	—
Proceeds from issuance of ordinary shares, net of offering costs	30,000	11,631	5,585
Proceeds from issuance of Series B preferred shares, net of offering costs	—	62,532	—
Proceeds from government grant	—	112	34
Payments on capital lease obligation	(62)	(126)	—
Proceeds from the exercise of share options	258	—	—
Net cash provided by financing activities	29,121	175,593	5,619
Effect of foreign exchange rates on cash	(14)	15	(327)
Net increase (decrease) in cash and cash equivalents	(10,927)	160,172	609
Cash and cash equivalents at beginning of period	161,220	1,048	439
Cash and cash equivalents at end of period	$ 150,293	$ 161,220	$ 1,048
Supplemental disclosure of cash flow information:			
Deferred offering costs in accounts payable and accrued expenses at period end	$ —	$ 1,075	$ 72
Cash paid for interest	$ 29	$ —	$ 86
Cash paid for taxes, net of refunds	$ 554	$ —	$ —
Equipment acquired for capital lease obligation	$ —	$ 268	$ —
Conversion of related party notes payable into ordinary and Series A preferred shares	$ —	$ —	$ 9,602
Property and equipment purchases in accounts payable and accrued expenses at period end	$ 1,653	$ 306	$ 3

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

1. THE COMPANY

Organization

WAVE Life Sciences Ltd. (together with its subsidiaries, "WAVE," "we" or the "Company") is a genetic medicines company with an innovative and proprietary synthetic chemistry drug development platform that we are using to design, develop and commercialize a broad pipeline of first-in-class or best-in-class nucleic acid therapeutic candidates for genetically defined diseases. We are initially developing oligonucleotides that target genetic defects to either reduce the expression of disease-promoting proteins or transform the production of dysfunctional mutant proteins into the production of functional proteins.

The Company was incorporated in Singapore on July 23, 2012 and has its principal U.S. office in Cambridge, Massachusetts. The Company was incorporated with the purpose of combining two commonly held companies, WAVE Life Sciences USA, Inc. ("WAVE USA"), a Delaware corporation (formerly Ontorii, Inc.), and WAVE Life Sciences Japan, Inc. ("WAVE Japan"), a company organized under the laws of Japan (formerly Chiralgen., Ltd.), which occurred on September 12, 2012. On May 31, 2016, WAVE Life Sciences Ireland Limited ("WAVE Ireland") was formed as a wholly-owned subsidiary of WAVE Life Sciences Ltd. It was formed as a private company limited by shares and the company number is 583482.

The Company's primary activities since inception have been developing a synthetic chemistry drug development platform to design, develop and commercialize nucleic acid therapeutic programs, advancing the Company's neurology franchise, expanding the Company's research and development activities to enter the clinic, building the Company's intellectual property, recruiting personnel and raising capital to support these activities.

Risks and Uncertainties

The Company is subject to risks common to companies in the biotechnology industry including, but not limited to, new technological innovations, protection of proprietary technology, developing internal manufacturing capabilities, dependence on key personnel, compliance with government regulations and the need to obtain additional financing. The Company's therapeutic programs will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercialization of any product candidates. These efforts require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance-reporting capabilities. The Company's therapeutic programs are currently in the development or discovery stage. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained, that any products developed will obtain necessary government regulatory approval or that any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from product sales. The Company operates in an environment of rapid change in technology and substantial competition from pharmaceutical and biotechnology companies. In addition, the Company is dependent upon the services of its employees and consultants.

Basis of Presentation

The Company has prepared the accompanying consolidated financial statements in conformity with U.S. GAAP and in U.S. dollars.

2. SIGNIFICANT ACCOUNTING POLICIES

Cash Equivalents

The Company considers all highly liquid securities with original final maturities of three months or less from the date of purchase to be cash equivalents. Cash equivalents are comprised of funds in money market accounts.

Principles of Consolidation

The Company's consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All significant intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated

financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include the valuation of its Series A preferred shares on conversion of the related party notes payable, the valuation of the Company's ordinary shares prior to the initial public offering, the assumptions used to determine the fair value of share-based awards, the valuation allowance required for the Company's deferred tax assets, and determining uncertain tax positions and the related liabilities. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Actual results could differ from the Company's estimates.

Segment Data

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's singular focus is on developing its proprietary synthetic chemistry platform to develop and commercialize a broad pipeline of nucleic acid-based therapeutics.

Foreign Currency Translation

The functional currency of the Company's Japanese subsidiary is the Japanese Yen and the functional currency for both the Company's U.S. subsidiary and the Company's Singapore entity is the U.S. dollar. Assets and liabilities of WAVE Japan are translated at period end exchange rates while revenues and expenses are translated at average exchange rates for the period. Intercompany loans that are not expected to be settled in the foreseeable future are translated at the historical rate for the date of each capital transaction. Net unrealized gains and losses from foreign currency translation are reflected as accumulated other comprehensive (loss) income within Series A preferred shares and shareholders' equity and consolidated statements of comprehensive loss. Gains and losses on foreign currency transactions are included in the consolidated statements of operations within other income (expenses), net.

Fair Value of Financial Instruments

The Company is 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. The fair value hierarchy is 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 financial instrument based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the financial instrument and are developed based on the 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 hierarchy defines three levels of valuation inputs:

Level 1—Unadjusted quoted prices in active markets that are accessible at the measurement date of identical, unrestricted assets.

Level 2—Quoted prices for similar assets, or inputs that are observable, either directly or indirectly, for substantially the full term through corroboration with observable market data. Level 2 includes investments valued at quoted prices adjusted for legal or contractual restrictions specific to the security.

Level 3—Pricing inputs are unobservable for the asset, that is, inputs that reflect the reporting entity's own assumptions about the assumptions market participants would use in pricing the asset. Level 3 includes private investments that are supported by little or no market activity.

There were no financial instruments recorded at fair value as of December 31, 2016 and 2015. The carrying amounts of accounts receivable, accounts payable, and accrued expenses approximate their fair values due to their short-term maturities.

Concentration of Credit Risk

Cash and cash equivalents are financial instruments that potentially subject the Company to concentration of credit risk. The Company uses several financial institutions to maintain its cash and cash equivalents, all of which are high quality, accredited financial institutions and, accordingly, such funds are subject to minimal credit risk. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. The Company has no financial instruments with off-balance sheet risk of loss.

Restricted Cash

Restricted cash consists primarily of cash placed in separate restricted bank accounts as required under the terms of the Company's lease agreements for its Cambridge, Massachusetts facility and the newly leased facility in Lexington, Massachusetts (refer to Note 8).

As of December 31, 2016, the Company had $3.6 million of restricted cash, of which $2.6 million was related to the Lexington facility and the remaining $1.0 million was related to the Cambridge facility. As of December 31, 2015, the Company had $1.1 million of restricted cash, which was primarily related to the Cambridge facility.

Property and Equipment

Property and equipment, which consists of furniture and equipment and leasehold improvements are stated at cost less accumulated depreciation and amortization. Depreciation is calculated on a straight-line basis over the following estimated useful lives of the assets:

Equipment, Furniture and Software	3-7 years
Leasehold Improvements	Shorter of life of lease or useful life

Depreciation and amortization begins at the time the asset is placed in service. Maintenance and repairs are charged to operations as incurred. Upon retirement or sale, the cost of the disposed asset and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is reflected in the consolidated statements of operations.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. Long-lived assets are reviewed for impairment whenever events or other changes in circumstances indicate that the carrying amount may not be recoverable. Certain factors may exist or events may occur that indicate that impairment exists including, but not limited to, the following: significant underperformance relative to historical or projected future operating results; significant changes in the manner of use of the underlying assets; and significant adverse industry or market economic trends.

