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, 2017

☐ **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.)**
7 Straits View #12-00, Marina One East Tower	
Singapore	**018936**
(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, a smaller reporting company, or emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the 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, 2017) was $288,724,657. The number of outstanding ordinary shares of the registrant as of March 1, 2018 was 27,992,244.

DOCUMENTS INCORPORATED BY REFERENCE

If the Registrant's Definitive Proxy Statement relating to the 2018 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," "target," "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 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 you 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 timeframe, 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 biotechnology company with an innovative and proprietary synthetic chemistry drug development platform that we are using to rationally 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. Nucleic acid therapeutics, or 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 that 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 or in development by others. In nucleic acid therapeutics, the modification of the backbone of oligonucleotides with a PS linkage is a common alteration, where one non-bridging oxygen is replaced with a sulfur atom at each phosphate. In PS-modified oligonucleotides, 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. In traditionally synthesized PS-modified oligonucleotides, chiral configurations are not purposefully designed or controlled, creating mixtures of many thousands of molecules, each having distinct three-dimensional atomic arrangements. Such variations may convey differing pharmacological 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 pharmacological properties compared with 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 linkages 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 product candidates. 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 and commercialize 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. Our initial focus for our clinical development programs is in neurology, which we broadly define as genetic diseases within the central nervous system ("CNS") and neuromuscular system. We have initiated clinical trials of our two lead programs in Huntington's disease ("HD") and our lead program in Duchenne muscular dystrophy ("DMD") targeting exon 51. In 2018, we expect to initiate three additional development programs, targeting exon 53 in DMD and *C9ORF72* in amyotrophic lateral sclerosis ("ALS") and frontotemporal dementia ("FTD"). In addition to neurology, we continue to advance discovery research in ophthalmologic and hepatic diseases. 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 that we are well positioned to achieve our goals and attain our objective of becoming a fully integrated biotechnology company because our team is comprised of leaders in the field of nucleic acid therapeutics, including world renowned scientists, leading researchers and executives with proven track records in drug discovery, development and commercialization of innovative therapeutics.

Recent Developments

In February 2018, we entered into a global strategic collaboration (the "Takeda Collaboration") that provides Takeda Pharmaceutical Company Limited ("Takeda") with the option to co-develop and co-commercialize our CNS development programs in HD, ALS and FTD, as well as a discovery-stage program targeting *ATXN3* for the treatment of spinocerebellar ataxia type 3 ("SCA3"). In addition, Takeda has the right to license multiple preclinical programs for CNS indications including Alzheimer's disease ("AD") and Parkinson's disease ("PD"). Subject to customary closing conditions, including the expiration or early termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 (the "HSR Act"), the Takeda Collaboration is expected to become effective during Q1 2018. A description of the Takeda Collaboration is included under "*Business – Licensing Arrangements and Research Collaborations – Our Partnerships*."

We continue to independently advance development programs and research in neuromuscular diseases, including our lead programs for the treatment of DMD. We also have ongoing programs to further leverage our stereochemistry platform in other therapeutic areas, including ophthalmology, with our wholly-owned discovery programs and hepatic diseases in collaboration with Pfizer.

Our Current Programs

	TARGET	BIOMARKER	ESTIMATED U.S. PREVALENCE [1]	MECHANISM	DISCOVERY	CANDIDATE	CLINICAL	WAVE'S COMMERCIAL RIGHTS	PARTNER	NEXT ANTICIPATED EVENT
CNS										
Huntington's disease	mHTT SNP1	mHTT	~10k / ~35k	A	●	●	Phase 1b/2a	50% Global [4]	Takeda [4]	Top line data H1 2019
Huntington's disease	mHTT SNP2	mHTT	~10k / ~35k	A	●	●	Phase 1b/2a	50% Global [4]	Takeda [4]	Top line data H1 2019
Amyotrophic lateral sclerosis	C9orf72	Dipeptide	~1,800	A	●	●		50% Global [4]	Takeda [4]	Trial initiation Q4 2018
Frontotemporal dementia	C9orf72	Dipeptide	~7,000	A	●	●		50% Global [4]	Takeda [4]	Trial initiation Q4 2018
Spinocerebellar ataxia 3	ATXN3		~4,500	●	●	○		50% Global [4]	Takeda [4]	Candidate by YE 2018
CNS diseases	Multiple [2, 4]			○	●	○		Milestones & Royalties [4]	Takeda [4]	
MUSCLE										
Duchenne muscular dystrophy	Exon 51	Dystrophin	~2,000	E	●	●	Phase 1	100% Global	–	Top line data Q3 2018
Duchenne muscular dystrophy	Exon 53	Dystrophin	~1,250	E	●	○		100% Global	–	Trial initiation Q1 2019
Neuromuscular diseases	Multiple			○	●	○		100% Global	–	
OPHTHALMOLOGY										
Retinal diseases	Multiple			○	●	○		100% Global	–	
HEPATIC										
Metabolic liver diseases	APOC3	Triglyceride		●	●	○		Milestones & Royalties	Pfizer	
Metabolic liver diseases	Multiple (2) [3]			○	●	○		Milestones & Royalties	Pfizer	

● = silencing. A = allele-specific silencing. E = exon skipping.

1. Estimates of U.S. prevalence and addressable population by target based on publicly available data and are approximate; for Huntington's disease, numbers approximate manifest and pre-manifest populations, respectively
2. During a four-year term, Wave and Takeda may collaborate on up to six preclinical targets at any one time
3. Pfizer has nominated two undisclosed targets in addition to APOC3
4. Wave's collaboration agreement with Takeda is not effective until satisfaction of customary closing conditions, including the requirements of the Hart-Scott-Rodino Antitrust Improvements Act of 1976

Additional details regarding our programs are set forth below.

Neurology: CNS

- In HD, we are advancing two separate programs, WVE-120101 and WVE-120102, each targeting a disease-associated single nucleotide polymorphism ("SNP") within the huntingtin gene ("HTT"): rs362307 ("HTT SNP1") and rs362331 ("HTT SNP2"), respectively. 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 associated with the expression of a disease-causing protein. We have shown that by targeting HTT SNP1 and HTT SNP2 in preclinical models, the production of disease-causing proteins associated with HD can be reduced. In July 2017, we initiated PRECISION-HD1 and PRECISION-HD2, global Phase 1b/2a clinical trials for WVE-120101 and WVE-120102, respectively. We expect top-line data from these trials in H1 2019.

- In ALS and FTD, we are advancing WVE-3972-01, which targets the transcript containing the GGGGCC (“G4C2”) expansion in the C9ORF72 gene. The G4C2 expansion in the C9ORF72 gene is the most common cause of familial ALS and FTD and is a strong genetic risk factor for non-inherited (sporadic) forms of ALS and FTD. We expect to initiate clinical trials of WVE-3972-01 in ALS and FTD in Q4 2018.
- In SCA3, we expect to have a candidate targeting ATXN3 identified by the end of 2018.
- Upon satisfaction of customary closing conditions, we will collaborate with Takeda to advance genetically defined targets for the treatment of CNS disorders, including AD and PD. Under the terms of the agreement, we may collaborate with Takeda on up to six preclinical programs at any one time, during a four-year term. Takeda is entitled to exclusively license multiple preclinical programs during the term.

Neurology: Muscle

- In DMD, we are advancing WVE-210201, which targets exon 51, a region within the precursor messenger RNA (“pre-mRNA”) that is transcribed from the *dystrophin* gene (also referred to as the “*DMD*” gene). DMD is a genetic disorder caused by mutations in the *DMD* gene that results in dysfunctional dystrophin protein. In November 2017, we initiated a global Phase 1 clinical trial of WVE-210201 administered intravenously. Safety data from the Phase 1 clinical trial are anticipated in Q3 2018.
- We also are advancing programs targeting additional *DMD* exons. In September 2017, we announced that our next DMD development program will target exon 53, and we expect to initiate clinical trials in Q1 2019. In addition, we are exploring subcutaneous administration for all of our DMD programs.
- We have initiated research to identify potential targets for additional neuromuscular diseases.

Ophthalmology

- In genetic ophthalmologic diseases, we have conducted preclinical research into the development of stereopure compounds and tested the hypothesis that controlling the chirality of PS linkages in the backbones of oligonucleotides will provide benefits in potency, distribution and duration of effect in the eye. In these studies, we have employed *MALAT1* as a surrogate target. We have evaluated lead stereopure oligonucleotides *in vivo* following single intravitreal injection in mouse and non-human primate (“NHP”) eyes.

Hepatic

- We are collaborating with Pfizer to advance 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. Under the terms of the agreement, Pfizer may select, and we will advance, up to five targets from discovery through 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 (“APOC3”). In Q3 2016, Pfizer nominated its third target. Per the terms of the agreement amended in November 2017, Pfizer is entitled to nominate up to two additional targets by May 2018.

Our R&D Platform and Proprietary Technology

We believe that our proprietary synthetic chemistry platform is an engine for nucleic acid drug development and places us in a unique position to deliver medicines to patient populations where no meaningful therapies are available. We believe that, in combination with our candidate discovery, design and selection process, our platform technology can potentially be applied to treat a significant number of indications, which span multiple therapeutic areas and are addressable by employing the most suited modality based on the biology and our empirical evidence.

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 acids. Prior to the development of our technology, it was not possible to synthesize stereopure nucleic acids with position-specific PS modifications, meaning drugs where the configuration of each chiral PS linkage is precisely controlled during chemical synthesis, at scale. Our unique approach also enables us to use rational drug design, whereby we either employ the conventional wisdom of small-molecule drug development or discover new design principles that govern nucleic acids and apply these insights to therapeutic development. After identifying a target sequence, we determine the most suitable modality, such as RNAi, antisense or exon skipping, and we precisely control the stereochemistry of our oligonucleotides based on the target and the modality. 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 that our platform technology can be broadly applied as it is not limited to a particular chemistry or nucleotide sequence, thereby creating opportunities to optimize it across a larger number of therapeutic areas.

We also 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 a 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. Our initial programs are focused in neurology and are aimed at addressing HD, DMD, ALS and FTD. In parallel to our neurology programs, we are exploring additional therapeutic areas that may benefit from the application of our platform.

The key components of our strategy are as follows:

- ***Maintain and extend our leadership in oligonucleotides***. We intend to establish a dominant position in the field of oligonucleotides, advancing basic research and pharmacology using stereochemistry across multiple therapeutic modalities and target classes. Our efforts are already revealing structure-activity relationships amongst chemical modification, stereochemistry and pharmacology that may allow us to tune the activity of our oligonucleotides in a previously unexplored modality-specific manner.
- ***Rapidly advance our clinical development programs.*** We are advancing three programs currently in clinical development: WVE-120101 and WVE-120102, targeting HTT SNP1 and HTT SNP2, respectively, in HD, and WVE-210201 targeting exon 51 in DMD. We expect to deliver safety data from our Phase 1 trial in DMD in Q3 2018 and top-line data from our two Phase 1b/2a trials in HD in H1 2019. We intend to initiate clinical trials of WVE-3972-01 in ALS and FTD in Q4 2018 and of our program targeting exon 53 in DMD in Q1 2019.
- ***Sustain our leadership in neurology.*** We are committed to transforming the care of rare genetic diseases in neurology, which we broadly define as CNS and the neuromuscular system. Our current neurology development programs offer a foundation from which to transform our company into a fully integrated commercial organization. We also believe there are additional areas within neurology, specifically neurodegenerative movement disorders, neuromuscular diseases beyond DMD and neurodegenerative dementias, that we can uniquely address with our chemistry platform to reach underserved patient populations.
- ***Expand our pipeline.*** We remain intent on making disciplined investments in our platform to enable a sustainable discovery and development engine for future growth. We believe our platform will yield optimized nucleic acid therapeutic candidates to deepen our pipeline in neurologic and hepatic diseases, as well as to allow us to broaden our pipeline into additional therapeutic areas, such as ophthalmology. We will continue to pursue these investments through wholly-owned programs as well as through potential partnerships and collaborations.
- ***Leverage manufacturing leadership in stereopure oligonucleotides.*** We expect that our manufacturing capabilities based in our Lexington, Massachusetts facility, and our growing internal expertise in current good manufacturing practices (“cGMP”), specifically for stereopure oligonucleotides, will better facilitate our growth and enhances our ability to secure drug product for current and future development activities and, potentially, commercial-scale manufacturing. In July 2017, we took occupancy of the approximately 90,000 square foot multi-use Lexington facility and began manufacturing production in Q4 2017.

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. In contrast, we believe that directing medicines to the 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 are an innovative class of drugs that can modulate the function of target RNAs to ultimately affect the production of disease-associated proteins or prevent the accumulation of pathogenic RNA species, which are emerging as important factors in human disease. Nucleic acid therapeutics can regulate protein and RNA via several different molecular mechanisms. These mechanisms can be broadly categorized as silencing, those that promote degradation of the target RNA, including antisense and RNAi; splicing, those that involve binding to the target RNA and modulating its function by promoting exon skipping; and RNA-guided gene editing.

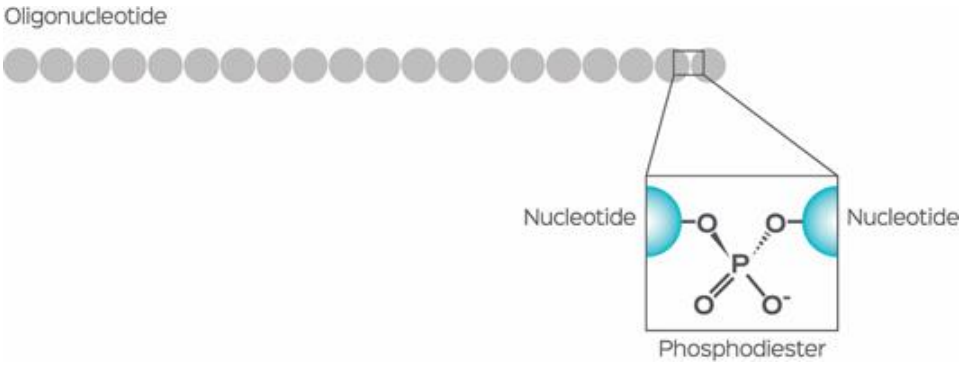
The unique capability of nucleic acid therapeutics to address a wide range of genomic targets that impact multiple therapeutic areas creates potentially significant market opportunities for us to develop drugs to treat a broad spectrum of human diseases, including diseases where no medicines currently 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 or pathogenic RNA. 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 RNAi machinery known as the RNA-induced silencing complex ("RISC") to silence a target RNA that is either pathogenic itself or encodes a disease-associated protein, thereby preventing the accumulation of the pathogenic species (RNA or protein).
- **Splicing**, which is the processing of a nascent pre-mRNA transcript into messenger RNA ("mRNA") by removing introns and joining exons together.
- **Exon skipping**, which uses a therapeutic oligonucleotide designed to bind to a particular sequence within a target pre-mRNA and direct the cellular machinery to delete, or splice out, certain specific regions 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 yields no functional protein. Use of the exon-skipping modality 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.

Design of Nucleic Acid Therapeutics

Nucleic acid therapeutics are largely 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 distributed in the human body, are rapidly cleared by the kidneys and are taken up poorly by targeted cells. The industry has employed chemical modifications of the nucleotides and PO bonds that improve the stability, biodistribution and cellular uptake of nucleic acid therapeutics.

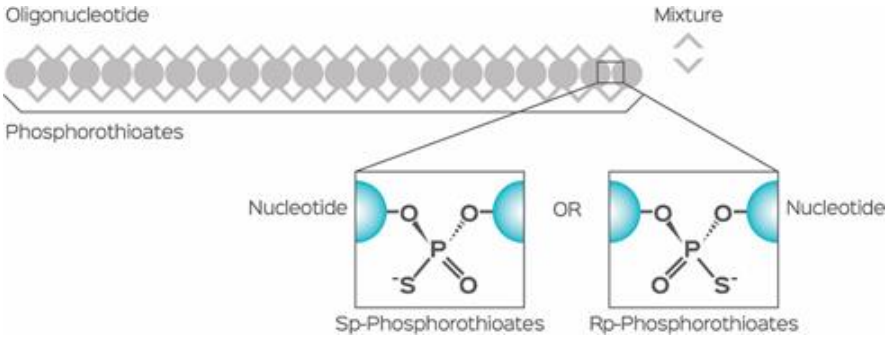
The phosphorothioate ("PS") modification was one of the earliest and remains one of the most common backbone modifications used in nucleic acid therapeutics. When introducing a PS modification, one of the nonbridging oxygen (O) atoms bonded to a phosphorus (P) atom is replaced with a sulfur (S) atom. This modification improves 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 chemistry platforms for nucleic acid therapeutics require the full replacement of the naturally occurring PO with PS, we can judiciously use a combination of PO and PS in our stereopure nucleic acids. We believe this flexibility to selectively employ PS modifications only where desired may provide control over pharmacodynamics and may improve the safety of our drugs.

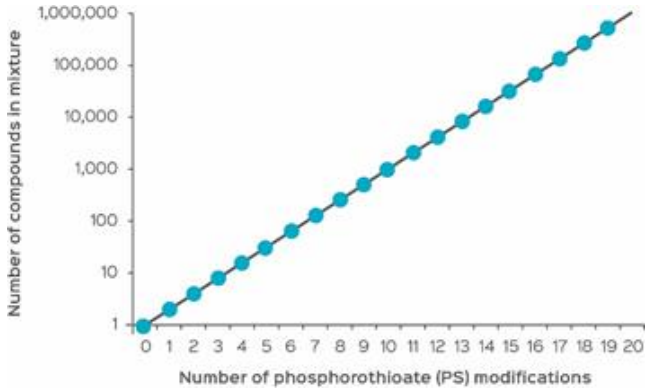
Nucleic acid therapeutics are a relatively "new" class of drugs from the perspective of regulatory approvals. The first U.S. Food and Drug Administration ("FDA") approval of a nucleic acid therapeutic occurred in 1998, and the most recent was in 2016. Nucleic acid therapeutic candidates that employ PS modifications are being developed by several different companies. PS modification is accepted as a state-of-the-art advancement in the field. 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 introducing PS modifications into an oligonucleotide is that it also introduces a chiral center at each phosphorus, creating stereoisomers designated as either an "Sp" or "Rp" isomer. As shown below, these stereoisomers have identical chemical compositions but different three-dimensional arrangements of their atoms and consequently different chemical and biological properties.



The isomeric configuration at each PS modification is random (either Rp or Sp) during conventional nucleic acid therapeutic synthesis. Because oligonucleotides contain a string of nucleotides with associated PS modifications, the synthesis process generates a complex mixture containing many stereoisomers. Specifically, each PS linkage doubles the number of stereoisomers in the product, so that a conventional preparation of a PS-containing oligonucleotide contains 2^N stereoisomers, where N represents the number of PS modifications. As shown below, a conventional, fully PS-modified oligonucleotide (20 nucleotides in length, 19 PS modifications) is a mixture of over 500,000 stereoisomers, each having the same nucleotide sequence but differing in the stereochemistry along their backbones.



Stereoisomers can possess different chemical and pharmacological 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 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 for nucleic acid therapeutic drug mixtures, which can contain tens of thousands to millions of distinct pharmacological entities. Based on our published and ongoing preclinical studies, we believe that we can design and synthesize stereopure PS-modified nucleic acid therapeutics that demonstrate superior pharmacological properties compared with mixture-based nucleic acid therapeutics. We believe that 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 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 optimized stereopure nucleic acid therapeutics. We have published both our proprietary chemistry platform and its application to synthesize stereopure oligonucleotides in *Nature Biotechnology* (Iwamoto N, et al. Nature Biotechnol. 2017;35(9):845-851).

We have discovered and expect to continuously elaborate on the relationships between the chemical makeup of an oligonucleotide, including the three-dimensional orientation or arrangement of its atoms, and its pharmacology (i.e., stability of the drug, activity against the target, specificity for the target and immunogenicity of the drug). Our initial findings relating the stereochemical make up of oligonucleotides to their pharmacology were also featured in our *Nature Biotechnology* publication. In addition, we have defined relationships between various 2'-sugar modifications to the nucleotide (such as methoxy, methoxyethyl, fluoro, locked), and the stereochemistry of the backbone that enhances oligonucleotide pharmacology, providing an enhanced therapeutic profile.

Our rational process for designing stereopure oligonucleotides combining chemistry, stereochemistry and natural phosphate linkages allows us to selectively optimize for the molecular mechanism in order to generate best-in-class nucleic acid therapeutics. We are using these ongoing discoveries to guide our drug development activities that we believe will lead to drugs that can be dosed at lower concentrations, less frequently, or both, as well as with improved therapeutic profiles.

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 compared with traditional oligonucleotide therapeutics (stereomixtures or stereorandom oligonucleotides), and optimizes their interactions with proteins that mediate their activity, as well as those that affect their safety and tolerability. Our ability to improve pharmacological 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. Our ability to improve activity against and selectivity for our intended target mRNA, which in combination with stability, translates into improved *in vivo* target engagement and durability of response.
- ***Broad applicability***. Our platform is applicable to nucleic acid therapeutics acting via multiple molecular mechanisms, 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

In preclinical models, which we believe are predictive of human biology, we have demonstrated that stereochemistry and pharmacology are directly related, and that these relationships inform the rational design and production of nucleic acid therapeutics. In proof-of-concept studies, we have used our platform to design and synthesize diverse sets of oligonucleotides, which allowed us to characterize and compare the behavior of various stereoisomers. These preclinical studies, some of which have been published in *Nature Biotechnology*, have demonstrated that by controlling stereochemistry, we can optimize multiple aspects of pharmacology, including stability, catalytic activity, efficacy, specificity, immunogenicity and enhanced delivery, which in turn, we believe will lead to an enhanced therapeutic profile. As with any drug under development, we cannot be certain that the same favorable pharmacological properties we have observed in preclinical studies for our stereopure nucleic acid therapeutics will translate to humans. 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.

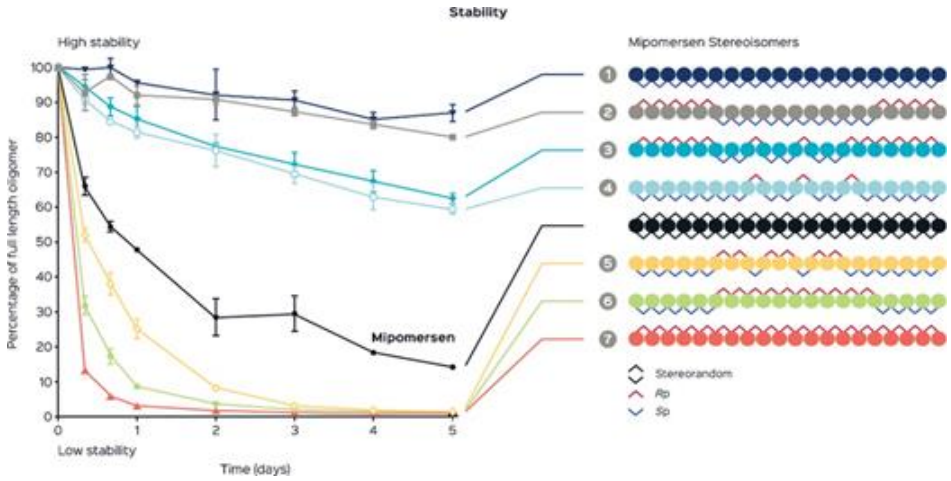
In our *Nature Biotechnology* paper, we describe our studies using stereopure oligonucleotides and oligonucleotide mixtures based on mipomersen. We studied mipomersen because, at that time, it was the only systemically administered nucleic acid therapeutic approved for commercialization, and documents from the regulatory bodies that evaluated mipomersen for marketing approval were publicly available. Mipomersen (currently marketed by Kastle Therapeutics and formerly marketed by Sanofi Genzyme, under the brand name Kynamro®) is approved for the treatment of homozygous familial hypercholesterolemia and is designed to silence production of Apolipoprotein B ("APOB") via an antisense mechanism. Although mipomersen received marketing authorization in the United States in 2012, concerns about the drug's tolerability and liver and cardiovascular safety led the European Medicines Agency ("EMA") to refuse to grant marketing authorization for the drug 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 to maintain its cholesterol-lowering effect.

Mipomersen, an oligonucleotide containing 20 nucleotides and 19 PS modifications, is synthesized by traditional oligonucleotide chemistry; thus, it is actually a mixture of over 500,000 different stereoisomers (2^{19} = 524,288). We rationally designed and synthesized individual stereoisomers of mipomersen, each having position-specific and distinct stereochemistry, and conducted studies comparing these defined stereoisomers with the mipomersen stereomixture.

Stability

We investigated the relationship between stereochemistry and stability by exposing our panel of individual stereoisomers and the stereomixture to metabolic enzymes, including nucleases, in rat liver homogenate or rat serum. We incubated each stereoisomer or the stereomixture separately in rat whole-liver homogenate for five days at physiological temperature and measured the percentage of each full-length stereoisomer and the stereomixture remaining daily. We found that stereochemistry had a profound impact on oligonucleotide stability.

As shown in the graph below, by day five, less than 15% of the stereomixture (mipomersen) remained. By contrast at day five, over 50% of our stereopure isomers 1, 2, 3 and 4 remained, with isomer 1 showing minimal degradation, indicating that these individual stereopure isomers have greater stability than the stereomixture. The mipomersen stereomixture, however, was more stable than several other stereoisomers (i.e., 5, 6 and 7).



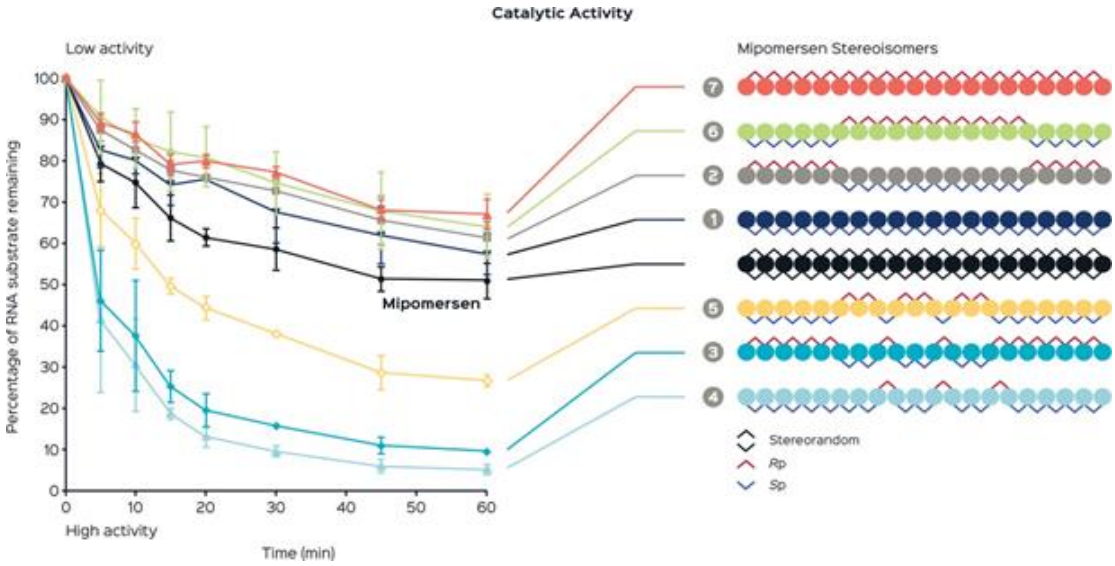
We obtained similar results when we assessed the stability of the stereomixture and selected stereoisomers in rat serum. Overall, we found that increasing the proportion of Sp isomers increased the stability of the oligonucleotides.

Catalytic Activity

We investigated the relationship between stereochemistry and catalytic activity, which, in the case of the antisense modality, is a measure of the efficiency with which the drug leads to the knockdown of the target. In the human body, antisense drugs like mipomersen rely on the enzyme RNase H to degrade or knockdown the target mRNA. Yielding efficient RNase H catalytic activity is an essential pharmacological feature for drugs like mipomersen.

We evaluated the catalytic activity of the same panel of stereoisomers described above in *in vitro* enzymatic assays using human RNase H. We added RNase H to pre-formed duplexes containing the stereoisomers or the stereomixture bound to the target *APOB* mRNA, and we assessed the relative rates of target RNA degradation. To do this, we stopped the reactions at designated time points and quantified the amount of full-length *APOB* mRNA remaining.

As shown below, the catalytic activity of the stereoisomers and the stereomixture differed considerably, as demonstrated by their efficiency in reducing the amount of the full-length target remaining over time. Certain stereoisomers, most notably stereoisomer 4, was far more catalytically active than the stereomixture as well as other stereoisomers. Importantly, stereoisomer 4 contains a pattern of PS stereochemistry denoted 3'-SpSpRp-5' ("SSR"). We also identified stereoisomers with distinct patterns of PS stereochemistry that were less catalytically active than the stereomixture, most notably isomer 7.



Based on these and other data, we have established key design principles (i.e., the SSR motif) relating stereochemistry to RNase H catalytic activity. These principles can now be applied across antisense therapeutics and are compatible with a broad range of additional chemical modifications to the drug molecule.

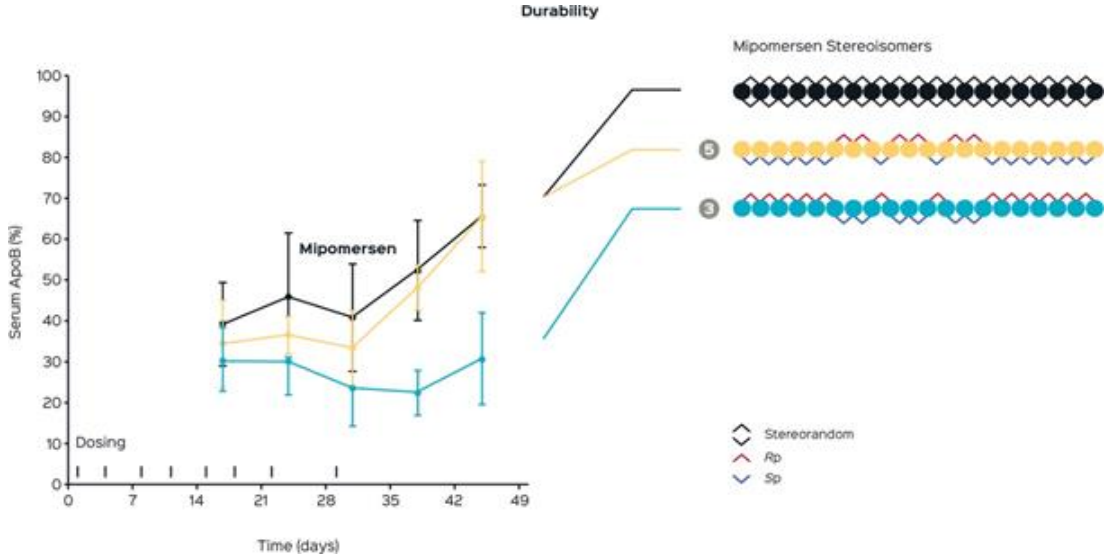
Based on these studies and others, we believe we can synthesize stereopure versions of any PS-modified nucleic acid therapeutic that possesses increased stability and catalytic activity, independent of nucleotide sequence.

Efficacy

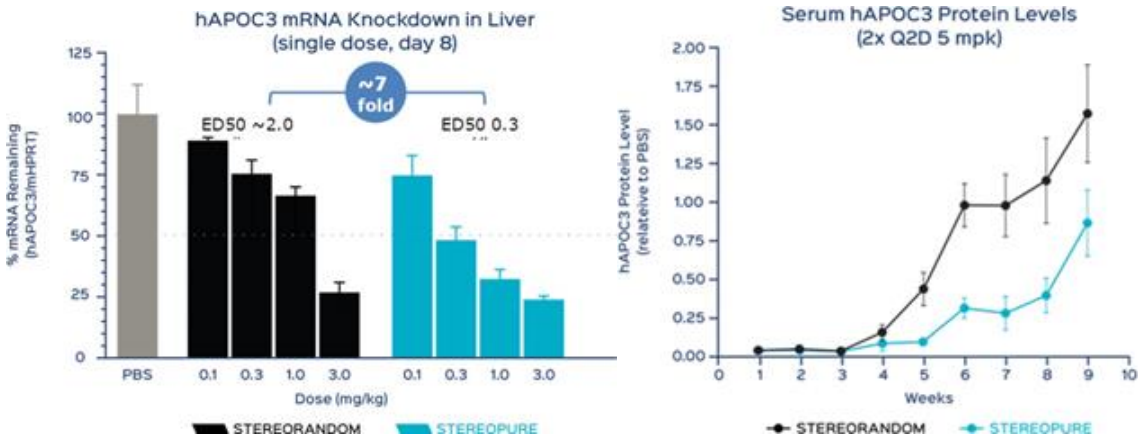
We assessed whether improved stability and catalytic activity of our stereoisomers would translate into greater efficacy in an *in vivo* pharmacological study. We administered our panel of stereoisomers and the stereomixture to transgenic mice that express human *APOB*. This validated animal model was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

We injected mice twice weekly with 10 mg/kg of stereoisomer 3, stereoisomer 5, or the stereomixture over a four-week period. We measured APOB protein levels in the serum weekly for six weeks. This treatment protocol and study design replicates the preclinical *in vivo* pharmacology study that was included in the regulatory submission for mipomersen.

In the experiment, stereoisomer 3, which demonstrated increased catalytic activity and stability *in vitro* compared with the stereomixture and stereoisomer 5, led to greater reduction in serum APOB protein than either the stereomixture or stereoisomer 5. These data are illustrated in the graph below, where levels of APOB in serum, expressed as a percentage of APOB at baseline, is plotted with respect to time (days). Knockdown of APOB by the stereomixture (mipomersen) and stereoisomer 5 decreased dramatically following final dose (after day 28). In contrast, stereoisomer 3 demonstrated efficient and sustained target engagement, as evidenced by the magnitude and duration of knockdown, which persisted for over two weeks after the final dose.



To demonstrate that stereochemistry can be deployed as a generalizable feature, we applied our design to an antisense nucleic acid with a different sequence and chemistry. In this experiment, we generated a single stereopure stereoisomer, containing the SSR motif, and compared it with a stereorandom isomer of the same sequence. Both were designed to target *APOC3* mRNA, which is predominately expressed in the liver. These isomers were also chemically modified with a GalNAc moiety, which improves their access to the liver. To demonstrate *in vivo* efficacy and durability of response, we administered the isomers to mice harboring a human *APOC3* transgene (B6.Cg-Tg(APOC3)2Bres/J), and we assessed knockdown activity by measuring serum APOC3 protein. Similar to the results shown above, the stereopure isomer led to more efficient knockdown of APOC3 (ED_{50}=0.3 mg/kg for stereopure vs. ED_{50}=~2.0 mg/kg for the stereorandom isomer) (left panel in figure below) that persisted much longer than that for the stereorandom isomer (right panel in figure below).