When performing the impairment assessment for long-lived assets, the Company compares the carrying value of such assets to the estimated undiscounted future net cash flows expected from the use of the assets and their eventual disposition. In the event that the carrying value of the assets is determined to be unrecoverable, the Company would estimate the fair value of the assets and record an impairment charge for the excess of the carrying value over the fair value.

Through December 31, 2016, the Company has not recognized any impairment charges.

Revenue Recognition

To date, the Company's only significant source of revenue is derived from the Pfizer Collaboration Agreement (as defined in Note 5), pursuant to which the Company and Pfizer (as defined in Note 5) have agreed to collaborate on the discovery, development and commercialization of stereopure oligonucleotide therapeutics for the Pfizer Programs (as defined in Note 5), each directed at a genetically-defined hepatic target selected by Pfizer. The Company entered into the Pfizer Collaboration Agreement in May 2016.

The Company presents revenue from the Pfizer Collaboration Agreement under Financial Accounting Standards Board ("FASB"), Accounting Standards Codification ("ASC") Topic 808, Collaborative Arrangements ("ASC 808"). In addition, the Company recognizes revenue in accordance with ASC Topic 605, Revenue Recognition ("ASC 605"). Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met:

- persuasive evidence of an arrangement exists;
- delivery has occurred or services have been rendered;
- the seller's price to the buyer is fixed or determinable; and
- collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Pursuant to the accounting guidance in ASC 605-25, the Company evaluates multiple-element arrangements to determine (1) the deliverables included in the arrangement and (2) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires the Company to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of

the contractual relationship. Deliverables are considered separate units of accounting provided that the delivered item has value to the customer on a standalone basis and, if the arrangement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the Company's control. In assessing whether an item has standalone value, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can use a deliverable for its intended purpose without the receipt of the remaining deliverable, whether the value of the deliverable is dependent on the undelivered item and whether there are other vendors that can provide the undelivered items.

Under the Pfizer Collaboration Agreement (as defined in Note 5), the Company and Pfizer agreed to collaborate on the discovery, development and commercialization of up to five Pfizer Programs, two of the five targets were declared upon initiation of the agreement. The Collaboration Agreement provides Pfizer with certain options to nominate up to three remaining programs and the Company is required to consider whether such options are substantive. Options are considered substantive if, at the inception of the arrangement, the Company is at risk as to whether the collaboration partner will choose to exercise the option. Factors that the Company considers in evaluating whether an option is substantive include whether the optional elements are essential to the functionality of other programs nominated, whether economic factors compel Pfizer to purchase the optional elements, the cost to exercise the option, the overall objective of the arrangement and, the benefit Pfizer might obtain from the arrangement without exercising the option. As December 31, 2016 Pfizer had declared three targets. Pfizer is entitled to nominate two additional targets by November 2017.

When an option is considered substantive and there is no significant incremental discount, the option is not considered a deliverable in the arrangement and no consideration is allocated to it. Conversely, when an option is not considered substantive or it is considered substantive but is priced at an incremental discount, it is analyzed to determine if it should be combined with other deliverables in the arrangement. Options that are substantive and priced at a significant and incremental discount are further assessed to determine whether a portion of the upfront payment should be allocated to the option and other deliverables in the arrangement.

At the inception of an arrangement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (1) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from its performance to achieve the milestone, (2) the consideration relates solely to past performance and (3) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone and the level of effort and investment required to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. Revenue from substantive milestones will be recognized in its entirety upon successful accomplishment of the milestone.

Aside from the program nomination payments, which relate to the options described above, the remaining milestone payments required under the Pfizer Collaboration Agreement are contingent upon the Company's performance under the Pfizer Collaboration Agreement, including in certain instances, regulatory approval. The Company views these milestones as substantive and has excluded the amounts as allocable consideration at the outset of the arrangement. All commercial milestones will be accounted for in the same manner as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

The Company recognizes arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605 are satisfied for that particular unit of accounting. In the event that a deliverable does not represent a separate unit of accounting, the Company recognizes revenue from the combined unit of accounting over the Company's contractual or estimated performance period for the undelivered elements, which is typically the term of the Company's research and development obligations. If there is no discernible pattern of performance or objectively measurable performance measures do not exist, then the Company recognizes revenue under the arrangement on a straight-line basis over the period the Company is expected to complete its performance obligations. Conversely, if the pattern of performance in which the service is provided to the customer can be determined and objectively measurable performance measures exist, then the Company recognizes revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method or proportional performance method, as applicable, as of the period ending date.

The Company has concluded that the deliverables under the Pfizer Collaboration Agreement relate primarily to the research and development required by the Company for each of the programs nominated by Pfizer. The remaining deliverables, including sample supplies provided by each party to fulfill its obligation as a licensee, participation on a joint steering committee to oversee the research and development activities, and regulatory responsibilities related to filings and obtaining approvals related to the products that may

result from each program do not represent separate units of accounting based on their dependence on the research and development efforts.

Because there is no discernible pattern of performance given the nature of the research and development efforts, the Company recognizes the allocated revenue for each deliverable under the Pfizer Collaboration Agreement on a straight-line basis over the period the Company is expected to complete its performance obligations for each deliverable, or unit of accounting. For the first two Pfizer Programs, this period is expected to be from the initiation date of the Pfizer Collaboration Agreement, which was May 5, 2016, and for the other Pfizer Programs, the period is expected to be from the date that work commences on those programs through the earlier of (a) the termination of the research and development performance obligations under the Pfizer Collaboration Agreement, which is May 5, 2020 (the "Research Term"), or (b) the estimated date the Company expects to meet its research and development performance obligations under the Pfizer Collaboration Agreement. Given the uncertainty as to when the research and development performance obligations will be completed, the Company has used the Research Term for purposes of applying the straight-line method for revenue recognition for the year ended December 31, 2016.

Product Revenue

The Company has had no product revenue to date.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs include salaries, share-based compensation and other employee benefit expenses, third-party license fees and other operational costs related to the Company's research and development activities, including allocated facility-related expenses and external costs of outside vendors engaged to conduct preclinical studies and other research and development activities. Costs associated with licenses of technology and patent costs are expensed as incurred and are generally included in research and development expense in the consolidated statement of operations.

Net Loss per Share

Basic net loss per share is computed using the weighted-average number of ordinary shares outstanding during the period. Diluted net loss per share is computed using the sum of the weighted-average number of ordinary shares outstanding during the period and, if dilutive, the weighted-average number of potential ordinary shares, including the assumed exercise of share options.

The Company applies the two-class method to calculate its basic and diluted net loss per share attributable to ordinary shareholders, as its Series A preferred shares are participating securities. The two-class method is an earnings allocation formula that treats a participating security as having rights to earnings that otherwise would have been available to ordinary shareholders. However, for the periods presented, the two-class method does not impact the net loss per ordinary share as the Company was in a net loss position for each of the periods presented and holders of Series A preferred shares do not participate in losses.

The Company's Series A preferred shares contractually entitle the holders of such shares to participate in dividends but do not contractually require the holders of such shares to participate in losses of the Company. Accordingly, for periods in which the Company reports a net loss attributable to ordinary shareholders, diluted net loss per share attributable to ordinary shareholders is the same as basic net loss per share attributable to ordinary shareholders, since dilutive ordinary shares are not assumed to have been issued if their effect is anti-dilutive.

License Agreements and Patent Costs

Costs associated with licenses of technology and patent costs are expensed as incurred and are generally included in research and development expense in the consolidated statements of operations.

Share-Based Compensation

The Company measures and recognizes share-based compensation expense, for both employee and director option awards, based on the grant date fair value of the awards. The Company calculates the fair value of restricted share awards based on the grant date fair value of the underlying ordinary shares. The Company recognizes share-based compensation expense on a straight-line basis over the requisite service period of the awards, which is generally the vesting period.