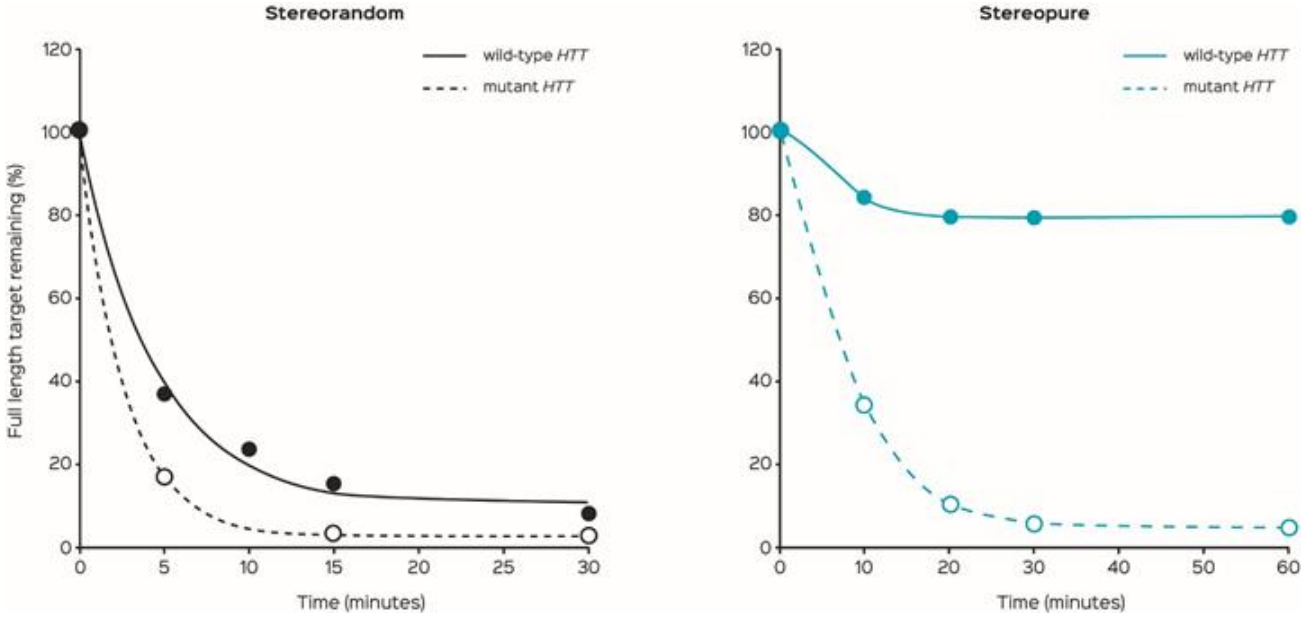
These data demonstrate that two pharmacological properties that we can control through stereochemistry, increasing *in vitro* stability with Sp isomers and increasing *in vitro* catalytic activity with the SSR motif, translate to improvements in important *in vivo* pharmacological properties, including target engagement and durability of response. In addition to these findings, we have also observed significant target engagement of our stereoisomers in numerous tissues, including eye, liver, muscle and CNS.

Specificity

By controlling stereochemistry, we have discovered that we can change the pattern of RNase H cleavage in the target mRNA that is caused by PS-modified antisense. Indeed, we can use stereochemistry to direct cleavage toward specific positions within the target. This precision control enables us to design PS-modified nucleic acids that can direct RNase H to differentiate between two very similar targets. This level of specificity is desirable in cases where cleavage of one target is expected to have disease-modifying impacts, but cleavage of a closely related target is undesirable or potentially unsafe.

For example, HD is caused by mutations in one allele (which is one of two or more versions of a gene) of the *HTT* gene, resulting in the production of a disease-causing protein, while the other allele encodes a healthy protein. By optimizing stereochemistry, we can direct cleavage towards the mutated *HTT* allele based on a single-nucleotide difference between the disease-causing allele and the normal allele.

In the experiment illustrated below, we performed *in vitro* RNase H enzymatic reactions similar to those presented previously. As before, we added RNase H to stereopure oligonucleotides or stereorandom oligonucleotides that were duplexed with mutant or healthy *HTT* RNA. We stopped the reactions at designated time points and quantified the amount of full-length mutant or healthy *HTT* RNA remaining. The stereorandom oligonucleotide (left panel) caused substantial reductions in both the mutant and healthy *HTT* RNA, whereas the optimized stereopure oligonucleotide (right panel) preferentially cleaved mutant *HTT* RNA while largely sparing the healthy *HTT* RNA.



We believe that our ability to use stereochemistry to precisely control the RNase H cleavage patterns resulting from PS-modified nucleic acids allows us to mitigate unwanted activity *in vivo*. This affords us a unique position to make allele-specific targeting (meaning the preferential interaction of an oligonucleotide with RNA transcribed from only one allele of a given gene) possible.

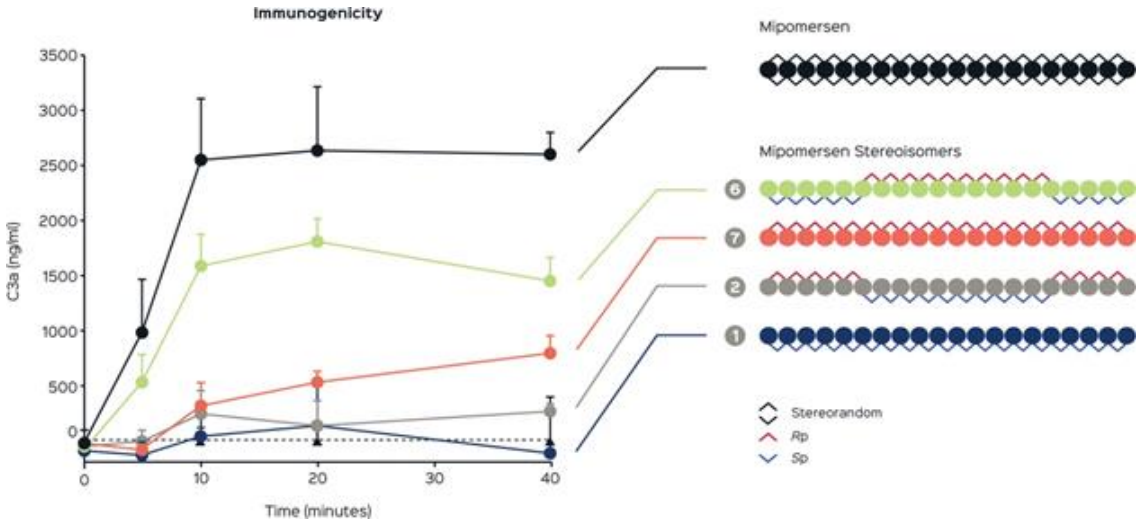
Through these preclinical studies, we have demonstrated the ability to use stereochemistry to precisely control cleavage and reduce off-target cleavage. We believe these findings can be applied in the design of nucleic acid therapies for a range of disease targets.

Immunogenicity

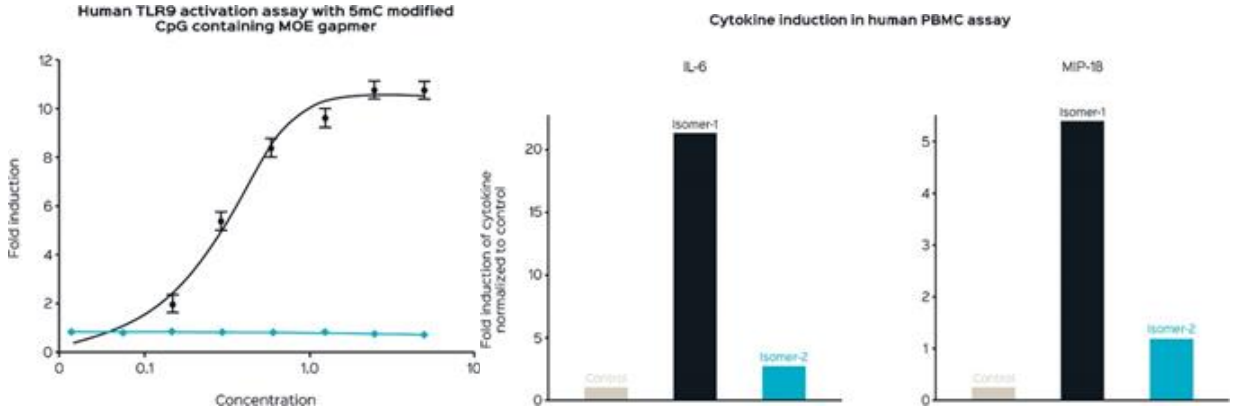
We investigated the relationship between stereochemistry and immunogenicity, which is the ability of a substance to activate an immune response. Immune activation has been observed with PS-modified oligonucleotides in preclinical toxicology studies. Flu-like symptoms and injection-site reactions in clinical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

Using NHP serum, we analyzed the activation of the complement system following exposure to our panel of individual stereopure isomers and the parent stereomixture. We incubated each isomer and stereomixture at physiological temperature in NHP serum from three individual animals. We removed samples from these incubations at designated times, and we assessed complement activation by measuring the increase in the amount of protein C3a. Protein C3a is formed when the complement system is activated and complement component 3 is cleaved. C3a levels in serum increase in direct proportion to the amount of pathway activation. We quantified serum C3a levels 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.

As shown below, the stereoisomers and the stereomixture yielded different levels of complement pathway activation as measured by C3a production. Certain stereoisomers, such as stereoisomers 1 and 2, showed less than half of the C3a production compared with the stereomixture (shown in black).



We have also assayed immune activation of stereoisomers and the parent stereomixture in a human TLR9 reporter assay (left panel below) and a human peripheral blood mononuclear cell ("PBMC") cytokine panel (right panel below, IL-6 and MIP-1β are key cytokines in B-cell and macrophage activation, respectively). In the TLR9 assay, the 5'methylcytosine ("5mC")-modified stereomixture activated TLR9 activity, whereas our stereopure isomer did not. Similarly, the 5mC-modified stereomixture (Isomer-1) led to IL-6 and MIP-1β secretion from PBMCs, where our stereopure isomer (Isomer-2) did not. Prior research has indicated that 5mC and 2'-modifications to a nucleic acid therapeutic containing the immune-activating CpG motif are sufficient to limit immune activation. However, substantial immune activation persists even when these modifications are incorporated, as seen in these experiments. Our chemistry platform allows us to design stereoisomers that yield notably less activation of the immune system.

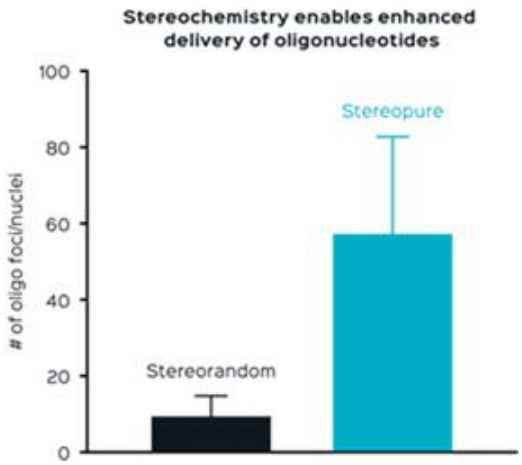


Based on these studies, we believe that it is possible to modulate complement activation and potentially reduce the immunogenicity of PS-modified oligonucleotides by controlling stereochemistry.

Enhanced Delivery

We have also investigated the relationship between stereochemistry and cellular uptake, which is the ability of nucleic acid therapeutics to penetrate cells and access the appropriate subcellular compartment (i.e., the nucleus) for them to engage with their intended target. Designing oligonucleotides that enter cells at sufficient concentrations to provide a therapeutic effect has been a challenge for the nucleic acid therapeutics field.

As shown below, we performed an intracellular trafficking assay using differentiating myoblast cell lines to compare the cellular localization of stereopure and stereorandom oligonucleotides *in vitro*. We washed and fixed treated cells and detected the oligonucleotides using a ViewRNA assay and an immunofluorescence microscope with deconvolution capabilities. Z-stacks were taken to eliminate artifacts. We compared the number of oligonucleotide foci (red, left panel below) in the nucleus (blue) of cultured cells that we treated with either a stereorandom oligonucleotide or one of our stereopure oligonucleotides. We detected substantially more foci per nucleus for our stereopure oligonucleotide compared with a stereorandom oligonucleotide of comparable sequence (right panel below).



Our Initial Therapeutic Programs

Our most advanced therapeutic programs are in neurology, which we broadly define as genetic diseases within the CNS and neuromuscular system. Within neurology, we are focused on HD, DMD, ALS, FTD and we have initiated discovery research in SCA3. We have initiated clinical trials of our two lead programs in HD and our lead program in DMD targeting exon 51. In 2018, we expect to initiate three additional development programs, targeting exon 53 in DMD and *C9ORF72* in ALS and FTD. As a component of our neurology focus, we continue to advance research to identify potential candidates for the treatment of SCA3 and explore additional targets relevant to CNS and neuromuscular disorders.

See below for more information on these programs and the respective diseases we are targeting.

Huntington's Disease

Background and Market Opportunity

HD is a rare hereditary neurodegenerative disease that results in early death and for which there is no cure. HD is caused by a mutation (i.e. an expanded CAG triplet repeat) in the *HTT* gene, which results in production of mutant HTT ("mHTT") protein. Accumulation of mHTT protein causes progressive loss of neurons in the brain, and can lead to neuronal cell death, causing cognitive, psychiatric and motor disability. HD patients still possess wild-type (healthy) HTT ("wtHTT") protein, which is believed to be critical for neuronal function. Accordingly, suppression of wtHTT may have detrimental long-term consequences. Absence of wtHTT protein has been shown to be embryonically lethal in mice.

Symptoms of HD 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 similar to having ALS, PD and AD simultaneously. Patients experience a reduction in motor function and psychological disturbances. Life expectancy after symptom onset is approximately 20 years. In the most symptomatic stages, often lasting over ten years, affected persons become fully dependent upon others to manage all activities of daily living; they lose the ability to make decisions, feed themselves and walk, often requiring premature placement in a long-term care facility. It is estimated that approximately 30,000 people in the United States have symptomatic HD and more than 200,000 others have a 50% risk for inheriting the disorder from their affected parent.

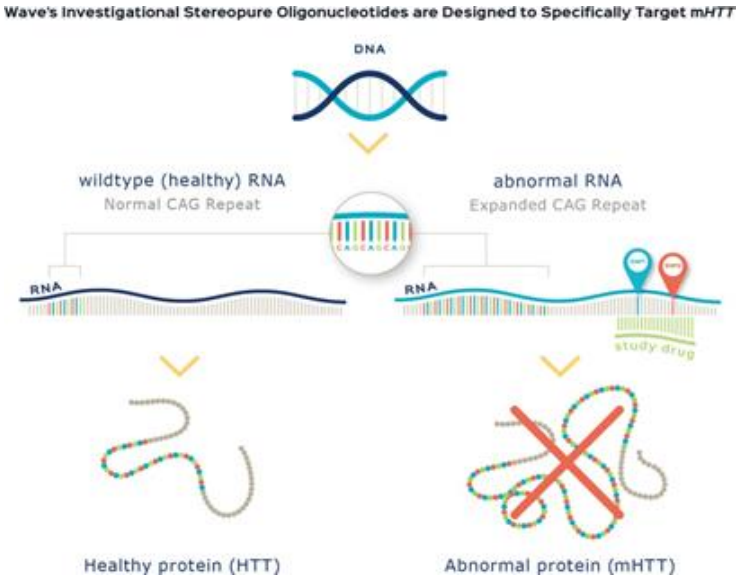
Current Treatments

There are no approved treatments that can reverse or slow HD progression. Current pharmacological therapies only address HD symptoms. Antipsychotics are used to manage depression, irritability and chorea (involuntary movements). Xenazine® (tetrabenazine) and Austedo™ (deutetrabenazine) are the only two therapies approved for the treatment of chorea associated with HD in the United States.

Our Programs

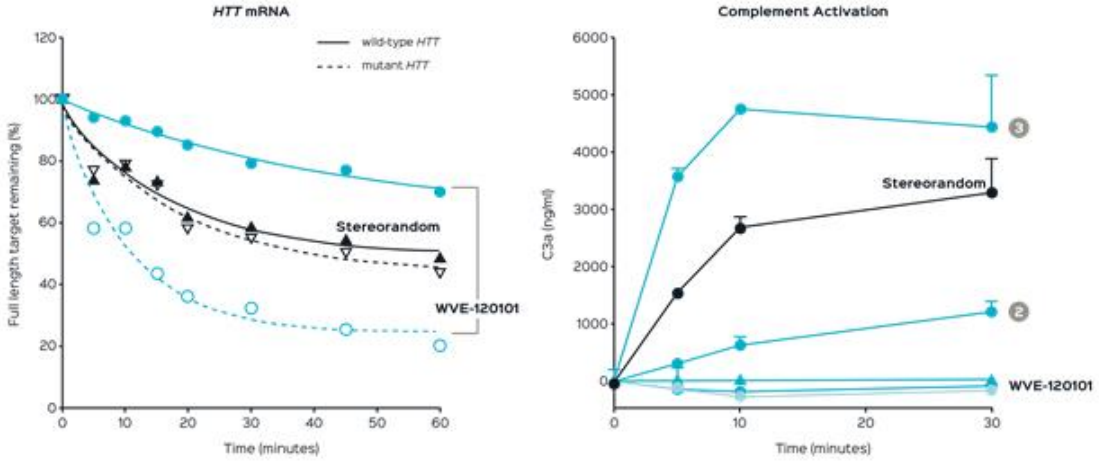
We have advanced two investigational stereopure oligonucleotides into clinical trials, WVE-120101 and WVE-120102, which target SNPs associated with the mutant allele of the *HTT* gene. The precise targeting of the mutant allele by stereopure oligonucleotides should allow discrimination and selective silencing of the m*HTT* mRNA transcripts that lead to the production of the mHTT protein associated with disease manifestations, while leaving wild-type (healthy) *HTT* transcripts and protein relatively intact (see figure below).

WVE-120101 and WVE-120102 are designed to selectively target HTT SNP1 and HTT SNP2 on the m*HTT* allele, respectively. These are two of the most common SNPs associated with the m*HTT* allele, which are believed to encompass up to 70% of the HD patient population. If approved, WVE-120101 and WVE-120102 would be the first allele-specific disease-modifying therapies for HD patients. Our allele-specific approach may also enable us to address the pre-manifest HD patient population in the future.



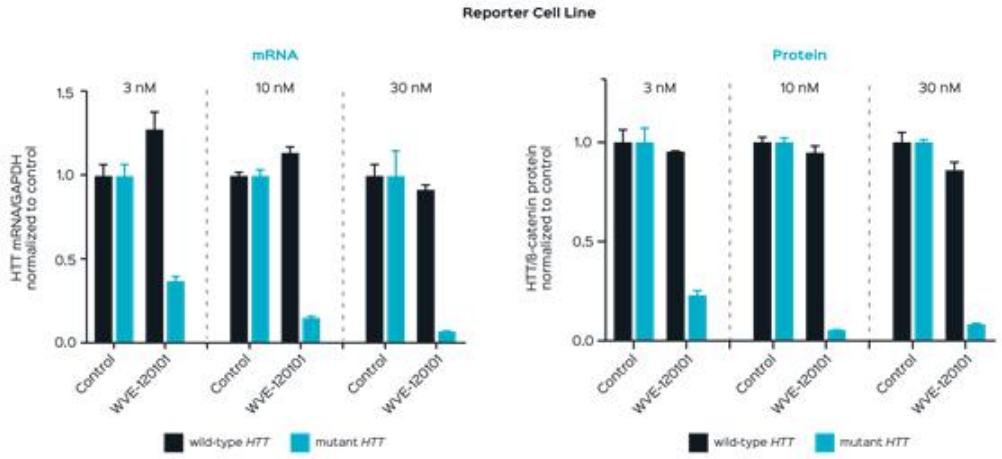
In July 2017, we initiated our clinical trial program for HD, PRECISION-HD. PRECISION-HD1 and PRECISION-HD2 are global Phase 1b/2a clinical trials for WVE-120101 and WVE-120102, respectively. We expect top-line data from these clinical trials in H1 2019. PRECISION-HD1 and PRECISION-HD2 are multicenter, randomized, double-blind, placebo-controlled studies that primarily evaluate the safety and tolerability of single and multiple doses of WVE-120101 and WVE-120102, respectively, administered intrathecally in early manifest HD patients. Additional exploratory objectives include assessing the impact that each compound has on levels of mHTT protein, as well as evaluating potential clinical effects and impact on brain atrophy as measured by magnetic resonance imaging. We intend to enroll approximately 50 patients globally in each of the two studies at multiple clinical trial sites. In 2016 and 2017, we were granted orphan drug designation under the Orphan Drug Act by the FDA for our product candidates, WVE-120101 and WVE-120102, respectively, for the treatment of HD.

In our preclinical studies, as shown below, the stereopure oligonucleotide WVE-120101 (circles) or a stereorandom oligonucleotide (triangles) were bound to wt*HTT* or m*HTT* mRNA and incubated with human RNase H (left panel). WVE-120101 produced greater knockdown of m*HTT* compared with the stereorandom oligonucleotide. In addition, WVE-120101 was selective for m*HTT* over wt*HTT*, producing relatively little knockdown of wt*HTT*. The stereorandom oligonucleotide was not selective and knocked down both wt*HTT* and m*HTT*.

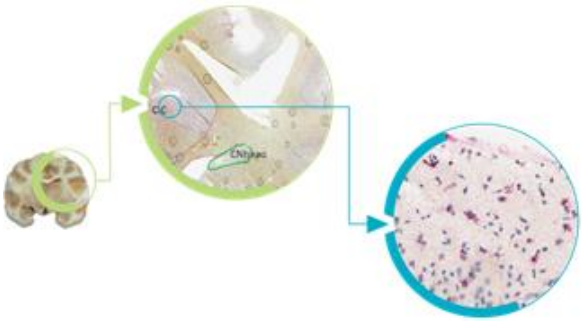


Using NHP serum, we analyzed the activation of the complement system following exposure to a panel of stereopure oligonucleotides and the parent stereorandom oligonucleotide, which were designed to target *HTT*. Each oligonucleotide was incubated at physiological temperature in NHP serum from three individual 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 panel), certain stereopure oligonucleotides and the stereorandom oligonucleotide demonstrated increased production of C3a; however, there was no production of C3a following exposure to WVE-120101, which also discriminated between wild-type and mutant *HTT*.

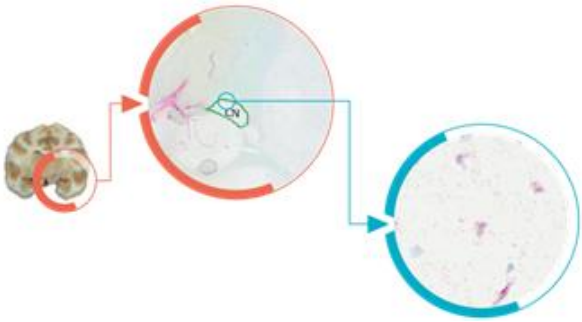
WVE-120101 was tested for potency and selectivity of knocking down m*HTT* mRNA in a cellular reporter assay. WVE-120101 targeting the m*HTT* mRNA was co-transfected into HEK293 cells with two reporter plasmids: a plasmid with V5-tagged full-length *HTT* containing the U-variant SNP1 (mutant) and a plasmid with FLAG-tagged full-length HTT containing the C-variant SNP1 (wild-type). Knockdown of m*HTT* 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 oligonucleotide as a control. As shown below, WVE-120101 potently reduced m*HTT* mRNA (left panel) and mHTT protein (right panel), and exhibited significant selectivity for m*HTT* at all doses tested. This study demonstrates the ability to knock down the m*HTT* allele while leaving the wt*HTT* (healthy) allele relatively unaffected.



Following these promising preclinical experiments, we investigated distribution characteristics of WVE-120101 in NHPs. Based on our preclinical studies, we believe stereochemistry enables improved protein binding and distribution. The figure below demonstrates meaningful distribution of WVE-120101 in an NHP study. In this preclinical study, we employed an *in situ* hybridization ("ISH") ViewRNA assay. The ViewRNA assay provides us with the ability to stain oligonucleotides, allowing increased visibility and understanding of the distribution of WVE-120101 in the brain. As shown below, we found 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 in the cortex and striatum. These findings are encouraging as we believe that distribution and penetration into several areas of the brain will be critical for the successful treatment of HD.



Red dots are WVE-120101 oligonucleotide.
Arrow points to nuclear and perinuclear distribution of WVE- 120101 in cingulate cortex



Red dots are WVE-120102 oligonucleotide.
Arrow points to nuclear and perinuclear distribution of WVE-120102 in caudate nucleus

Preclinical studies on WVE-120102 showed similar results with regard to RNase H-mediated activity, m*HTT* allele specificity, and distribution in NHP brain.

Duchenne Muscular Dystrophy

Background and Market Opportunity

DMD is a rare, genetic progressive neuromuscular disorder caused by mutations in the *DMD* gene on the X chromosome that affects approximately one in 3,500 newborn boys around the world (approximately 20,000 new cases annually). 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 a 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. Patients with DMD 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 thirties.

Current Treatments

While there are approved therapies for DMD, there is no cure, and there continues to be significant unmet medical need. In most countries, corticosteroids are the standard drug therapy, which slows the progression of muscle weakness and delays loss of ambulation by two to three years. In February 2017, the FDA approved Emflaza (deflazacort), the first corticosteroid approved as a treatment in the United States for DMD patients older than five years of age.

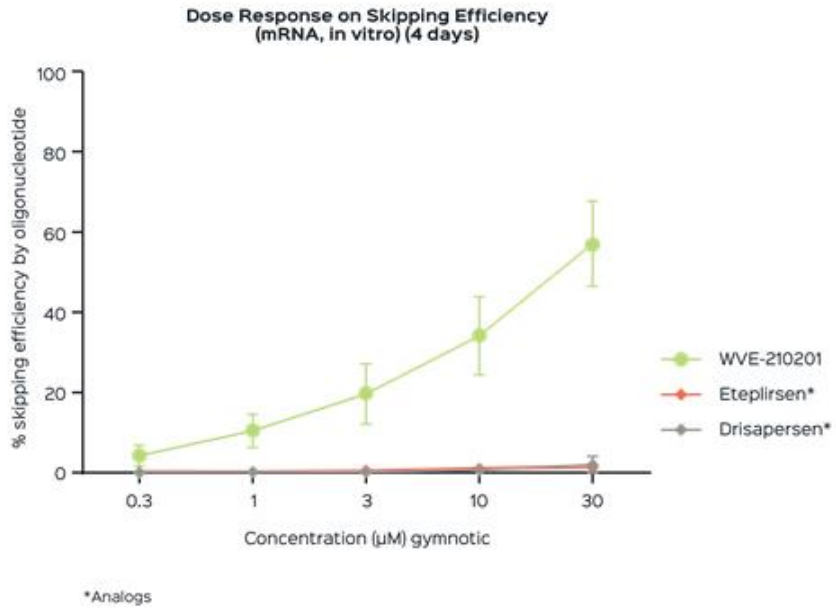
In 2016, Sarepta Therapeutics' Exondys 51™ *(*eteplirsen) received accelerated approval in the United States. The FDA concluded that the data submitted demonstrated an increase in dystrophin production that is reasonably likely to confer clinical benefit in some patients with DMD, who have a confirmed mutation of the *DMD* 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 being evaluated in 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, who have a confirmed mutation of the *DMD* gene amenable to exon 51 skipping. Another exon-skipping nucleic acid therapeutic candidate for DMD, BioMarin Pharmaceutical's drisapersen, received a complete response letter ("CRL") from the FDA in January 2016, indicating that the review cycle was complete and that the application was not ready for approval in its present form.

In 2014, PTC Therapeutics' Translarna™ (ataluren) was the first disease-modifying treatment to receive conditional approval by the EMA for the treatment of ambulatory DMD patients over 5 years of age who have a nonsense mutation (12% of DMD cases) in the *DMD* gene. In 2016, the EMA did not allow ataluren to convert to full marketing authorization, rather it granted a renewal of the conditional approval.

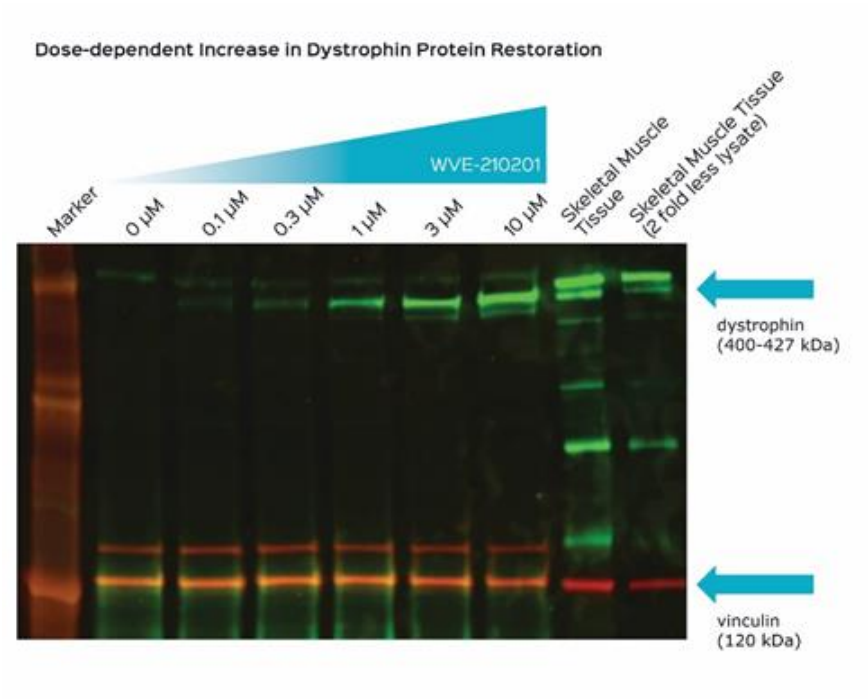
Our Programs

Based on our interactions with the DMD patient community and DMD patient advocacy groups, we believe that there continues to be a significant unmet medical need in DMD patients despite the availability of eteplirsen in the United States and ataluren in the European Union. We initiated a global Phase 1 clinical trial in WVE-210201, our investigational stereopure oligonucleotide, in November 2017. Approximately 13% of DMD patients have genetic mutations that are amenable to treatment with exon 51 skipping therapy. In addition, we are advancing our next DMD development program of a stereopure oligonucleotide for patients amenable to exon 53 skipping. Available data indicate that a molecule that skips exon 53 could address approximately 8% of DMD patients. We expect to initiate clinical trials of our exon 53 program in Q1 2019. In addition, we are exploring subcutaneous formulations for all of our DMD programs.

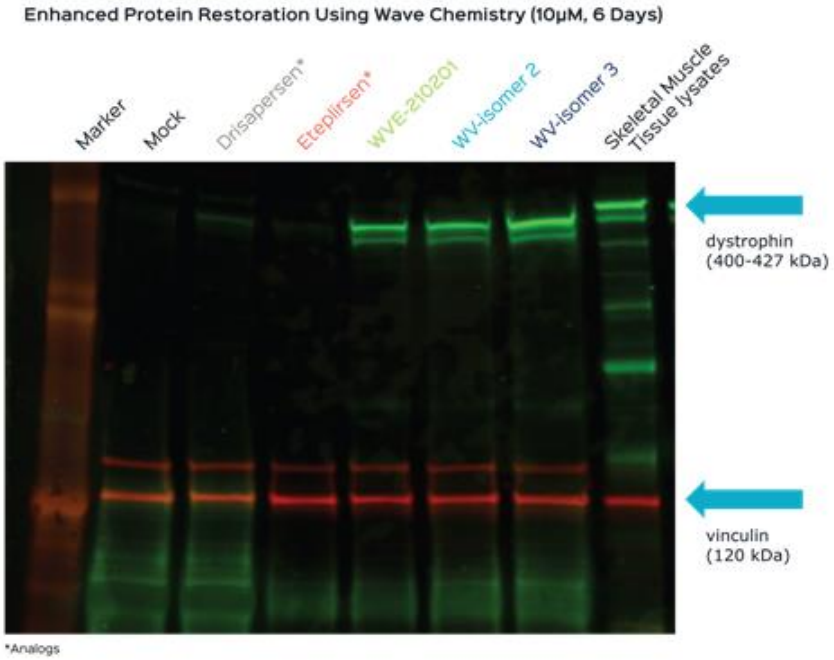
WVE-210201 was selected for clinical development, in part, based on its ability to demonstrate high exon 51 skipping efficiency and dystrophin protein restoration in patient-derived muscle cells. Efficiency at skipping exon 51 was determined by quantitative RT-PCR following exposure to equal concentrations of oligonucleotides. As shown below, WVE-210201 demonstrated dose-dependent and more potent increases in exon skipping efficiency compared with analogs of eteplirsen and drisapersen.



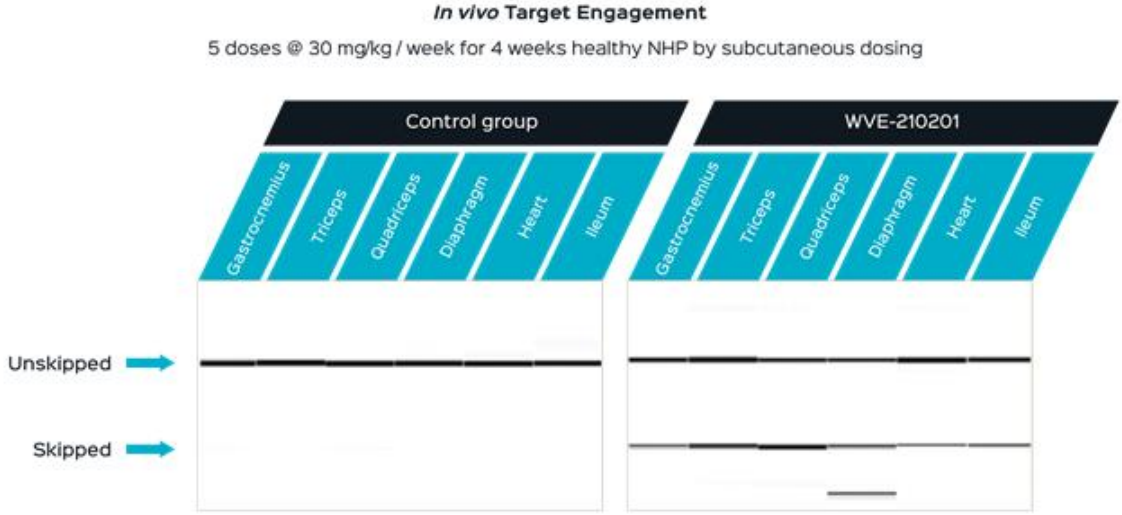
Using patient-derived muscle cells, we analyzed WVE-210201's impact on protein expression by Western blot after gymnotic uptake, meaning delivery of drug candidate to the cell in the absence of any carriers or conjugation. Results show that WVE-210201 induced a clear dose-dependent restoration of dystrophin protein expression (Western blot shown below).