The Company determines the fair value of share-based awards granted to non-employees as either the fair value of the consideration received or the fair value of the equity instruments issued, whichever is more reliably measurable. All issuances of equity instruments

issued to non-employees as consideration for goods or services received by the Company are accounted for based on the fair value of the equity instruments issued. These awards are recorded in expense and additional paid-in capital in shareholders' equity over the applicable service periods based on the fair value of the options at the end of each period.

The Company classifies share-based compensation expense in its consolidated statements of operations in the same manner in which the award recipient's payroll costs are classified or in which the award recipients' service payments are classified.

Prior to the Company's initial public offering ("IPO") in November 2015, the fair value of the ordinary shares underlying its share-based awards was estimated on each grant date by the board of directors. The board of directors determined the estimated per share fair value of the Company's ordinary shares at various dates considering contemporaneous and retrospective valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation* ("the Practice Aid"). After the closing of our IPO, the board of directors determined that the fair value of the ordinary shares underlying our share-based awards be based on the closing price of the Company's ordinary shares as reported by the NASDAQ Global Market on the date of grant.

The fair value of each share option grant was determined using the methods and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment and estimation by management.

- *Fair Value of Ordinary Shares*. As discussed above, prior to our IPO, the fair value of the Company's ordinary shares underlying our share options was historically determined by the board of directors. Because prior to our IPO, there was no public market for our ordinary shares, the board of directors determined the fair value of our ordinary shares at the time of grant of the option by considering a number of objective and subjective factors, including valuations of comparable companies, sales of its shares to unrelated third parties, operating and financial performance and general and industry specific economic outlook. Following the completion of our IPO, the board of directors determined that the fair value of each ordinary share underlying our share-based awards would be based on the closing price of the Company's ordinary shares as reported by the NASDAQ Global Market on the date of grant.
- *Expected Term*. The expected term of share options represents the weighted-average period that the share options are expected to remain outstanding. The Company estimated the expected term using the simplified method, which is an average of the contractual term of the option and the vesting period.
- *Expected Volatility*. Since there is limited historical data for the Company's ordinary shares and limited company-specific historical volatility, it has determined the share price volatility for options granted based on an analysis of the volatility used by a peer group of publicly traded companies. In evaluating similarity, the Company considers factors such as industry, stage of life cycle and size.
- *Risk-free Interest Rate*. The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of the grant for zero-coupon U.S. Treasury notes with remaining terms similar to the expected term of the options.
- *Dividend Rate*. The expected dividend was assumed to be zero as the Company has never paid dividends and has no current plans to do so.

Income Taxes

The Company accounts for income taxes using an asset and liability approach, which requires recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements, but have not been reflected in taxable income. A valuation allowance is established to reduce deferred tax assets to their estimated realizable value. Therefore, the Company provides a valuation allowance to the extent that it is more likely than not that all or a portion of the deferred tax assets will not be realized in the future.

The Company accounts for uncertainty in income taxes recognized in the financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

The Company recognizes interest and penalties related to uncertain tax positions in the income tax provision on the consolidated statements of operations.

The Company has certain service arrangements in place between our U.S and Singapore entities, which include transfer pricing assumptions. The determination of the appropriate level of transfer pricing requires judgment based on transfer pricing analyses of comparable companies. The Company monitors the nature of their service arrangements for changes in our operations as well as economic conditions. The Company also periodically reviews the transfer pricing analyses for changes in the composition in the pool of comparable companies as well the related ongoing results of the comparable companies.

Early Adoption of Accounting Standards Update No. 2016-09

Effective for the quarter ended December 31, 2016, the Company adopted a change in accounting principle related to the early adoption of ASU 2016–09, Compensation – Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting ("ASU 2016-09"). This revised standard affects forfeitures, cash flow presentation and income taxes. Additionally, this standard requires all excess tax benefits and deficiencies on share-based payment awards to be recognized as income tax expense or benefit in the statement of operations. In addition, the tax effects of exercised or vested awards should be treated as discrete items in the reporting period in which they occur and excess tax benefits should be classified with other income tax cash flows as an operating activity. The standard permits early adoption in any annual or interim period and will be applied by means of a cumulative-effect adjustment to the balance sheet as of the beginning of the fiscal year of adoption. The Company notes that it did not have any off-balance sheet attributes as of January 1, 2016 and therefore did not record a cumulative-effect adjustment to retained earnings. The standard permits the changes to the classification of the statement of cash flows to be applied either prospectively or retrospectively. The Company has elected to treat the change in classification of cash flows resulting from excess tax benefits or deficiencies on a retrospective basis and elected to recognize forfeitures as they occur on a modified-retrospective basis. There was an immaterial cumulative effect adjustment on forfeitures as a result of the adoption. The adoption of this standard also resulted in a current year tax benefit of $0.3 million which previously would have been recognized in the current period in additional paid-in capital.

Recently Issued Accounting Pronouncements

In May 2014, the FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606) ("ASU 2014-09"), which supersedes all existing revenue recognition requirements, including most industry-specific guidance. The new standard requires a company to recognize revenue when it transfers goods or services to customers in an amount that reflects the consideration that the company expects to receive for those goods or services. The new standard will be effective on January 1, 2018 and earlier application is permitted only for annual reporting periods beginning after December 15, 2016, including interim reporting periods within that reporting period. For the year ended December 31, 2016, revenue was generated exclusively from the Pfizer Collaboration Agreement. The Company is currently evaluating the potential impact that ASU 2014-09 may have on its financial position and results of operations as it relates to this single arrangement, and expects to elect the modified retrospective application as its transition method.

In August 2014, the FASB issued ASU 2014-15, Presentation of Financial Statements – Going Concern ("ASU 2014-15"), which requires a company to evaluate the existence of conditions or events that raise substantial doubt about its ability to continue as a going concern within one year of the issuance date of its financial statements. The standard is effective for interim and annual periods ending after December 15, 2016 with early adoption permitted. The Company has evaluated the impact of ASU 2014-15 and has concluded that it does not have a material effect on the consolidated financial statements or footnote disclosures as of the December 31, 2016 adoption date, but may require additional disclosures in future periods.

In February 2015, the FASB issued ASU 2015-02, Consolidation (Topic 810) ("ASU 2015-02"), to address financial reporting considerations for the evaluation as to the requirement to consolidate certain legal entities. ASU 2015-02 is effective for fiscal years and for interim periods within those fiscal years beginning after December 15, 2015. The Company has evaluated the impact of ASU 2015-02 and has concluded that it has no effect on the consolidated financial statements.

In April 2015, the FASB issued ASU 2015-03, Interest—Imputation of Interest (Subtopic 835-30) ("ASU 2015-03"), as part of the initiative to reduce complexity in accounting standards. The update requires that debt issuance costs related to a recognized debt liability be presented in the balance sheet as a direct deduction from the carrying amount of that debt liability, consistent with debt discounts. The Company has evaluated the impact of ASU 2015-03 and has concluded that it has no effect on the consolidated financial statements.

In November 2015, the FASB issued ASU 2015-17, Balance Sheet Classification of Deferred Taxes ("ASU 2015-17"), which requires entities to present deferred tax assets and deferred tax liabilities as noncurrent in a classified balance sheet. The ASU simplifies the current guidance in ASC Topic 740, Income Taxes, which requires entities to separately present deferred tax assets and liabilities as current and noncurrent in a classified balance sheet. ASU 2015-17 is effective for fiscal years beginning after December 31, 2016, and interim periods within those annual periods. Early adoption is permitted for all entities as of the beginning of an interim or annual reporting period. The Company does not expect the impact of ASU 2015-17 to be material to its consolidated financial statements.

In February 2016, the FASB issued ASU 2016-02, Leases ("ASU 2016-02"), which requires a lessee to recognize assets and liabilities on the balance sheet for operating leases and changes many key definitions, including the definition of a lease. The update includes a short-term lease exception for leases with a term of 12 months or less, in which a lessee can make an accounting policy election not to recognize lease assets and lease liabilities. Lessees will continue to differentiate between finance leases (previously referred to as capital leases) and operating leases, using classification criteria that are substantially similar to the previous guidance. For lessees, the recognition, measurement, and presentation of expenses and cash flows arising from a lease have not significantly changed from previous U.S. GAAP. Lessees and lessors are required to recognize and measure leases at the beginning of the earliest period presented using a modified retrospective approach. The modified retrospective approach includes a number of optional practical expedients that entities may elect to apply as well as transition guidance specific to nonstandard leasing transactions. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years. The Company is currently evaluating the potential impact that the adoption of ASU 2016-02 may have on its consolidated financial statements.

In October 2016, the FASB issued ASU 2016-16, Income Taxes (Topic 740): Intra-Entity Transfers of Assets Other Than Inventory ("ASU 2016-16"). The ASU requires companies to recognize the income tax consequences of an intra-entity transfer of an asset other than inventory when the transfer occurs. Prior to the issuance of this ASU, existing guidance prohibited the recognition of current and deferred income taxes for an intra-entity asset transfer until the asset has been sold to an outside party. ASU 2016-16 will be effective for the Company in the first quarter of 2018 with early adoption permitted. The Company is currently evaluating the potential impact that the adoption of ASU 2016-16 may have on its consolidated financial statements.

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash ("ASU 2016-18"). The ASU requires an entity to explain the changes in the total of cash, cash equivalents, restricted cash, and restricted cash equivalents on the statement of cash flows and to provide a reconciliation of the totals in that statement to the related captions in the balance sheet when the cash, cash equivalents, restricted cash, and restricted cash equivalents are presented in more than one line item on the balance sheet. This ASU is effective for annual and interim periods beginning after December 15, 2017, and is required to be adopted using a retrospective approach, with early adoption permitted. The Company is currently evaluating the potential impact that the adoption of ASU 2016-18 may have on its consolidated financial statements.

Other accounting standards that have been issued or proposed by the FASB or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on the Company's consolidated financial statements upon adoption.

3. PROPERTY AND EQUIPMENT, NET

Property and equipment, net, consists of the following

	December 31,	
	2016	2015
	(in thousands)	
Furniture and equipment	$ 7,231	$ 3,936
Software	43	—
Leasehold improvements	1,964	267
Fixed assets in progress	1,863	198
Total	11,101	4,401
Less accumulated depreciation and amortization	(2,494)	(1,612)
Property and equipment, net	$ 8,607	$ 2,789

Leasehold improvements made during the year ended December 31, 2016 consisted of costs related to the Company's leased facility in Cambridge, Massachusetts and the newly leased facility in Lexington, Massachusetts.

Leasehold improvements made during the year ended December 31, 2015 consisted primarily of costs related to the Company's leased facility in Cambridge, Massachusetts.

Depreciation and amortization expense was $0.8 million, $0.6 million, and $0.3 million for the years ended December 31, 2016, 2015 and 2014, respectively.

4. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

Accrued expenses and other current liabilities consist of the following:

	December 31,	
	2016	2015
	(in thousands)	
Accrued compensation	$ 2,480	$ —
Accrued professional fees	417	401
Accrued vacation	589	191
Other	959	353
Total accrued expenses and other current liabilities	$ 4,445	$ 945

5. PFIZER COLLABORATION AND SHARE PURCHASE AGREEMENT

On May 5, 2016, the Company entered into a Research, License and Option Agreement (the "Pfizer Collaboration Agreement") with Pfizer Inc. ("Pfizer"). Pursuant to the terms of the Pfizer Collaboration Agreement, the Company and Pfizer agreed to collaborate on the discovery, development and commercialization of stereopure oligonucleotide therapeutics for up to five programs (the "Pfizer Programs"), each directed at a genetically-defined hepatic target selected by Pfizer (the "Collaboration"). The Company received $10.0 million as an upfront license fee under the Pfizer Collaboration Agreement. Subject to option exercises by Pfizer, assuming five potential products are successfully developed and commercialized, the Company may earn up to $871.0 million in potential research, development and commercial milestone payments, plus royalties, tiered up to low double-digits, on sales of any products that may result from the Collaboration. None of the payments under the Pfizer Collaboration Agreement are refundable.

Simultaneously with the entry into the Pfizer Collaboration Agreement, the Company entered into a Share Purchase Agreement (the "Pfizer Equity Agreement," and together with the Pfizer Collaboration Agreement, the "Pfizer Agreements") with C.P. Pharmaceuticals International C.V., an affiliate of Pfizer (the "Pfizer Affiliate"). Pursuant to the terms of the Pfizer Equity Agreement, the Pfizer Affiliate purchased 1,875,000 of the Company's ordinary shares (the "Shares") at a purchase price of $16.00 per share, for an aggregate purchase price of $30.0 million. The Company did not incur any material costs in connection with the issuance of the Shares.

Under the Pfizer Collaboration Agreement, the parties agreed to collaborate during the four-year Research Term. During the Research Term, the Company is responsible to use its commercially reasonable efforts to advance up to five programs through to the selection of clinical candidates. At that stage, Pfizer may elect to license any of these Pfizer Programs exclusively and to have exclusive rights to undertake the clinical development of the resulting clinical candidates into products and the potential commercialization of any such products thereafter. In addition, the Company receives a non-exclusive, royalty-bearing sublicenseable license to use Pfizer's hepatic targeting technology in any of the Company's own hepatic programs that are outside the scope of the Collaboration (the "WAVE Programs"). If the Company uses this technology on the WAVE Programs, Pfizer is eligible to receive potential development and commercial milestone payments from the Company. Pfizer is also eligible to receive tiered royalties on sales of any products that include Pfizer's hepatic targeting technology.

Pfizer nominated two hepatic targets upon entry into the Collaboration in May 2016. In August 2016, Pfizer nominated the third hepatic target under the Collaboration and has the option to nominate two additional targets by November 5, 2017. The Company received a $2.5 million milestone payment related to the nomination of third target.

The Company has determined that the options held by Pfizer under the Pfizer Collaboration Agreement are substantive and priced at a significant incremental discount. Accordingly, $3.0 million of the upfront payment has been allocated to the options to nominate the three remaining targets. The amount allocated to the three options will be recognized as the research and development are provided commencing from the date that Pfizer exercises each respective option, or immediately as each option expires unexercised. The portion of the upfront payment allocated to the initial two targets was $7.0 million and will be recognized as the research and development services are provided from the inception of the arrangement. Subsequently, in 2016, Pfizer exercised its option to nominate a third program. The Company will recognize $3.5 million of revenue (which is comprised of $1.0 million allocated to the option at inception of the arrangement and $2.5 million paid by Pfizer at the time of exercising the option) as the research and development services are provided.

The Collaboration is managed by a joint steering committee in which both parties are represented equally, which will oversee the scientific progression of each Pfizer Program up to the clinical candidate stage. During the four-year Research Term and for a period of two years thereafter, the Company has agreed to work exclusively with Pfizer with respect to using any of the Company's stereopure oligonucleotide technology that is specific for the applicable hepatic target which is the basis of any Pfizer Program.

The stated term of the Pfizer Collaboration Agreement commenced on May 5, 2016 and terminates on the date of the last to expire payment obligation with respect to each Pfizer Program and with respect to each WAVE Program, expires on a program-by-program basis accordingly. Pfizer may terminate its rights related to a Pfizer Program under the Pfizer Collaboration Agreement at its own convenience upon 90 days' notice to the Company. The Company may also terminate its rights related to a WAVE Program at its own convenience upon 90 days' notice to Pfizer. The Pfizer Collaboration Agreement may also be terminated by either party in the event of an uncured material breach of the Collaboration Agreement by the other party.