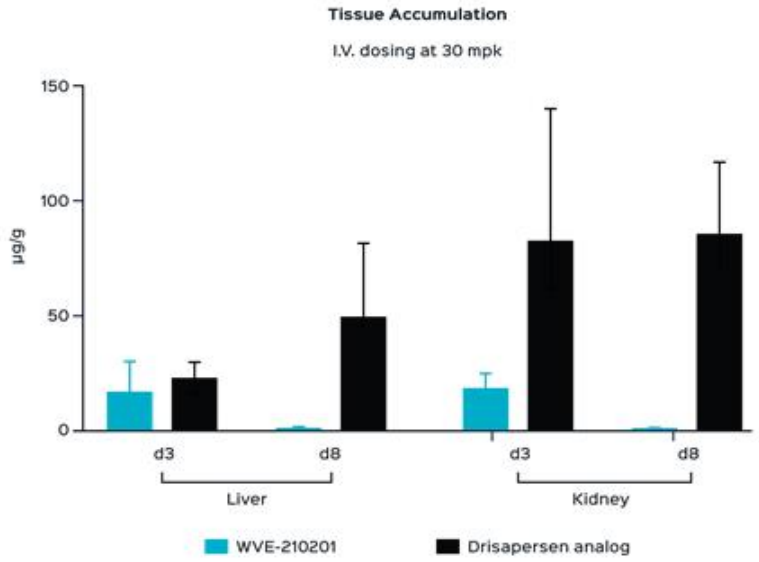
At a 10 µM concentration of each compound (WVE-210201, other Wave isomers and analogs of drisapersen and eteplirsen), we quantified the extent of dystrophin protein restoration *in vitro*, and found that WVE-210201 and other Wave isomers (WV-isomer 2 and WV-isomer 3) restored dystrophin protein expression to between 50% and 100% of that in normal skeletal lysates (Western blot shown below). Specifically, WVE-210201 restored dystrophin protein expression to 52% of the levels found in normal skeletal muscle tissue lysates versus the approximate 1% restoration observed with other exon-skipping compounds.



We have confirmed target engagement of WVE-210201 in an NHP study. We dosed animals with five 30 mg/kg weekly subcutaneous injections of WVE-210201 over four weeks. Tissue samples were collected two days after the final dose, and nested PCR was performed to assess the presence of skipped RNA transcripts. As shown below, we detected skipped transcripts in all treated muscles that we assessed (right panel), indicating that WVE-210201 successfully engaged with *DMD* pre-mRNA *in vivo*.



As conventional oligonucleotides tend to accumulate in the liver and kidney, we also assessed the accumulation of WVE-210201 in the liver and kidney of a dystrophin-deficient mouse model (mdx-23 mice) after a single intravenous 30 mg/kg dose. As shown below, there was significantly less accumulation of WVE-210201 in these tissues up to eight days after dosing compared with an analog of drisapersen.

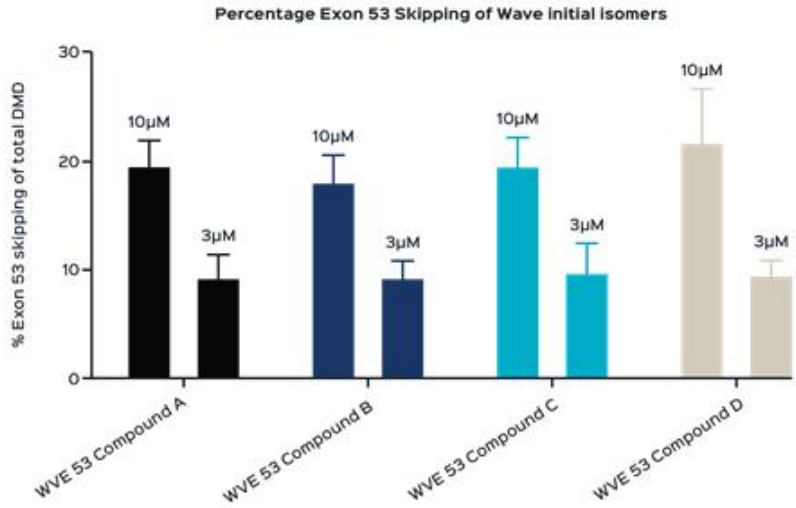


WVE-210201 is being studied in a global multicenter, double-blind, placebo-controlled Phase 1 clinical trial. The objective of this clinical trial is to evaluate the safety, tolerability and plasma concentrations of single ascending doses of WVE-210201 administered intravenously in DMD patients who have *DMD* gene mutations that are amenable to exon 51 skipping therapies. The trial is expected to enroll up to 40 patients between the ages of 5 and 18 years, and the inclusion criteria allow for participation of both ambulatory and non-ambulatory patients, as well as patients who were previously treated with eteplirsen, following an appropriate washout period. Intravenous doses tested in the Phase 1 trial will escalate through a range expected to be clinically relevant. In the United States, we are required to provide data from preclinical studies to the FDA in order to progress to the highest-dose cohorts and planned multi-dose studies.

Safety data from the Phase 1 clinical trial for WVE-210201 are expected in Q3 2018 and will facilitate the rapid transition to a double-blind, placebo-controlled, multi-dose efficacy study in which dystrophin expression and clinical outcomes will be assessed. The clinical program is designed to allow patient participants from the Phase 1 trial to enroll in an open-label extension study in which dosing with WVE-210201 will continue. The open-label extension study and the planned efficacy study are intended to follow the Phase 1 trial and are expected to include an interim efficacy readout of dystrophin expression from muscle biopsies in H2 2019.

We are leveraging our stereochemistry platform to advance investigational therapies targeting additional DMD-related exons. In September 2017, we announced that our next DMD development program will target exon 53, and we expect to initiate clinical trials in Q1 2019.

In our *in vitro* research studies using exon 53-skipping candidates, we have shown that several of our stereopure isomers (WVE 53 Compounds A-D, shown below) induce dose-dependent increases in pre-mRNA skipping in DMD patient-derived myoblasts carrying a deletion of exons 45–52. In these experiments, cells were exposed to stereopure isomers for four days under gymnotic conditions. These initial data, using un-optimized stereopure isomers, show that we can achieve ~20% skipping.



Amyotrophic Lateral Sclerosis and Frontotemporal Dementia

A hexanucleotide G_4C_2 expansion found in the *C9ORF72* gene is the most common cause of familial ALS and FTD and is a strong genetic risk factor for non-inherited (sporadic) forms of ALS and FTD. Some patients exhibit characteristics of both ALS and FTD, indicating that these diseases form part of a continuum of neurological disease with some overlap in symptoms between them.

ALS Background and Market Opportunity

ALS is a neurodegenerative disease characterized by the progression and degeneration of motor neurons in the brain and spinal cord. Diagnosis may take up to 12 months and is made clinically by assessing the signs of upper and lower motor neuron degeneration in the same region of the body. Patients initially present with limb-onset disease (approximately 70% of patients), bulbar-onset disease (approximately 25% of patients) or with initial trunk or respiratory involvement (approximately 5% of patients). Age of onset is generally in the mid-to-late 50's, and median survival is three years; however, up to 24% of patients survive for five to ten years. Survival in patients with *C9ORF72* ALS may be shorter than in patients with sporadic ALS.

In the United States and Europe combined, there are approximately three to five ALS patients per 100,000 people. This translates to approximately 13,000 diagnosed patients in the United States, although the total prevalence may be around 20,000. There are one or two newly diagnosed cases of ALS per year, per 100,000 people in the United States and Europe combined, resulting in approximately 5,000 newly diagnosed patients in the United States each year. While the majority of ALS cases are sporadic, approximately 10% of cases are found to be familial in nature. The *C9ORF72* gene mutation is currently the most common demonstrated mutation related to ALS and is present in approximately 40% of familial ALS and 8-10% of sporadic ALS patients.

ALS Current Treatments

There is significant unmet need for the treatment of ALS. Two drugs are currently approved in the United States for the treatment of ALS. Rilutek® (riluzole), an inhibitor of glutamate release, was approved in 1995 for the treatment of patients with ALS. It was demonstrated to extend survival by three to six months. Radicava® (edaravone) was approved in 2017 for the treatment of ALS. Administration of edaravone resulted in a significantly smaller decline in the ALS Functional Ration Scale-Revised (ALSFRS-R) through six months of treatment.

FTD Background and Market Opportunity

FTD is a neurodegenerative disorder of the frontal and anterior temporal lobes of the brain. It is characterized by changes in personality, cognition (e.g., language impairment and executive dysfunction), and behavior (e.g., disinhibition, apathy and compulsivity). Diagnostic criteria categorize FTD into either the behavioral variant (approximately 60% of patients) or speech/language variant (approximately 40% of patients) based on the primary symptom observed at presentation; however, FTD results in dementia in all patients. The majority of FTD associated with the G_4C_2 expansion in the *C9ORF72* gene is categorized as the behavioral variant. FTD frequently has an onset in mid-life, and death typically occurs within three to 14 years of onset. FTD is the second most common form of early-onset dementia in people under the age of 65, after AD.

In FTD, the *C9ORF72* gene mutations appear in 38% of familial cases and 6% of sporadic cases. FTD affects approximately 55,000 people in the United States.

FTD Current Treatments

There are currently no disease-modifying therapies approved for the treatment of FTD. Treatment to date has involved use of medications for symptomatic management.

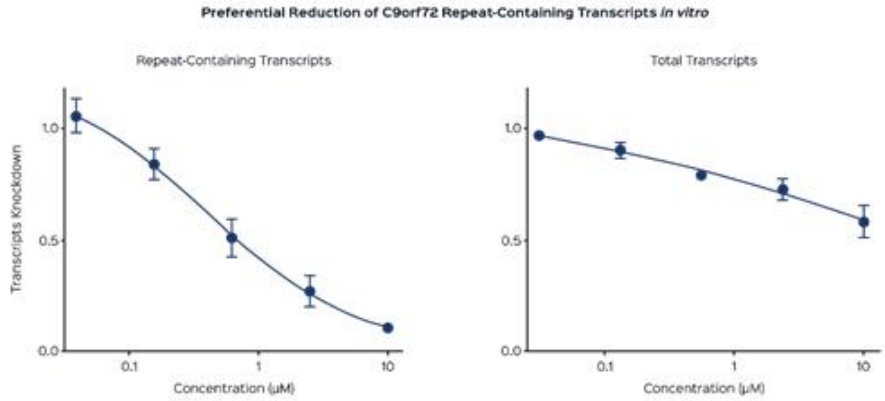
Our Program

WVE-3972-01 is an investigational oligonucleotide that was designed to preferentially knockdown G_4C_2 repeat-containing *C9ORF72* mRNA transcripts, which are associated with ALS and FTD. Expansion of the G_4C_2 repeat alters the normal expression of the *C9ORF72* gene and causes the production of repeat-containing RNAs. These RNAs accumulate in cellular nuclei in the form of RNA foci and can be translated into dipeptide repeat (“DPR”) proteins. Neuronal degeneration associated with the expression of the repeat expansion is hypothesized to arise either from a toxic loss-of-function mechanism due to a reduction in C9ORF72 protein or a toxic RNA gain-of-function mechanism through the accumulation of RNA foci and/or DPRs in the brain and spinal cord.

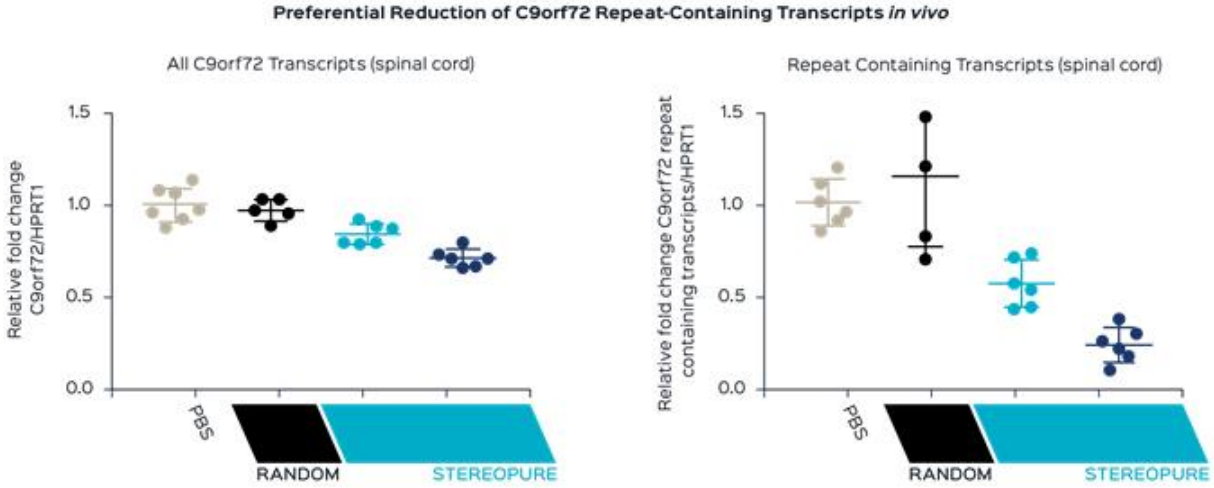
By targeting the mRNA transcripts that contain the G_4C_2 expansion found in the *C9ORF72* gene, WVE-3972-01 has the potential to reduce both RNA-based and protein-based toxicity, thereby impacting the disease course and slowing the progression of ALS or FTD. As WVE-3972-01 preferentially targets the transcripts containing the G_4C_2 expansion, it is designed to minimize the impact on normal C9ORF72 protein levels in patients, thereby reducing potential on-target risk.

Our data suggest that preferential targeting of repeat-containing transcripts using WVE-3972-01 may be a viable therapeutic approach for the treatment of ALS and FTD associated with *C9ORF72*-repeat expansions. We expect to initiate clinical trials of WVE-3972-01 in ALS and FTD in Q4 2018.

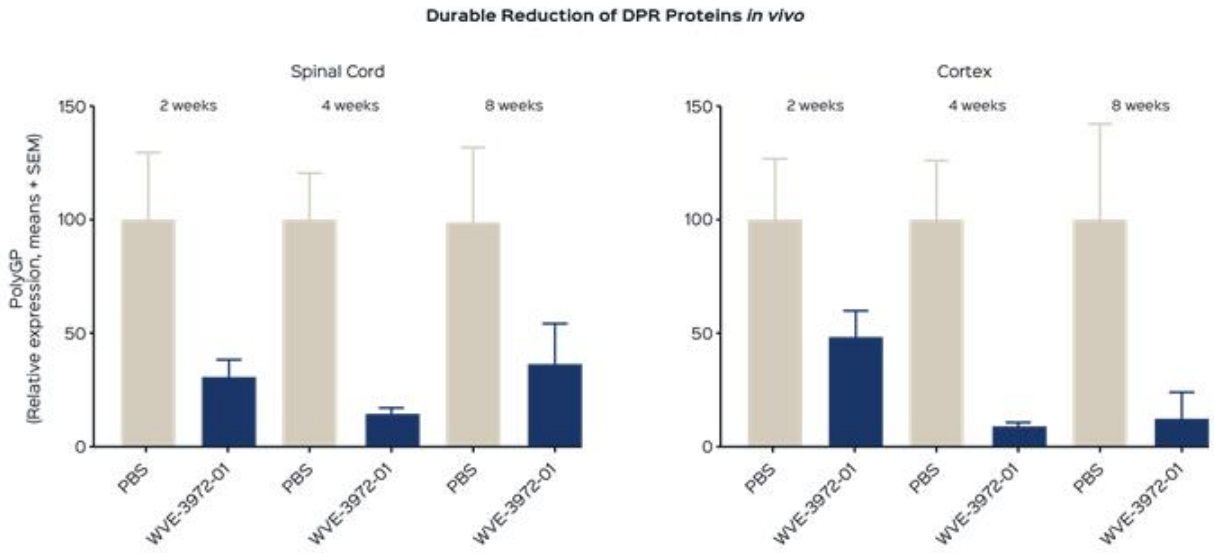
WVE-3972-01 preferentially reduces G_4C_2-repeat containing transcript levels in several *in vitro* models. For example, as shown below, administration of WVE-3972-01 to C9ORF72-ALS patient-derived induced pluripotent stem cell (iPSC) neurons under gymnotic conditions showed preferential knock down of *C9ORF72* repeat-containing transcripts relative to total transcripts. A clear dose-dependent decrease in repeat-containing transcripts was observed, with a calculated IC_{50} of 0.4 µM. In contrast, total transcripts were only slightly reduced and only at the highest doses tested, with a maximal reduction of 42% at 10 µM. Notably, approximately 20% of the reduction in *C9ORF72* total transcripts can be attributed to the reduction in the repeat-containing transcripts.

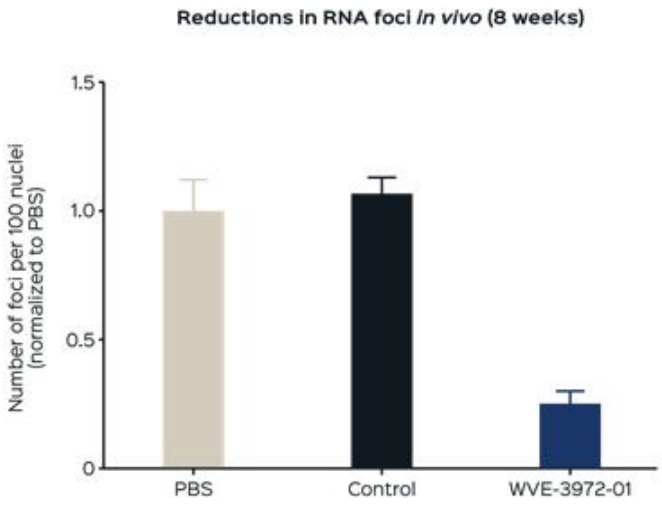


Importantly, WVE-3972-01 led to preferential knockdown of repeat-containing *C9ORF72* transcripts in a mouse model. In the transgenic model, mice express the human *C9ORF72* gene from a bacterial artificial chromosome ("BAC"). In these mice, WVE-3972-01 engaged *C9ORF72* across cell types in regions of the CNS critically implicated in ALS. The figure below shows that our stereopure oligonucleotides (stereopure) led to preferential reduction of repeat-containing *C9ORF72* transcripts (right panel) in the spinal cord compared with all transcripts (left panel) in *C9ORF72* transgenic mice. The stereorandom oligonucleotide (random) was neither selective for the repeat-containing transcripts nor as potent as the stereopure oligonucleotides against repeat-containing transcripts.