During the year ended December 31, 2016, the Company recognized revenue of $1.5 million under the Pfizer Collaboration Agreement. Deferred revenue amounted to $11.0 million as of December 31, 2016, of which $2.7 million is included in current liabilities.

6. SHARE CAPITAL

Ordinary Shares

The following represents the historical ordinary share transactions of the Company from December 31, 2013 through December 31, 2016:

- In February 2014, the Company issued 2,263,291 ordinary shares to a third-party investor at $2.47 per share for net proceeds of $5.6 million. In connection with this financing, holders of $9.6 million of related party notes payable agreed to convert such notes into 2,365,139 Series A preferred shares and 1,515,596 ordinary shares.
- In January 2015, the Company issued 4,769,077 ordinary shares to a third-party investor and an existing investor at $2.47 per share for net proceeds of $11.6 million.
- In March 2015, the Company granted 190,856 fully-vested ordinary shares to an executive of the Company.
- In November 2015, the Company completed an initial public offering of its ordinary shares, in which the Company issued and sold 6,375,000 ordinary shares at a price to the public of $16.00 per share. In December 2015, the Company issued an additional 618,126 ordinary shares at a price of $16.00 per share pursuant to a partial exercise of the underwriters' over-allotment option. The aggregate net proceeds to the Company from the initial public offering, inclusive of the over-allotment exercise, were $100.4 million after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.
- In May 2016, the Company granted 1,875,000 ordinary shares to Pfizer under the Pfizer Agreements (Note 5) at a purchase price of $16.00 per share, for an aggregate purchase price of $30.0 million.

Features of the Ordinary Shares

The ordinary shares have no par value and there is no authorized share capital under Singapore law. The rights, preferences, and privileges of ordinary shares are as follows:

New Share Offering

Prior to the closing of the Company's initial public offering, any new ordinary shares or securities convertible into ordinary shares were required to be offered in the first instance to all the then holders of any class of shares, other than the Series A preferred shares, prior to issuance and each shareholder had the right of pre-emption with respect to any issuance of new ordinary shares or securities convertible into ordinary shares. This right of pre-emption did not apply to shares sold in the Company's initial public offering and terminated immediately prior to the closing of the Company's initial public offering.

Voting

The holders of ordinary shares are entitled to one vote for each ordinary share held at all meetings of shareholders and written actions in lieu of meetings provided, however, that except as otherwise required by law, holders of ordinary shares shall not be entitled to implement the following without the approval of more than 75% of the Company's issued and outstanding ordinary shares:

(i) effect a merger, split, corporate reorganization, liquidation, dissolution, or winding up of the Company or any member of the group;

(ii) authorize or issue any additional shares, other equity interests in the Company or any convertible securities into such equity interests;

(iii) effect any public offering or listing of the equity securities of the Company; or

(iv) purchase, redeem, pay or declare any dividend on any shares or other equity interests in the Company.

Dividends

All dividends shall be declared and paid pro rata according to the number of shares held by each member entitled to receive dividends. The Company's board of directors may deduct from any dividend all sums of money presently payable by the member to the Company on account of calls.

Liquidation

In the event of a liquidation, dissolution or winding up of, or a return of capital by the Company, the ordinary shares will rank equally with the Series A preferred shares after the payment of the liquidation preference of $10.00 for Series A preferred shares.

Series A Preferred Shares

The following represent the Series A preferred share transactions of the Company from December 31, 2013 through December 31, 2016:

- In February 2014, holders of $9.6 million of related party notes payable agreed to convert such notes into 2,365,139 Series A preferred shares and 1,515,596 ordinary shares.
- In connection with the private placement of Series B preferred shares on August 14, 2015, holders of the Company's preference shares agreed to rename the existing "preference shares" as "Series A preferred shares." In addition, as further described below, the terms of the Series A preferred shares were amended to remove their right of first refusal and to provide for their right to convert on a one-for-one basis into an aggregate of 3,901,348 ordinary shares at any time at the election of the holder. The rights of the Series A preferred shares are identical to the ordinary shares except that the Series A preferred shares have: (1) no voting rights other than in limited circumstances, (2) the right to a non-cumulative dividend if and when declared by the Company's board of directors and (3) the right to convert the Series A preferred shares at any time on a one-for-one basis into ordinary shares at the discretion of the holder. The Company's shareholders, including holders of Series A preferred shares, entered into an investors' rights agreement and a voting agreement with the Company in connection with the private placement. Pursuant to the terms of the voting agreement, which terminated in connection with the Company's IPO, investors who held at least 1,212,477 shares of registerable securities, including holders of Series A preferred shares and Series B preferred shares, had a right to purchase certain new securities offered by the Company. Additionally, in the event of the sale of 50% or more of the voting power of the Company or a deemed liquidation event, if the holders of at least a majority of the ordinary shares and the holders of 56% of the Series B preferred shares had voted for a sale of the Company, they had the right to force the other shareholders, including the holders of Series A preferred shares, to agree to such a sale.
- In September 2015, the terms of the Series A preferred shares were further amended to provide that, upon the mandatory conversion of Series B preferred shares, which occurred on the completion of the initial public offering, the existing right of Series A preferred shares to a non-cumulative dividend if and when declared by our board of directors ceased and was replaced by a liquidation preference consisting of $0.0024743 per Series A preferred share, or an aggregate of $10.00 based on the number of Series A preferred shares outstanding at the date of the amendment.

The Company has accounted for the September 2015 amendment to the Series A preferred shares as a modification of the preferred shares based on upon a qualitative assessment of the amendment. The Company has not adjusted the carrying value of the Series A preferred shares since the fair value of the Series A preferred shares immediately prior and subsequent to the modification date resulted in an immaterial change in fair value.

The addition of the liquidation preference to the Series A preferred shares, however, resulted in the reclassification of the Series A preferred shares from permanent shareholders' equity to temporary shareholders' equity since the holders of the Series A preferred shares are entitled to a liquidation preference upon a deemed liquidation event, which is outside the control of the Company. In the event a deemed liquidation event were to occur, the Company would adjust the carrying value of the Series A preferred shares to their liquidation value, which amounts to $10.00 in the aggregate.

The Series A preferred shares have no par value and there is no authorized share capital under Singapore law. The Series A preferred shares are not redeemable.

Series B Preferred Shares Converted in Connection with Initial Public Offering

The following represents the historical Series B preferred share transactions of the Company from January 1, 2015 through the completion of our initial public offering:

- On August 14, 2015, the Company issued an aggregate of 5,334,892 Series B preferred shares at a purchase price of $12.37 per share to certain third-party investors for $62.5 million of net proceeds.
- Upon the completion of the initial public offering on November 16, 2015, all of the outstanding Series B preferred shares of the Company automatically converted into 5,334,892 of the Company's ordinary shares.

Prior to the conversion of the Series B preferred shares into ordinary shares, the Series B preferred shares had a liquidation preference over the Series A preferred shareholders and ordinary shareholders equal to the original per share amount paid of $12.37 per share, plus any declared plus unpaid dividends, if any. Additionally, the holders of Series B preferred shares were entitled to voting rights, however, the Series B preferred shareholders were not entitled to any preferential dividends and their shares were not redeemable.

7. SHARE-BASED COMPENSATION

In December 2014, the Company's board of directors adopted the WAVE Life Sciences Ltd. 2014 Equity Incentive Plan (the "2014 Plan"), and reserved 1,763,714 ordinary shares for issuance under this plan, which, as approved, was increased to 5,064,544 in 2015.

The 2014 Plan authorizes the board of directors or a committee of the board to grant incentive share options, non-qualified share options, share appreciation rights and restricted share awards to eligible employees, outside directors and consultants of the Company. Options generally vest over a period of three or four years, and options that lapse or are forfeited are available to be granted again. The contractual life of all options is ten years from the date the option begins to vest.

During the years ended December 31, 2016 and 2015, the Company granted options to purchase 1,479,200 and 2,215,342 ordinary shares, respectively, to employees, directors and non-employees. During the year ended December 31, 2016, there were forfeitures of options to purchase 41,030 ordinary shares. There were no forfeitures of options during the year ended December 31, 2015. During the years ended December 31, 2016 and 2015 there were no cancellations of options. The Company did not grant any share options in 2014. In July 2016, the Company granted 22,750 restricted share units ("RSUs") with a grant date fair value of $21.69 per unit. The RSUs fully vest upon the first anniversary of the grant date. Share-based compensation expense related to the RSUs is included in research and development expenses on the consolidated statements of operations. As of December 31, 2016, 1,197,426 ordinary shares remained available for future grant.

The Company recorded share-based compensation expense of $6.8 million and $4.0 million for the years ended December 31, 2016 and 2015, respectively, of which $2.7 million and $1.6 million respectively related to options granted to non-employees. The Company did not have any share-based compensation expense in 2014. The Company measures and records the value of options granted to non-employees over the period of time services are provided and, as such, unvested portions are subject to re-measurement at subsequent reporting periods.

Share option activity under the 2014 Plan is summarized as follows:

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)(1)
Options outstanding as of January 1, 2016	2,215,342	$ 3.88	9.30	$ 26,740
Granted	1,479,200	20.79		
Exercised	(75,746)	3.42		1,887
Cancelled or forfeited	(41,030)	10.23		
Outstanding as of December 31, 2016	3,577,766	$ 10.58	8.68	$ 56,780
Options exercisable as of December 31, 2016	1,248,343	$ 3.10	8.24	$ 28,775
Options unvested as of December 31, 2016	2,329,423	$ 14.58	8.92	$ 28,006

(1) The aggregate intrinsic value of options is calculated as the difference between the exercise price of the share options and the fair value of the Company's ordinary shares for those share options that had exercise prices lower than the fair value of the ordinary shares as of the end of the period.

RSU activity for the year ended December 31, 2016 is summarized as follows:

	RSUs	Average Grant Date Fair Value (in dollars per share)
RSUs Outstanding as of January 1, 2016	—	$ —
Granted	22,750	21.69
RSUs Outstanding at December 31, 2016	22,750	$ 21.69

The assumptions used in the Black-Scholes option pricing model to determine the fair value of share options granted to employees during the period were as follows:

	For the Year Ended December 31,	
	2016	2015
Risk-free interest rate	1.15% – 2.18%	1.56% - 1.89%
Expected term (in years)	3.00 – 6.25	5.52 - 6.12
Expected volatility	60.89% – 68.76%	62.14% - 71.02%
Expected dividend yield	0%	0%
Exercise price	$14.11 – 36.43	$2.47 - 13.08
Fair value of ordinary share	$14.11 – 36.43	$4.41 - 13.08

The assumptions used in the Black-Scholes option pricing model to determine the fair value of share options granted to non-employees during the period were as follows:

	Year Ended December 31, 2015
Risk-free interest rate	2.06% - 2.35%
Expected term (in years)	9.19 - 10.00
Expected volatility	62.65% - 69.80%
Expected dividend yield	0%
Exercise price	$2.47
Fair value of ordinary share	$4.41 - 15.95

There were no options granted to non-employees in 2016.

As of December 31, 2016, the unrecognized compensation cost related to outstanding options was $18.0 million for employees and $3.8 million for non-employees. The unrecognized compensation cost for employees and non-employees is expected to be recognized over a weighted-average period of approximately 2.23 years. The unrecognized compensation costs related to outstanding RSUs was $0.3 million as of December 31, 2016, and is expected to be recognized expense over a weighted-average period of approximately 0.53 years. For the years ended December 31, 2016 and 2015, the weighted-average grant date fair value per granted option was $30.23 and $6.64, respectively. For the year ended December 31, 2016, the weighted-average grant date fair value per granted RSU was $21.69. The aggregate fair value of options that vested during the year ended December 31, 2016 was $4.7 million.

In March 2015, the Company granted 190,856 fully-vested ordinary shares to an executive of the Company and the Company recorded compensation expense in the amount of $0.9 million.

Share-based compensation expense for the year ended December 31, 2016 and 2015 was classified in the consolidated statements of operations as follows:

	For the Year Ended December 31,	
	2016	2015
	(in thousands)	
Research and development expenses	$ 4,936	$ 2,268
General and administrative expenses	1,911	1,756
Total share-based compensation	$ 6,847	$ 4,024

8. COMMITMENTS AND CONTINGENCIES

Lease Arrangements

The Company enters into lease arrangements for its facilities as well as certain equipment. A summary of the arrangements are as follows:

Operating Leases

On September 26, 2016, and as amended on December 31, 2016 the Company entered into a 10 year and 9 month lease, which includes two successive five year renewal options, for its manufacturing function in Lexington, Massachusetts. Throughout the term of the Lease, the Company is responsible for paying certain costs and expenses, in addition to the rent, as specified in the Lease, including a proportionate share of applicable taxes, operating expenses and utilities. In connection with the lease agreement, the Company issued the lessor a letter of credit in the amount of $2.6 million, which is included in restricted cash at December 31, 2016.

In connection with the lease agreement, the Company is entitled to receive $11.5 million of tenant improvement allowances. The Company has received $0.1 million as of December 31, 2016, which is amortized over the period from the commencement of tenant improvement construction through to the end of the lease term.

As of December 31, 2016, property and equipment, net, includes $0.9 million related to construction costs for the facility in Lexington.

In April 2015, the Company entered into a lease agreement for an office and laboratory facility in Cambridge, Massachusetts, which commenced in October 2015 with a term of 7.5 years with a five-year renewal option to extend the lease. In connection with the lease, the Company issued the lessor a letter of credit in the amount of $1.0 million, which is recorded as restricted cash on the consolidated balance sheets at December 31, 2016 and 2015.

Previously, the Company leased its corporate office space in Boston, Massachusetts under a non-cancellable operating sublease with SNBL, a related party. On September 22, 2015, the Company terminated its sublease with SNBL and exited the premises on October 2, 2015. As a result of the termination of the sublease, the Company recorded approximately $0.2 million of additional depreciation and $0.1 million of exit costs during the year ended December 31, 2015. In connection with the termination, the Company agreed to guarantee SNBL certain obligations of an unrelated third party who entered into a sublease agreement with SNBL effective October 2, 2015. The guarantee provides that in the event the sub-lessee does not meet its lease obligations to SNBL, the Company will make the required payments. The guarantee agreement is effective through August 2019, when the final lease payments are due, and coincides with the original expiration of the lease. The Company simultaneously entered into an indemnification agreement with the sub-lessee to indemnify the Company for any costs incurred under the guaranty made by the Company to SNBL. The maximum amount of the guarantee over the three year and six month sub-lease period is $0.6 million, exclusive of any indemnification from the sub-lessee.

Future minimum lease payments under the Company's non-cancelable operating leases as of December 31, 2016, are as follows:

For the Year Ended December 31,	Amount (in thousands)
2017	1,954
2018	4,660
2019	5,798
2020	5,972
2021	6,151
Thereafter	33,418
	57,953

The Company recorded rent expense of $1.5 million, $0.5 million and $0.3 million for the years ended December 31, 2016, 2015 and 2014, respectively.

Capital Lease

In April 2015, the Company entered in a three year lease to acquire laboratory equipment, which has been accounted for as a capital lease. The capital asset was valued at $0.3 million and is included in property and equipment, net, along with accumulated amortization of $0.1 million and less than $0.1 million as of December 31, 2016 and 2015, respectively.