In addition, in *in vivo* animal models, WVE-3972-01 produced substantial reductions in DPR proteins and RNA foci, which remained low through eight weeks, the last observed time point (shown in the figures below). DPR proteins were reduced 76% and 87% in the spinal cord and the cortex, respectively. RNA foci were reduced by 70% in the spinal cord. These data have been replicated in blinded preclinical studies in an independent laboratory through our collaboration with Dr. Robert H. Brown, Jr., the Leo P. and Theresa M. LaChance Chair in Medical Research and Chair of the Department of Neurology at the University of Massachusetts Medical School ("UMMS"), Worcester, MA.





Spinocerebellar ataxia 3

Background and Market Opportunity

SCA3 is a rare, hereditary (autosomal dominant) progressive neurodegenerative disorder that results in a lack of muscle control and coordination of the upper and lower extremities. Signs and symptoms of SCA3 may begin between childhood and late adulthood, and they vary greatly. Symptoms may include progressive clumsiness in the arms and legs, spasticity, difficulty with gait, and impaired speaking, swallowing and eye movements. Symptoms of the disease worsen over time, eventually leading to paralysis. Some patients with SCA3 develop dystonia or symptoms similar to those of PD, including twitching of the face or tongue, and nerve damage (neuropathy). Life expectancy ranges from the mid-30s (more severe forms) to a nearly normal life expectancy for those with milder forms of the disease.

SCA3 is caused by a CAG-repeat expansion in the *ATXN3* gene, resulting in an abnormally long polyglutamine stretch in the encoded ataxin-3 protein. Mutant ataxin-3 protein is thought to cause widespread neuronal loss in the brain and spinal cord, likely through a toxic gain-of-function mechanism. SCA3 is the most common dominantly inherited form of ataxia. The prevalence of SCA3 is believed to be one to two cases in 100,000 people with significant geographic and ethnic variations.

Current Treatments

There are currently no disease-modifying therapies approved for treatment of SCA3. Treatment to date has involved the use of medications for symptomatic management.

Our Program

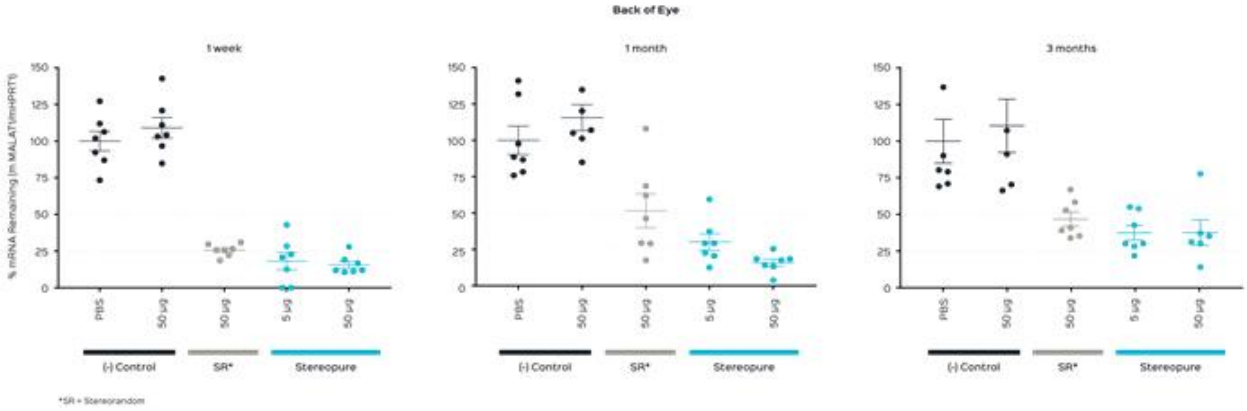
We have initiated research to identify potential candidates targeting *ATXN3* for the treatment of SCA3. Early research suggests there are multiple target sites for oligonucleotides that allow us to knock down the *ATXN3* gene in allele-specific or non-discriminatory ways. Further studies are in progress to assess the efficacy and benefits of each of these approaches. We expect to have a candidate identified by the end of 2018.

Emerging Franchises

We believe that our platform will drive the discovery and advancement of stereopure therapeutic candidates in our initial focus area of neurology and additional therapeutic areas. We continue to explore ways that our multi-modality chemistry may be optimized to address a multitude of rare genetic diseases. Based on our design principles, we have demonstrated our ability to rapidly design and select lead therapeutic candidates with optimized pharmacological properties in preclinical studies. Outside of neurology, we have early-stage discovery programs focused on screening activities and lead optimization for potential drug candidates in ophthalmologic and hepatic diseases. We intend to continue to advance these discovery programs and explore opportunities to expand to other areas independently and through collaborations and partnerships.

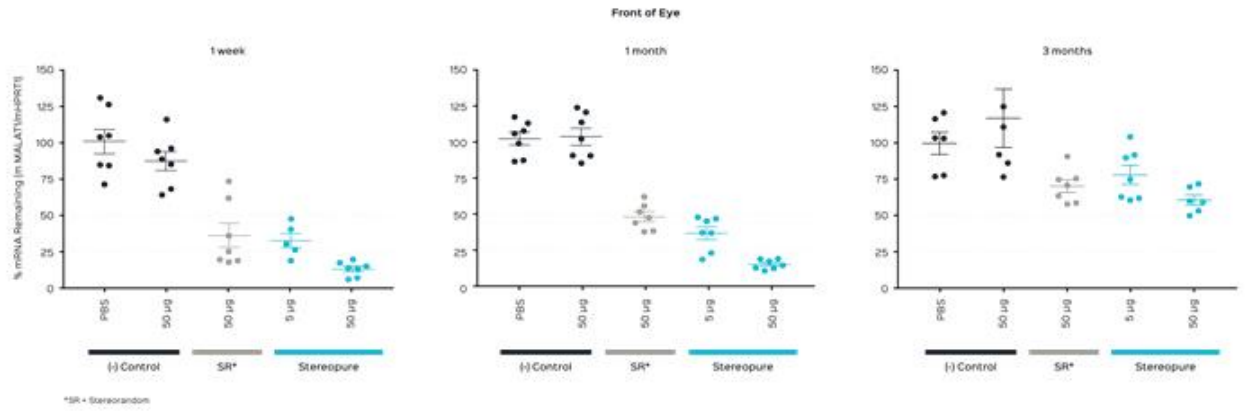
Ophthalmology

We are advancing the development of stereopure compounds to target genetic ophthalmologic diseases, with initial emphasis on retinal diseases. Our discovery research has tested the hypothesis that controlling the chirality of PS linkages in the backbones of oligonucleotides will provide a benefit in potency, distribution and duration of effect in the eye. In these studies, we have employed *MALAT1* as a surrogate target. We generated stereopure compounds targeting the long non-coding *MALAT1* RNA and evaluated them *in vitro* in iCell neurons under gymnotic conditions. We then evaluated lead stereopure oligonucleotides *in vivo* following single intravitreal injection (5 µg and 50 µg) in the mouse eye. We are assessing reduction of *MALAT1* RNA by qPCR, levels and distribution of oligonucleotides by hybridization ELISA and IHC, and duration of effect over a six-month period.

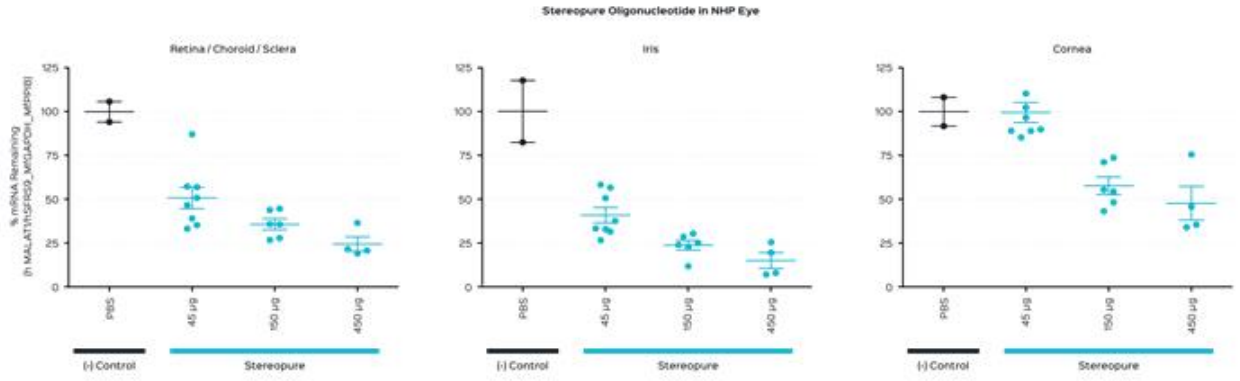


We successfully delivered stereopure *MALAT1* oligonucleotides under gymnotic conditions to iCell neurons with our best-performing compounds exhibiting IC_{50} values approximately 24-fold lower than those of stereorandom oligonucleotides. In the back of the eye (shown in the figure above), the stereorandom oligonucleotide (SR+, 50 µg) produced a 75% knockdown of *MALAT1* mRNA, which was maintained for two weeks. At one month, this fell to a 50% reduction, and at three months, a 53% reduction. At the same dose (Stereopure, 50 µg), the stereopure oligonucleotide achieved an 85% reduction in *MALAT1* mRNA as early as seven days post-single intravitreal injection, which was maintained at one month. At three months post-dose, a 62% reduction persisted. At a 10-fold lower dose (5 µg), the stereopure oligonucleotide still exhibited greater knockdown of *MALAT1* RNA through one month (70 % vs. 50% knockdown) and three months (62% vs. 53%) than the stereorandom oligonucleotide. In summary, a 10-fold enhancement in potency was achieved *in vivo* with a stereopure oligonucleotide compared with a stereorandom oligonucleotide, and this effect was sustained through three months.

Similar results were observed in the front of the eye (figure below).



In a preliminary *in vivo* experiment in NHPs, the stereopure oligonucleotide achieved a clear dose-dependent knockdown of *MALAT1* mRNA in three separate eye tissues (retina/choroid/sclera, iris and cornea) one week following a single intravitreal injection (figure below).



These studies support the hypothesis that stereopure compounds can be designed to increase the potency, distribution and duration of effect in the eye compared with stereorandom oligonucleotides. Additional research is being conducted to develop stereopure oligonucleotides against specific genetic targets to treat diseases of the eye, including retinal diseases.

Hepatic

Our collaboration with Pfizer continues to make progress toward developing genetically targeted therapies for the treatment of metabolic liver diseases, such as nonalcoholic steatohepatitis. The collaboration has accelerated the application of our stereochemistry platform across antisense and RNAi modalities with the incorporation of GalNAc and Pfizer's hepatic-targeting technology to address metabolic diseases of the liver. As part of the collaboration, three targets have been declared, including APOC3. Our stereopure GalNAc-conjugated APOC3 antisense oligonucleotide demonstrated a potency equivalent to state-of-the-art GalNAc-conjugated double-strand RNAi with a median effective dose of 0.3mg/kg *in vivo*. In addition, our stereopure GalNAc-conjugated APOC3 antisense oligonucleotide demonstrated a 7- to 10-fold improvement in potency and an increase in durability *in vivo* compared with stereorandom GalNAc-conjugated APOC3 antisense oligonucleotides. In November 2017, we achieved a milestone under our collaboration with Pfizer by demonstrating significant activity of stereopure GalNAc-conjugated APOC3 antisense oligonucleotides over stereorandom oligonucleotides in *in vivo* studies and meeting other milestone criteria.

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 may enter into new partnership and collaboration agreements as a means of advancing our own nucleic acid therapeutic programs, 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 where our chemistry platform demonstrates a competitive advantage.

Our Partnerships

Takeda

In February 2018, Wave Life Sciences USA, Inc. and Wave Life Sciences UK Limited (collectively as used in this description, "we"), two of our direct, wholly-owned subsidiaries, entered into a Collaboration and License Agreement (the "Takeda Collaboration Agreement") with Takeda. Subject to customary closing conditions, including the expiration or early termination of the applicable waiting period under the HSR Act, the Takeda Collaboration Agreement is expected to become effective during Q1 2018.

Pursuant to the terms of the Takeda Collaboration Agreement, we and Takeda have agreed to collaborate on the research, development and commercialization of oligonucleotide therapeutics for disorders of the CNS. The collaboration provides Takeda with the option to globally co-develop and commercialize programs targeting HD, ALS, FTD and SCA3, (collectively, the "Category 1 Programs"), which we will have the right to co-commercialize in the United States. In addition, Takeda will have the right to exclusively license multiple preclinical programs for CNS disorders, including AD and PD (collectively, the "Category 2 Programs").

With respect to Category 1 Programs, we will be responsible for researching and developing products and companion diagnostics for Category 1 Programs through completion of the first proof of mechanism study for such products. Takeda will have an exclusive option for each target and all associated products and companion diagnostics for such target, which it may exercise at any time through completion of the proof of mechanism study. If Takeda exercises this option, we will receive an opt-in payment and will lead manufacturing and joint clinical co-development activities; Takeda will lead joint co-commercial activities in the United States and all commercial activities outside of the United States. Global costs and potential profits will be shared 50:50 and we will be eligible to receive development and commercial milestone payments. In addition to its 50% profit share, we are eligible to receive option exercise fees and development and commercial milestone payments for each of the Category 1 Programs.

With respect to Category 2 Programs, we have granted Takeda the right to exclusively license multiple preclinical programs during a four-year research term (subject to limited extension for programs that were initiated prior to the expiration of the research term, in accordance with the Takeda Collaboration Agreement). During that term, the parties may collaborate on preclinical programs for up to six targets at any one time. We will be responsible for researching and preclinically developing products and companion diagnostics directed to the agreed upon targets through completion of IND-enabling studies in the first major market country. Thereafter, Takeda will have an exclusive worldwide license to develop and commercialize products and companion diagnostics directed to such targets, subject to our retained rights to lead manufacturing activities for products directed to such targets. Takeda will fund our research and preclinical activities in the amount of $60 million during the research term and will reimburse us for any collaboration-budgeted research and preclinical expenses incurred by us that exceed that amount. We are also eligible to receive tiered high single-digit to mid-teen royalties on Takeda's global commercial sales of products from each Category 2 Program.

In addition to the research support funding of $60 million over four years and the profit and loss sharing and royalty payments described above, Takeda will make an upfront payment of $110 million and an upfront equity investment of $60 million when the Takeda Collaboration Agreement takes effect.

Under the Takeda Collaboration Agreement, each party grants to the other party specific intellectual property licenses to enable the other party to perform its obligations and exercise its rights under the Takeda Collaboration Agreement, including license grants to enable each party to conduct research, development and commercialization activities pursuant to the terms of the Takeda Collaboration Agreement.

The term of the Takeda Collaboration Agreement runs from the date on which the closing has occurred under the share purchase agreement for the Takeda Equity Investment (as described below), which is conditioned upon the expiration or early termination of the applicable waiting period under the HSR Act, and, unless terminated earlier, will continue until the date on which: (i) with respect to each Category 1 Program target for which Takeda does not exercise its option, expiration or termination of the development program with respect to such target; (ii) with respect to each Category 1 Program target for which Takeda exercises its option, the date on which neither party is researching, developing or manufacturing any products or companion diagnostics directed to such target; or (iii) with respect to each Category 2 Program target, the date on which royalties are no longer payable with respect to products directed to such target.

Takeda may terminate the Takeda Collaboration Agreement for convenience on 180 days' notice, in its entirety or on target-by-target basis. Subject to certain exceptions, each party has the right to terminate the Takeda Collaboration Agreement on a target-by-target basis if the other party or, a third party related to such party, challenges the patentability, enforceability or validity of any patents within the licensed technology that cover any product or companion diagnostic that is subject to the Takeda Collaboration Agreement. In the event of any material breach of the Takeda Collaboration Agreement by a party, subject to cure rights, the other party may terminate the Takeda Collaboration Agreement in its entirety if the breach relates to all targets or on a target-by-target basis if the breach relates to a specific target. In the event that Takeda and its affiliates cease development, manufacturing and commercialization activities with respect to compounds or products subject to the Takeda Collaboration Agreement and directed to a particular target, we may terminate the Takeda Collaboration Agreement with respect to such target. Either party may terminate the Takeda Collaboration Agreement for the other party's insolvency. In certain termination circumstances, we would receive a license from Takeda to continue researching, developing and manufacturing certain products, and companion diagnostics.

Simultaneously with our entry into the Takeda Collaboration Agreement, we entered into a share purchase agreement with Takeda pursuant to which we agreed to sell to Takeda 1,096,892 of our ordinary shares at a purchase price of $54.70 per share, for an aggregate purchase price of approximately $60.0 million (the "Takeda Equity Investment"). Subject to customary closing conditions, including the expiration or early termination of the applicable waiting period under the HSR Act, the Takeda Equity Investment is expected to close during Q1 2018. The shares being purchased by Takeda are subject to lock-up and standstill restrictions and carry certain registration rights, customary for transactions of this kind.

Pfizer

In May 2016, we entered into a research, license and option agreement with Pfizer Inc. (the "Pfizer Collaboration Agreement"). Pursuant to the terms of the Pfizer 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 "Pfizer 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, we may earn 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 Pfizer Collaboration.

Under the Pfizer 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 Pfizer Collaboration, we receive a non-exclusive, royalty-bearing sublicensable 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, 2017 with the Securities and Exchange Commission ("SEC"), Pfizer had declared three hepatic targets, including APOC3 and two undisclosed programs and has until May 2018 to declare up to two additional hepatic targets. Also in connection with the Pfizer Collaboration, Pfizer agreed that it will be subject to certain standstill restrictions customary for transactions of this kind. The term of the Pfizer 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 Pfizer 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, 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 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 license is one of two maximum allowable co-exclusive licenses for these patents, the other of which is currently held by Ionis.

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 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 mRNA. His team has been investigating the potential of single-stranded antisense oligonucleotides for the modification of mRNA splicing, for example in DMD. In October 2016 we extended our research collaboration for an additional 27 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 and exon 44 beyond our lead DMD programs, which target exon 51 and exon 53. In October 2017, we expanded our research collaboration with Oxford beyond DMD to include spinal muscular atrophy, with a term of 18 months.

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 have received a five-year grant to support a collaborative research project entitled 'Delivering gene silencing therapy to the epidermic and ocular surface,' effective March 1, 2017.

University of Massachusetts Medical School

Since January 2017, we have been conducting research in collaboration with 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 focused on characterizing our proprietary isomers in order to improve the pharmacology of oligonucleotides for the treatment of ALS and FTD, and investigating the mechanisms of action of specific and efficient knockdown of the targeted mutant *C9ORF7*2 mRNA.

ReadCoor

Since April 2017, we have been collaborating with ReadCoor, Inc. ("ReadCoor") to develop a registry of brain cell network maps and advance our chemistry for targeted drug delivery to the brain. ReadCoor is a company focused on leading the next generation of 'omics by delivering the first panomic spatial sequencing platform to researchers, clinicians and pharmaceutical and diagnostics companies. The collaboration leverages ReadCoor's proprietary FISSEQ (Florescent In-Situ Sequencing) platform designed to provide critical spatial data by combining next generation sequencing and three-dimensional imaging.

Manufacturing

To provide internal cGMP manufacturing capabilities and increase control and visibility of our drug product supply chain, we entered into a lease in September 2016 for a multi-use facility of approximately 90,000 square feet in Lexington, Massachusetts and immediately initiated the build out of manufacturing space and related capabilities. In addition to manufacturing space, the Lexington facility includes additional laboratory and office space to support our growth. This facility supplements our existing Cambridge, Massachusetts laboratory and office space headquarters, enhances our ability to secure drug product for current and future development activities and may provide commercial-scale manufacturing capabilities. In July 2017, we took occupancy of the Lexington facility and began manufacturing production in Q4 2017.

We believe that we have sufficient manufacturing capacity through our third-party contract manufacturers and our internal 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 availability of capacity for the manufacture of drug substance and drug product and believe that our supply agreements with our contract manufacturers and the lead times for new supply agreements would allow us to access additional capacity if needed. We believe that our products can be manufactured at 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 $79.3 million, $40.8 million and $9.1 million during the fiscal years ended December 31, 2017, 2016 and 2015, 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 stereopure 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, 2018, our portfolio includes at least 12 issued U.S. patents, at least 37 issued foreign patents, and pending applications in at least 37 jurisdictions. The information contained in this *"Business – Intellectual Property"* subsection is current as of March 1, 2018.

Synthetic Methodologies

Our patent portfolio includes multiple families that protect synthetic methodologies and/or key reagents for generating stereopure 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 2022-2025.

Additional synthetic methodologies and/or reagents are protected by families that we own. Certain families have 20-year expiration dates that range from 2029 to 2037. Some of these families have issued patents in several jurisdictions, including in major relevant jurisdictions such as the United States, Europe, and/or Japan; all have pending applications either at the international stage or in multiple jurisdictions.

We also co-own with the University of Tokyo certain filings that are directed to certain methods and/or reagents for synthesizing oligonucleotides; their 20-year expiration dates fall in 2031.

Stereopure Oligonucleotide Compositions

Certain of our patent filings protect stereopure 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. Certain patent filings describe specific compositions designed for use in the treatment of particular diseases (e.g., HD, DMD). Several of our patent filings directed to stereopure compositions have entered national stage prosecution in multiple jurisdictions; others are in the international stage. Certain filings offer 20-year protection terms that extend into 2033-2037.

We also co-own with Shin Nippon Biomedical Laboratories, Ltd. various patent families that relate to stereopure oligonucleotide adjuvant compositions and have entered national stage prosecution in multiple jurisdictions; these have 20-year terms extending to 2033-2035.

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, and there may be instances where we undertake such filings in the future, 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 biotechnology and 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 HD. We believe, based on publicly available information, that Roche and Ionis (Phase 2) have an investigational drug in clinical development and several companies have ongoing preclinical programs in HD, including Sangamo Biosciences, ProQR, Nuredis, uniQure, Spark Therapeutics and Voyager Therapeutics.

A number of companies are developing drugs to treat symptoms associated with HD, including Teva Pharmaceutical Industries (Phase 2), Vaccinex (Phase 2), Prana Biotechnology (Phase 2), Omeros Corporation (Phase 2), Stealth BioTherapeutics (Phase 2) and Azevan Pharmaceuticals (Phase 2), among others.

Duchenne Muscular Dystrophy

Sarepta Therapeutics' 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 *DMD* gene amenable to exon 51 skipping. No clinical benefit of eteplirsen 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 eteplirsen improves motor function of DMD patients with a confirmed mutation of the *DMD* 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. Sarepta has submitted a market authorization application in the European Union and anticipates a decision from the EMA's Committee for Medicinal Products for Human Use.

For PTC Therapeutics, conditional market authorization has been granted in Europe for ataluren for the treatment of nonsense mutation DMD for ambulatory patients who are five years of age or older. In October 2017, PTC Therapeutics received a CRL from the FDA declining to approve their NDA for ataluren. PTC Therapeutics filed a formal dispute resolution request with the FDA appealing this decision. In February 2018, the FDA reiterated their prior position and denied PTC Therapeutics' appeal and recommended a possible path forward for ataluren based on the accelerated approval pathway. In addition, BioMarin Pharmaceutical's drisapersen is an exon-skipping nucleic acid therapeutic candidate for DMD for which the FDA issued a CRL in January 2016 indicating that the review cycle was complete and that the NDA was not ready for approval in its present form.

We believe, based on publicly available information, that a number of other companies are developing drugs that may alter the progression of the disease. Those with programs in clinical development include Roche (Phase 3), Catabasis Pharmaceuticals (Phase 3), Intalfarmaco (Phase 3), Pfizer (Phase 2 and Phase 1), Summit Therapeutics (Phase 2), FibroGen (Phase 2), Capricor Therapeutics (Phase 2), Sarepta Therapeutics (Phase 3 and Phase 1) and Solid Biosciences (Phase 1).

Amyotrophic Lateral Sclerosis and Frontotemporal Dementia

There are two treatments approved in the United States for the treatment of ALS, riluzole, approved in 1995, and edaravone, approved in 2017. There are a number of companies with potential therapeutics for the treatment of ALS in clinical development, including AB Sciences (Phase 3), Cytokinetics (Phase 2), Orphazyme (Phase 2), BrainStorm Cell Therapeutics (Phase 2), Genentech (Phase 1) and Biogen and Ionis (Phase 1). Currently, there are no investigational therapies in clinical development specifically targeting *C9ORF72*.

There are no approved treatments available to slow the progression of FTD. Few companies have investigational therapies in clinical development specifically for FTD. Ionis (Phase 1) and AlzProtect (Phase 1) appear to be including FTD in their broader AD or tauopathies clinical development plans.

Government Regulation

FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal 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 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 one or more clinical trial site(s) or the sponsor's site and/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 Prescription Drug User Fee Act ("PDUFA") program 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, first 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 three 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 and the contract research organization facilities with oversight of the trial, 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 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.

Expedited Review and Approval

The FDA has various programs, including Fast Track, priority review, and accelerated approval, which are intended to expedite or simplify the process for reviewing drugs, and/or provide for approval on the basis of surrogate endpoints. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Drugs that may be eligible for these programs are those for serious or life-threatening conditions, generally those with the potential to address unmet medical needs, or that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development, and expedite the review, of drugs to treat serious diseases and fill an unmet medical need. Priority review, which is requested at the time of NDA submission, is designed to give drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists, an initial review within six months from the time of filing as compared to a standard review time of ten months. Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug and expedite review of the application for a drug designated for priority review. Accelerated approval provides an earlier approval of drugs to treat serious diseases, and that fill an unmet medical need based on a surrogate endpoint. As a condition of accelerated approval, the FDA will require that a sponsor of a drug receiving accelerated approval perform post-marketing clinical trials to confirm that the drug confers a clinical benefit for the patient.

Under the Food and Drug Administration Safety and Innovation Act ("FDASIA"), one of the expedited programs added is that for Breakthrough Therapy. A Breakthrough Therapy designation is designed to expedite the development and review of drugs that are intended to treat a serious condition where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s). A drug that receives Breakthrough Therapy designation is eligible for all Fast Track designation features, intensive guidance on an efficient drug development program, beginning as early as Phase 1 and commitment from the FDA involving senior managers.

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 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 NME. 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, 3 years, and 7 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 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.

Pediatric Exclusivity and Pediatric Use

The Best Pharmaceuticals for Children Act ("BPCA") provides NDA holders a six-month period of exclusivity attached to any other exclusivity listed with FDA—patent or non-patent—for a drug if certain conditions are met. Conditions for pediatric exclusivity include a determination by the FDA that information relating to the use of a new drug in the pediatric population may produce health benefits in that population; a written request by the FDA for pediatric studies; and agreement by the applicant to perform the requested studies and the submission to the FDA, completion of the studies in accordance with the written request, and the acceptance by the FDA, of the reports of the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications.

In addition, under the Pediatric Research Equity Act ("PREA"), NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective, unless the sponsor has received a deferral or waiver from the FDA. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

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.

In Vitro Diagnostic Tests for Biomarkers

For some of our product candidates, we plan to work with collaborators to develop or obtain access to *in vitro* companion diagnostic tests to identify appropriate patients for these targeted therapies. If a sponsor or the FDA believes that a diagnostic test is essential for the safe and effective use of a corresponding therapeutic product, a sponsor will typically work with a collaborator to develop an *in vitro* diagnostic ("IVD"). IVDs are regulated by the FDA as medical devices, and it issued final and draft guidance documents that are intended to assist companies developing *in vitro* companion diagnostic devices and companies developing therapeutic products that depend on the use of a specific *in vitro* companion diagnostic for the safe and effective use of the product.

The two primary types of marketing pathways for medical devices are clearance of a premarket notification under Section 510(k) of the Federal Food, Drug, and Cosmetic Act, or 510(k), and approval of a premarket approval application, or PMA. If a company is required to perform clinical trials for the IVD diagnostic, and the IVD is viewed as a significant risk device, the sponsor will have to submit an investigational device exemption application, or IDE. If the diagnostic test and the therapeutic drug are studied together to support their respective approvals, the clinical trial must meet both the IDE and IND requirements.

The FDA expects that the therapeutic sponsor will address the need for an IVD companion diagnostic device in its therapeutic product development plan and that, in most cases, the therapeutic product and its corresponding IVD companion diagnostic device will be developed contemporaneously. If the companion diagnostic test will be used to make critical treatment decisions such as patient selection, treatment assignment, or treatment arm, it will likely be considered a significant risk device for which a clinical trial will be required. After approval, the use of an IVD companion diagnostic device with a therapeutic product will be stipulated in the instructions for use in the labeling of both the diagnostic device and the corresponding therapeutic product. In addition, a diagnostic test that was approved through the PMA process or one that was cleared through the 510(k) process and placed on the market will be subject to many of the same regulatory requirements that apply to approved drugs.

Other Healthcare Laws

Although we currently do not have any products on the market, we will 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 after a product is approved and commercialized. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations. 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, the 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. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. Both Congress and President Trump have expressed their intention to repeal or repeal and replace the ACA, and as a result certain sections of the ACA have not been fully implemented or effectively repealed. The uncertainty around the future of the ACA, and in particular the impact to reimbursement levels, may lead to uncertainty or delay in the purchasing decisions of our customers, which may in turn negatively impact our product sales. If there are not adequate reimbursement levels, our business and results of operations could be adversely affected. We continue to evaluate the effect that the 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. The 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, 2017, we employed 168 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

We were incorporated under the name Wave Life Sciences Pte. Ltd. (Registration No.: 201218209G) under the laws of Singapore on July 23, 2012. On November 16, 2015, we closed our initial public offering. In preparation for 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 four 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.); Wave Life Sciences Ireland Limited (“Wave Ireland”), a company organized under the laws of Ireland; and Wave Life Sciences UK Limited (“Wave UK”), a company organized under the laws of the United Kingdom.

Our registered office is located at 7 Straits View #12-00, Marina One East Tower, Singapore 018936, and our telephone number at that address is +65 6236 3388. Our principal office for Wave USA is located at 733 Concord Avenue, Cambridge, MA 02138, and our telephone number at that address is +1-617-949-2900. Our registered office for Wave Japan is 2438 Miyanoura-cho, Kagoshima-shi, Kagoshima pref. 891-1394, Japan. Our registered office for Wave Ireland is One Spencer Dock, North Wall Quay, Dublin 1, Ireland. Our registered office for Wave UK is Hays Galleria, 1 Hays Lane, London, SE1 2RD, United Kingdom.

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 “For 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 (“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 filed with the SEC. 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 “For 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 clinical-stage biotechnology 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 clinical-stage biotechnology company and have incurred significant operating losses since our incorporation in 2012. Our net loss was $102.0 million, $55.4 million, and $19.2 million for the fiscal years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017 and December 31, 2016, we had an accumulated deficit of $192.5 million and $90.5 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 currently have no products on the market and expect that it may be many years, if ever, before we have a product candidate ready for commercialization. In 2017, we initiated clinical trials of our product candidates WVE-120101 and WVE-120102 in patients with Huntington's disease ("HD") and WVE-210201 in patients with Duchenne muscular dystrophy ("DMD").

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, manufacturing, 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 believe that our existing cash and cash equivalents will be sufficient to fund our operations for at least the next twelve months.

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. 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. 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.

Our future capital requirements will depend on many factors, including, but not limited to, the following:

- our monthly spending levels, based on new and ongoing development and corporate activities;
- the scope, progress, results and costs of drug discovery, preclinical and clinical development for our product candidates;
- our ability to establish and maintain collaboration arrangements, and whether our collaboration partners decide to exercise option rights in connection with targets and development programs;
- the achievement of milestones and other development targets that trigger payments under our collaborations with Takeda Pharmaceutical Company Limited ("Takeda") and Pfizer Inc. ("Pfizer"), or any other strategic collaborations into which we may enter;

- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs or expenses and other costs and expenses associated with research and preclinical and clinical activities under our collaboration with Takeda, or any other future collaboration agreements, if any; and
- the costs of securing manufacturing arrangements internally or with third parties for drug supply.

To date, we have primarily financed our operations through sales of our securities and our collaborations with third parties. 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. On April 18, 2017, we closed a follow-on underwritten public offering of 4,166,667 ordinary shares that were registered on the universal shelf registration statement for gross proceeds of $100.0 million. Net proceeds to us from the offering were $93.5 million, after deducting underwriting discounts and commissions and offering expenses. Therefore, we have approximately $400.0 million of our securities registered and available for sale under our existing shelf registration statement.

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, 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 management has broad discretion over the use of proceeds received from sales of our securities and our collaborations with third parties and the proceeds may not be used effectively.

Our management has broad discretion as to the use of proceeds we receive from conducting sales of our securities and our collaborations with third parties and could use the proceeds for purposes other than those contemplated at the time of such transactions. It is also possible that the proceeds we have received, or may receive, from securities sales and collaborations will be invested in a way that does not yield a favorable, or any, return for us.

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 clinical-stage biotechnology company with a 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, manufacturing, preclinical and clinical development, patient advocacy activities, business planning and raising capital. Prior to 2017, all of our product candidates were in the preclinical development stage. In 2017, we initiated clinical trials of our product candidates WVE-120101 and WVE-120102 in patients with HD, and WVE-210201 in patients with DMD. We expect to initiate three additional development programs by the end of 2018, targeting exon 53 in DMD, and targeting *C9ORF72* in amyotrophic lateral sclerosis (“ALS”) and frontotemporal dementia (“FTD”). We have not yet demonstrated our ability to 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 and commercialize a therapeutic 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 biotechnology companies in the early stages of clinical development, 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, including risks and uncertainties associated with any of our current or future collaboration partners. We are transitioning from a company primarily with a research focus to a company capable of supporting multiple clinical trials and commercial preparation activities. We may not be successful in this transition.

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 oligonucleotide development efforts may increase skepticism in the marketplace regarding the potential for oligonucleotides.

Relatively few nucleic acid therapeutic product candidates have been tested in humans, and a number of clinical trials for such therapeutics conducted by other companies have not been successful. Few nucleic acid therapeutics have received regulatory approval. The pharmacological properties ascribed to the investigational compounds we are testing in laboratory studies may not be positively demonstrated in clinical trials in patients, 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. In addition, our approach, which focuses on using nucleic acid therapeutics for drug development, as opposed to multiple or other, more advanced proven technologies, may expose us to additional financial risks and make it more difficult to raise additional capital if we are not successful in developing a nucleic acid therapeutic that receives regulatory approval.