Unasserted Claims

In the ordinary course of business, the Company may be subject to legal proceedings, claims and litigation as the Company operates in an industry susceptible to patent legal claims. The Company accounts for estimated losses with respect to legal proceedings and claims when such losses are probable and estimable. Legal costs associated with these matters are expensed when incurred. The Company is not currently a party to any material legal proceedings.

9. NET LOSS PER ORDINARY SHARE

Basic loss per share is computed by dividing net loss attributable to ordinary shareholders by the weighted-average number of ordinary shares outstanding:

	Year Ended December 31,		
	2016	2015	2014
	(in thousands except share and per share data)		
Numerator:			
Net loss attributable to ordinary shareholders	$ (55,401)	$ (19,200)	$ (5,229)
Denominator:			
Weighted-average ordinary shares outstanding	22,800,628	10,501,455	3,911,556
Net loss per share, basic and diluted	$ (2.43)	$ (1.83)	$ (1.34)

The Company's potentially dilutive shares, which include outstanding share options to purchase ordinary shares, are considered to be ordinary share equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

The following potential ordinary shares, presented based on amounts outstanding at each period end, were excluded from the calculation of diluted net loss per share attributable to ordinary shareholders for the periods indicated because including them would have had an anti-dilutive effect:

	As of December 31,	
	2016	2015
Options to purchase ordinary shares	3,577,766	2,215,432
Restricted share units	22,750	—
Series A preferred shares	3,901,348	3,901,348

10. INCOME TAXES

The components of loss before income taxes were as follows:

	Year Ended December 31,		
	2016	2015	2014
	(in thousands)		
Singapore	$ (53,387)	$ (16,534)	$ (4,542)
Rest of world	(1,398)	(2,622)	(603)
Loss before income taxes	$ (54,785)	$ (19,156)	$ (5,145)

During the years ended December 31, 2016, 2015, and 2014, the Company recorded a tax provision of $0.6 million, less than $0.1 million, and $0.1 million, respectively, due to income taxed in the United States.

During the years ended December 31, 2016, 2015 and 2014, the Company recorded no income tax benefits for the net operating losses incurred in Japan and Singapore, due to its uncertainty of realizing a benefit from those items.

The deferred components of the benefit (provision) for income taxes were as follows:

	Year Ended December 31,		
	2016	2015	2014
	(in thousands)		
Current tax benefit (provision):			
Singapore taxes	$ —	$ —	$ —
Rest of world taxes	(1,180)	(8)	—
Total current benefit (provision) income taxes	$ (1,180)	$ (8)	$ —
Deferred tax benefit (provision):			
Singapore taxes	$ —	$ —	$ —
Rest of world taxes	564	(36)	(84)
Total deferred benefit (provision) income taxes	$ 564	$ (36)	$ (84)
Total benefit (provision) income taxes	$ (616)	$ (44)	$ (84)

A reconciliation of the Singapore statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2016	2015	2014
Singapore statutory income tax rate	17.0%	17.0%	17.0%
Research and development tax credits	3.1	2.3	2.2
Permanent differences	(0.9)	5.5	—
Foreign exchange loss	—	—	2.0
Changes in reserves for uncertain tax positions	(3.6)	(1.2)	(2.2)
Foreign rate differential	(0.1)	1.2	4.5
Other	(0.9)	0.2	—
Change in deferred tax asset valuation allowance	(15.7)	(25.2)	(25.1)
Effective income tax rate	(1.1)%	(0.2)%	(1.6)%

The components of the Company's deferred tax assets as of December 31, 2016 and 2015 are as follows:

	December 31,	
	2016	2015
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 16,046	$ 7,037
Research and development credits	449	460
Accrued expenses	242	58
Share-based compensation	1,024	218
Other	102	149
Total deferred tax assets	17,863	7,922
Valuation allowance	(15,999)	(7,466)
Net deferred tax assets	1,864	456
Depreciation	(1,090)	(246)
Total deferred tax liability	(1,090)	(246)
Net deferred tax asset (liability)	$ 774	$ 210

A roll-forward of the valuation allowance for the years ended December 31, 2016 and 2015 is as follows:

	Year Ended December 31,	
	2016	2015
	(in thousands)	
Balance at beginning of year	$ 7,466	$ 2,658
Increase in valuation allowance	8,774	4,818
Reversal of valuation allowance	(282)	—
Effect of foreign currency translation	41	(10)
Balance at end of year	$ 15,999	$ 7,466

As of December 31, 2016 and 2015, the Company also has United States research and development credit carryforwards of approximately $0.2 million and $0.7 million, respectively, available to offset future U.S. federal income taxes and approximately $0.3 million and $0.4 million, respectively, available to offset future state income taxes. The U.S. federal and state research and development credits will begin to expire in 2031 and 2028, respectively.

As of December 31, 2016 and 2015, the Company has net operating loss carryforwards in Japan of $5.3 million and $4.3 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2017.

As of December 31, 2016 and 2015, the Company has net operating loss carryforwards in Singapore of $84.0 million and $31.8 million, respectively, which may be available to offset future income tax liabilities and can be carried forward indefinitely.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize its deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets in Japan and Singapore. Accordingly, a full valuation allowance has been established against those deferred tax assets as of December 31, 2016 and 2015. Additionally, management has considered the Company's expected utilization of research and development credit carryforwards and has concluded that it is more likely than not that the Company will not realize the benefits of the U.S. state research and development carryforward. The $0.3 million valuation allowance previously recorded against the federal research and development credit carryforward has been released in 2016 based on management's assessment that the deferred tax asset is more-likely-than-not to be realized.

The valuation allowance increased by approximately $8.5 million in 2016, $4.8 million in 2015 and $1.3 million in 2014 primarily as a result of operating losses generated with no corresponding financial statement benefit. The Company may release this valuation allowance when management determines that it is more-likely-than-not that the deferred tax assets will be realized. Any release of valuation allowance will be recorded as a tax benefit increasing net income.

The Company's reserves related to taxes and its accounting for uncertain tax positions are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is more-likely-than-not to be realized following resolution of any potential contingencies present related to the tax benefit.

A summary of activity in the Company's unrecognized tax benefits is as follows:

	2016	2015	2014
		(in thousands)	
Unrecognized tax benefit during the year	$ 1,280	$ 1,025	$ 901
Tax positions released related to prior years	(1,066)	—	—
Tax positions related to the current year	2,129	255	124
Unrecognized tax benefit end of year	$ 2,343	$ 1,280	$ 1,025

As of December 31, 2016, 2015 and 2014, the total amount of gross unrecognized tax benefits in the United States, which excludes interest and penalties, was $2.3 million, $1.3 million, and $1.0 million, respectively. At December 31, 2016, $1.7 million of the net unrecognized tax benefits, would affect the Company's annual effective tax rate if recognized.

In 2015, the Company early adopted ASU 2013-11 and therefore unrecognized tax benefits related to net operating losses were netted against the related deferred tax asset. In 2016, the Company filed amended tax returns for tax years ended December 31, 2012 through December 31, 2014. As a result of the filing of the amended returns, the Company released $1.1 million of unrecognized tax benefits, which were previously netted with net operating loss deferred tax assets. As a result, the filing of the amended returns had no impact on the current year tax provision.

In 2016, the Company early adopted ASU 2016-09 which requires all excess tax benefits and deficiencies on share-based payment awards to be recognized as income tax expense or benefit in the statement of operations. The adoption of this standard resulted in a $0.3 million tax benefit that would have previously been recorded to additional paid-in capital.

The Company does not expect to record any material reductions in the measurement of its unrecognized tax benefits within the next twelve months.

The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision. As of December 31, 2016 and 2015, the Company had no accrued interest or penalties related to uncertain tax positions, and no amounts have been recognized in the Company's statements of operations or comprehensive loss.

The Company files income tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by various taxing authorities in the United States, Japan, and Singapore. There are currently no pending income tax examinations. Tax years from 2012 to the present are still open to examination in the United States, from 2008 to the present in Japan, and from 2012 to the present in Singapore. To the extent that the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the tax authorities to the extent utilized in a future period.

As of December 31, 2016 and 2015, $1.7 million and less than $0.1 million, respectively, of cash was held by the subsidiaries outside of Singapore. The Company does not provide for Singapore income tax or foreign withholding taxes on foreign unrepatriated earnings, as the Company intends to permanently reinvest undistributed earnings in its foreign subsidiaries. If the Company decides to change this assertion in the future to repatriate any additional foreign earnings, the Company may be required to accrue and pay taxes. Because of the complexity of Singapore and foreign tax rules applicable to the distribution of earnings from foreign subsidiaries to Singapore, the determination of the unrecognized deferred tax liability on these earnings is not practicable.

Utilization of the net operating loss carryforwards and research and development tax credit carryforwards in the United States may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"), due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the shares of a corporation by more than 50% over a three-year period. In 2015, the Company completed a study to assess whether an ownership change has occurred or whether there have been multiple ownership changes since its formation. The results of this study indicated that the Company experienced ownership changes as defined by Section 382 of the Code. Management has determined that the limitations will not have a material impact on the Company's ability to utilize its research and development credit carryforwards to offset future tax liabilities.

11. EMPLOYEE BENEFIT PLANS

The Company has a 401(k) retirement and savings plan (the "401(k) Plan") covering all U.S.-based employees. The 401(k) Plan allows employees to make pre-tax contributions up to the maximum allowable amount set by the IRS. Under the 401(k) Plan, the Company may make discretionary contributions as approved by the board of directors. The Company did not make contributions to the 401(k) Plan during the years ended December 2016, 2015, or 2014.

The Company has a J401(k) defined contribution pension plan covering all Japan-based permanent employees that was adopted in 2010. The J401(k) defined contribution pension plan allows the Company to make pre-tax contributions up to the maximum allowable amount set by the chief officer of the Kyushu Regional Bureau of Health and Welfare's approval and company's wage regulation. Under the J401(k) defined contribution pension plan, the Company may make discretionary contributions as approved by the board of directors. The Company has made contributions of approximately $7 thousand, $7 thousand, and $5 thousand during the years ended December 31, 2016, 2015 and 2014, respectively.

12. RELATED PARTIES

The Company had the following related party transactions for the periods presented in the accompanying consolidated financial statements, which have not otherwise been discussed in these notes to the consolidated financial statements:

- The Company had cash of $118 thousand and $115 thousand at December 31, 2016 and 2015, respectively, in depository accounts with one of its investors, Kagoshima Bank, Ltd., an affiliate of one of its shareholders, Kagoshima Shinsangyo Sousei Investment Limited Partnership.
- The Company made payments for lease rentals and other related expenses in the amount of $60 thousand and $178 thousand to Shin Nippon Biomedical Laboratories Ltd. ("SNBL"), a related party, for the years ended December 31, 2016 and 2015, respectively.
- Pursuant to the terms of various service agreements with SNBL, which the Company paid SNBL $362 thousand for the year ended December 31, 2016 for contract research services provided to the Company and its affiliates. There were no payments made to SNBL related to these agreements for the year ended December 31, 2015.
- In 2012, the Company entered into a consulting agreement with Dr. Gregory L. Verdine for services in the capacity as a scientific advisor. The consulting agreement does not have a specific term and may be terminated by either party upon 14 days' prior written notice. Pursuant to the consulting agreement, the Company pays Dr. Verdine approximately $13 thousand per month, plus reimbursement for certain expenses.

- The Company also has an informal consulting arrangement with Dr. Takeshi Wada for scientific advisory services in the amount of 250 thousand Japanese yen, or approximately $2 thousand, per month, plus reimbursement of certain expenses.

13. GEOGRAPHIC DATA

The Company's long-lived assets consist of property and equipment, net, and are located in the following geographical areas:

	December 31, 2016	December 31, 2015
	(in thousands)	
Asia	$ 136	$ 578
United States	8,471	2,211
Total long-lived assets	$ 8,607	$ 2,789

14. SELECTED QUARTERLY FINANCIAL INFORMATION (UNAUDITED)

Selected quarterly results from operations for the years ended December 31, 2016 and 2015 are as follows:

	2016 Quarter Ended			
	March 31	June 30	September 30	December 31
	(in thousands, except for per share data)			
Revenues	$ -	$ 417	$ 392	$ 676
Operating expenses	7,952	12,055	17,625	19,180
Loss from operations	(7,952)	(11,638)	(17,233)	(18,504)
Net loss	(7,847)	(11,565)	(17,535)	(18,454)
Basic and diluted net loss per ordinary share	$ (0.36)	$ (0.51)	$ (0.75)	$ (0.79)

	2015 Quarter Ended			
	March 31	June 30	September 30	December 31
	(in thousands, except for per share data)			
Revenues	$ 26	$ 126	$ —	$ —
Operating expenses	3,491	3,755	4,990	7,214
Loss from operations	(3,465)	(3,629)	(4,990)	(7,214)
Net loss	(3,465)	(3,700)	(4,936)	(7,099)
Basic and diluted net loss per ordinary share	$ (0.42)	$ (0.40)	$ (0.54)	$ (0.46)

Exhibit 21.1

WAVE LIFE SCIENCES LTD.

List of Subsidiaries

Name of Subsidiary	Ownership Percentage	State/Jurisdiction of Incorporation
WAVE Life Sciences USA, Inc.	100%	Delaware
WAVE Life Sciences Japan, Inc.	100%	Japan
WAVE Life Sciences Ireland Limited	100%	Ireland

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors
WAVE Life Sciences Ltd.

We consent to the incorporation by reference in the registration statements (No. 333-208598) on Form S-8 and (No. 333-215428) on Form S-3 of WAVE Life Sciences Ltd., of our report dated March 16, 2017, with respect to the consolidated balance sheets of WAVE Life Sciences Ltd. as of December 31, 2016 and 2015 and the related consolidated statements of operations, comprehensive loss, Series A preferred shares and shareholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2016, which report appears in the December 31, 2016 annual report on Form 10-K of WAVE Life Sciences Ltd.

/s/ KPMG LLP

Cambridge, Massachusetts
March 16, 2017

Exhibit 31.1

CERTIFICATION PURSUANT TO
SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, Paul B. Bolno, M.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of WAVE Life Sciences Ltd.;

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

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

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 16, 2017

/s/ Paul B. Bolno, M.D.
Paul B. Bolno, M.D.
President and Chief Executive Officer
(*principal executive officer*)

Exhibit 31.2

CERTIFICATION PURSUANT TO
SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, Keith C. Regnante, certify that:

1. I have reviewed this Annual Report on Form 10-K of WAVE Life Sciences Ltd.;

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

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

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 16, 2017

/s/ Keith C. Regnante
Keith C. Regnante
Chief Financial Officer
(*principal financial officer and principal accounting officer*)

Exhibit 32

WAVE LIFE SCIENCES LTD.
CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of WAVE Life Sciences Ltd. (the "Company") on Form 10-K for the fiscal year ended December 31, 2016, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of such officer's knowledge:

(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.

March 16, 2017

/s/ Paul B. Bolno, M.D.
Paul B. Bolno, M.D.
President and Chief Executive Officer
(*principal executive officer*)

March 16, 2017

/s/ Keith C. Regnante
Keith C. Regnante
Chief Financial Officer
(*principal financial officer and principal accounting officer*)

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of WAVE Life Sciences Ltd. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.