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 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 few 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.

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 early in our clinical development efforts, and we currently have no products on the market. Our product candidates are still in preclinical or early-stage clinical development. In 2017, we initiated clinical trials of our product candidates WVE-120101 and WVE-120102 in patients with HD, and WVE-210201 in patients with DMD. We have invested a significant portion of our efforts and financial resources in the identification and preclinical and clinical development of our 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;
- successfully conducting process development and manufacturing campaigns in accordance with current good manufacturing practice ("cGMP");
- receiving regulatory approvals from applicable regulatory authorities to market our product candidates and, to the extent necessary, our companion diagnostic tests;
- establishing commercial manufacturing capabilities or making arrangements with third party contract manufacturing organizations ("CMOs");
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- the degree to which we are successful in our collaborations with Takeda and Pfizer;
- 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
- continuing to maintain an 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.

The successful initiation 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, possible 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;
- develop companion diagnostic tests for use with certain of our product candidates;
- manufacture and maintain a sufficient amount of clinical material, internally or through third parties;
- 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 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 successfully, 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 clinical requirements and timelines, 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 multi-use facility of approximately 90,000 square feet in Lexington, Massachusetts to provide internal cGMP manufacturing capabilities and increase control and visibility of our drug product supply chain, and we immediately initiated the build out of manufacturing space and related capabilities. This facility supplements our existing Cambridge, Massachusetts laboratory and office space headquarters, enhances our ability to secure drug product for current and future development activities and may provide commercial-scale manufacturing capabilities. In July 2017, we took occupancy of the Lexington facility and began manufacturing production in Q4 2017. However, we have limited manufacturing experience as a company, and we will incur significant costs to develop this expertise internally.

In addition to the oligonucleotides that we manufacture internally, we continue to rely on CMOs to manufacture the oligonucleotides required for our preclinical studies and clinical trials. There are a limited number of manufacturers that supply oligonucleotides. There are risks inherent in pharmaceutical manufacturing that could affect the ability of us or 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 our facility or the CMOs' facilities 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 raw 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. There can be no assurance that we will be able to produce sufficient quantities of our oligonucleotides to meet our clinical trial demands on our projected timelines.

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 complex processes associated with the manufacture of our product candidates expose us to various manufacturing challenges and risks, which may include delays in manufacturing adequate supply of our product candidates, limits on our ability to increase manufacturing capacity, and the potential for product failure and product variation that may interfere with preclinical and clinical trials, along with additional costs. 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 current or 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 trials or at earlier portions of a trial to the product used in later clinical trials 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.

In 2017, we initiated clinical trials of our product candidates WVE-120101 and WVE-120102 in patients with HD, and WVE-210201 in patients with DMD. We expect to initiate three additional development programs by the end of 2018, targeting exon 53 in DMD, and C9orf72 in ALS and FTD. Although we have hired, and are continuing to hire, employees with experience in manufacturing nucleic acid therapeutics, we have limited 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, compliance with cGMP requirements and other quality issues may arise during our internal efforts to scale-up manufacturing, and with our current or any future CMOs. 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 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 and clinical development stages. 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 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 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, including results that may not meet the level of significance or clinical benefit required by the FDA or other regulators, 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;
- delays in developing and receiving regulatory approval for companion diagnostic tests to identify patients for our 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;
- results from future clinical trials may not confirm positive results, if any, from earlier preclinical studies and clinical trials;
- 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 side effects that may or may not be related to the product candidate being tested that are 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, investigators, or collaboration partners 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 we do not successfully conduct clinical development, we will not be able to market and sell products derived from our product candidates and to generate product revenues. Even if we do successfully complete clinical trials, those results are not necessarily predictive of results of additional trials that may be needed before we can submit an application for regulatory approval to the FDA or 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.

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. Although we have assembled a team of employees with experience designing clinical trials and obtaining regulatory approval to market therapeutics in neurology and in rare diseases, we have limited experience

as a company in designing clinical trials for oligonucleotide therapeutics and we may be unable to design and execute appropriate clinical trials 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, which we also refer to as a companion diagnostic test, for the presence or absence of a particular genetic sequence. For example, in HD, we are conducting clinical trials for WVE-120101 and WVE-120102, targeting SNPs associated with the mutant alleles of the *HTT* 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.

If we are unable to successfully develop or obtain regulatory approval for companion diagnostic tests for our product candidates, or experience significant delays in doing so, our clinical trials may be delayed and our business could be materially harmed.

The development programs for some of our product candidates contemplate the development of companion diagnostic tests, which are assays or tests to identify an appropriate patient population. The success of certain of our product candidates will depend on several factors, including the successful development of, and ability to obtain regulatory approval for, companion diagnostic tests that will be used to screen and identify the right patients for our product candidates. We are focused on the development of nucleic acid therapeutics for genetically-defined diseases. The target patient populations for several of our product candidates are relatively small, and it will be difficult to successfully identify the appropriate patients for whom our drugs are being designed without reliable, accessible, relatively inexpensive, easy-to-use companion diagnostic tests.

Companion diagnostic tests are subject to regulation by the FDA and similar regulatory authorities outside the United States as medical devices and require separate regulatory approval prior to commercialization. We are not a medical device company, and we have limited experience developing medical devices. A more detailed description of the FDA approval process for companion diagnostic tests is included under "*Business – In Vitro Diagnostic Tests for Biomarkers*." Given our limited experience in developing and commercializing companion diagnostic tests, we may rely collaborate with third parties to assist us in the design, manufacture, regulatory approval and commercialization of the companion diagnostic tests for some of our product candidates. We and any potential collaborators, may encounter difficulties in developing and obtaining approval for the companion diagnostic tests, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by us or any potential collaborators, to develop or obtain regulatory approval of the companion diagnostic tests could delay or prevent approval of our product candidates. If we, or any third parties that we engage to assist us, are unable to successfully develop and commercialize companion diagnostic tests for our drug candidates, or experience delays in doing so, our clinical trials and our business could be materially harmed.

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 limited experience as a company in conducting and managing the human clinical trials for oligonucleotide therapeutics that are 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 ("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 rights 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 of the United States and vice versa.

We have been granted orphan drug designation in the United States for WVE-120101 and WVE-120102, but there can be no guarantee that we will maintain orphan status for these product candidates or receive orphan drug approval.

In 2016 and 2017, we were granted orphan drug designation under the Orphan Drug Act by the FDA for our product candidates, WVE-120101 and WVE-120102, respectively, for the treatment of HD. Subject to receiving approval from the FDA of an NDA, products granted orphan drug status are 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 candidates that were granted orphan status were to lose their status as an orphan drug or the marketing exclusivity provided to 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 are conducting our clinical trials 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.

We, our CMOs, and the 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 CMOs, or our or their manufacturing processes or facilities, including failure to maintain compliance with cGMP requirements, 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 and our CMOs currently manufacture a limited supply of clinical trial materials. Reliance on CMOs entails risks to which we would not be subject if we manufactured all of our material ourselves, including reliance on the CMO 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;
- the 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
- the 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, service providers or other third parties 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.

We are currently, or may in the future, be subject to federal, state, local, and comparable foreign healthcare laws and regulations relating to areas such 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 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 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 could delay our commercial launch of the product and negatively impact any potential revenues we may be 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 will also 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. At this time, we are unable 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 (such as most 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 indications 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 (the “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. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. Both Congress and President Trump have expressed their intention to repeal or repeal and replace the ACA, and as a result, certain sections of the ACA have not been fully implemented or effectively repealed. The uncertainty around the future of the ACA, and in particular the impact to reimbursement levels, may lead to uncertainty or delay in the purchasing decisions of our customers, which may in turn negatively impact our product sales. We continue to evaluate the effect that the ACA has or any potential changes to the ACA could have on our business. 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 and reimbursement. 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 product 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 the 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, 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 continue to expand these operations. 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, in 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 or maintain 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. In addition, if any of our collaboration partners face product liability claims, our programs could also be affected and our business could be harmed. 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 or maintain 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 depend on collaborations with third parties for the development and commercialization of certain of our product candidates.

We depend on third-party collaborators for the co-development and co-commercialization of certain of our product candidates and we face significant competition to the extent we elect to collaborate with others. Our potential future 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 February 2018, we entered into a collaboration with Takeda to discover, develop and commercialize nucleic acid therapies for disorders of the CNS. The collaboration provides Takeda with the option to globally co-develop and commercialize programs targeting HD, ALS, FTD, and SCA3, which we will have the right to co-commercialize in the United States. In addition, Takeda will have the right to exclusively license multiple preclinical programs for CNS disorders, including Alzheimer's disease ("AD") and Parkinson's disease ("PD"). 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 may 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.

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 or collaboration 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.

Depending on the type of collaborations we enter into, we may 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 and efforts to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates may 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 may not be able to execute our business strategy optimally if we are unable to maintain our existing collaborations or enter into new collaborations with partners that can provide sales, marketing and distribution capabilities and funds for the development and commercialization of our product candidates.

We do not currently have any sales and marketing or distribution capabilities. Accordingly, we have entered into a collaboration with Takeda in CNS, which we believe can assist us in building these capabilities. We may also enter into additional alliances in the future. We have selectively chosen to enter into a collaboration in the field of CNS with Takeda and for certain hepatic targets with Pfizer. We have chosen these two partners because we believe this is the optimal way for us to broaden our platform, leverage our resources, and create significant value for ourselves and our shareholders, as we advance nucleic acid therapeutic candidates for genetically defined diseases.

Depending on the collaborations that we enter into, we may expect our collaborators to provide assistance with development, regulatory affairs, marketing, sales and distribution, among other areas. Our future revenues may depend heavily on the success of the efforts of these third parties. For example, under our collaboration with Takeda, if Takeda exercises its option with respect to any of our programs in HD, ALS, FTD or SCA3, we will rely on Takeda for commercialization of such optioned programs outside of the United States. In addition, Takeda will be solely responsible for the potential commercialization of additional to-be-identified preclinical CNS programs globally based on targets that Takeda identifies.

We may not be successful in our collaborations due to various factors, including our ability to successfully demonstrate proof of mechanism in humans, our ability to demonstrate the safety and efficacy of our specific product candidates, our ability to manufacture or have third parties manufacture our product candidates, the strength of our intellectual property and/or concerns about potential challenges to or limitations of our intellectual property. To the extent we have entered into, or enter into new, collaborations, we may not be able to maintain them if, for example, development or approval of a product candidate is delayed, challenges are raised as to the validity or scope of our intellectual property or sales of an approved drug are lower than we or our collaboration partner expected.

For certain product candidates that we may develop, we have formed collaborations to fund all or part of the costs of drug development and commercialization, such as our collaboration with Takeda. We may not, however, be able to enter into additional collaborations for certain other programs, and the terms of any collaboration agreement we do secure may not be favorable to us. If we are not successful in our efforts to enter into future collaboration arrangements with respect to one or more of our product candidates, we may not have sufficient funds to develop that or any other product candidate internally, or to bring any product candidates to market. If we do not have sufficient funds to develop and bring our product candidates to market, we will not be able to generate sales revenues from these product candidates, and this will substantially harm our business.

We rely, and expect to continue to rely, on third parties to conduct some aspects of our compound formulation, research, preclinical studies and clinical trials, 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, preclinical studies, or clinical trials 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 Dr. Matthew J.A. Wood's laboratory at the University of Oxford, the University of Dundee and Dr. Robert H. 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 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 and clinical trials of our product candidates. 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 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 continuing to build and expand our own internal manufacturing capabilities, we have not yet manufactured our product candidates on a commercial scale, and may not be able to do so for any of our product candidates. We also have limited experience manufacturing any of our products for our preclinical studies and clinical trials. In addition, 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 drug candidates 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. Furthermore, with the increase of companies developing nucleic acid therapeutics, there may be increased competition for the supply of the raw materials that are necessary to make our nucleic acid therapeutics, which could severely impact the manufacturing 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 they must be acceptable to the FDA or approved by foreign regulatory authorities. Suppliers and manufacturers, including us, must meet applicable manufacturing requirements, including compliance with cGMP regulations, 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 fail 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 have limited capabilities and 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;
- delays 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. In addition, while our collaboration with Takeda will provide us with know-how and experience related to commercialization, we have limited experience of our own. 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 rely on or enter into additional 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 may 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 or other key employees could delay our research and development programs and materially harm our business, financial condition, results of operations and prospects. In addition, we expect that we will continue to have an increased need to recruit and hire qualified personnel as we advance our programs and expand operations. Failure to successfully recruit and retain personnel could impact our anticipated development plans and timelines. 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 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 our preclinical studies and clinical trials and advance to further clinical development, 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 as a company in drug development. Prior to 2017, all of our product candidates were in the preclinical development stage. In 2017, we initiated clinical trials of our product candidates WVE-120101 and WVE-120102 in patients with HD and WVE-210201 in patients with DMD. We expect to initiate three additional development programs by the end of 2018, targeting exon 53 in DMD, and *C9ORF72* in ALS and FTD. As we advance product candidates through preclinical studies and 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 addition, we must manage our relationships with collaborators or partners, suppliers and other organizations, including our collaborations with Takeda and Pfizer. 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.

Security breaches, loss of data and other disruptions could compromise sensitive information related to our business, prevent us from accessing critical information or expose us to liability, which could adversely affect our business and our reputation.

In the ordinary course of our business, we, our CROs and other third parties on which we rely collect and store sensitive data, including legally protected patient health information, personally identifiable information about our employees, intellectual property, and proprietary business information. We manage and maintain our applications and data utilizing on-site systems. These applications and data encompass a wide variety of business critical information including research and development information and business and financial information.

The secure processing, storage, maintenance and transmission of this critical information by us, or our CROs and other third parties, is vital to our operations and business strategy. Although we take measures to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure, or that of our CROs or other third parties, may be vulnerable to attacks by hackers, viruses, breaches, interruptions due to employee error, malfeasance or other disruptions, lapses in compliance with privacy and security mandates, or damage from natural disasters, terrorism, war and telecommunication and electrical failures. Any such event could compromise our networks, or that of our CROs or other third parties, and the information stored there could be accessed by unauthorized parties, publicly disclosed, lost or stolen.

We have measures in place that are designed to detect and respond to such security incidents and breaches of privacy and security mandates. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, such as the HIPAA, government enforcement actions and regulatory penalties. Unauthorized access, loss or dissemination could also disrupt our operations, including our ability to conduct research and development activities, process and prepare company financial information, manage various general and administrative aspects of our business and damage our reputation, any of which could adversely affect our business. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, there can be no assurance that we, or our CROs and other third parties, will promptly detect any such disruption or security breach, if at all. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

Foreign currency exchange rates may adversely affect our results.

Due to our operations outside of the Unites States, we are exposed to market risk, related to changes in foreign currency exchange rates. Historically, we have not hedged our foreign currency exposure. Changes in the relative values of currencies occur regularly and, in some instances, could materially adversely affect our business, our financial condition, the results of our operations or our cash flows.

For the years ended December 31, 2017, 2016 and 2015, changes in foreign currency exchange rates did not have a material impact on our historical financial position, our business, our financial condition, the results of our operations or our cash flows. A hypothetical 10% change in foreign currency rates would not have a material impact on our historical financial position or results of operations.

However, there can be no assurance that changes in foreign currency exchange rates will not have a material adverse impact on us in the future.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act (the "Tax Act"), that significantly reforms the Internal Revenue Code of 1986, as amended (the "Code"). The Tax Act, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and puts into effect the migration from a "worldwide" system of taxation to a territorial system. For the year ended December 31, 2017, we re-evaluated the valuation of our net deferred tax assets and liabilities at the newly enacted U.S. corporate rate and the impact to our tax expense in light of the Tax Act. We will continue to examine the impact this tax reform legislation may have on our business. The impact of this tax reform is uncertain and could adversely affect our business and financial conditions.

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 or obtain patent protection 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 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 allow 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 ("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, uncertain, and sometimes unpredictable.

In addition, there are numerous recent changes to the patent laws and proposed changes to the rules of the USPTO that 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 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 license patent rights from third parties that we may use from time to time to protect certain aspects of our technology and programs. We may license additional third-party intellectual property in the future. To the extent that we use, and ultimately rely on, in-licensed technologies in our platform and our programs, our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for those in-licensed technologies. 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 that could allow them to develop, market and sell product candidates in competition with ours.

Our in-license of patent rights 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. (“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. 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.

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 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 ("PCT") application is usually filed within 12 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, different 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 and our product candidates have not yet reached commercialization, 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. We are aware of third party competitors in the oligonucleotide therapeutics space, whose patent filings and/or issued patents may include claims directed to targets and/or products related to some of our programs. It is possible that at the time that we commercialize our products these third-party patent portfolios may include issued patent claims that cover our products or critical features of their production or use. 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.

There are many issued patents and/or pending patent applications that claim aspects of oligonucleotide compositions, 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 the nucleic acid drugs we wish to develop. We are aware of third-party competitors in the oligonucleotide therapeutics space whose patent filings and/or issued patents may include claims directed to targets and/or product candidates related to some of our development programs. It is possible that these third-party

patent portfolios may include issued patent claims that cover our product candidates or critical features of their production or use. 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, or at all, we may not be able to market products or perform research and development or other activities covered by these patents.

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 directors are residents outside the United States. Moreover, a significant portion 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 such persons own or together with parties acting in concert with such person, 30% or more of our voting shares, or if such person holds, either on such person's own or together with parties acting in concert with such person, between 30% and 50% (both inclusive) of our voting shares, and if such person (or parties acting in concert with such person) 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 2017 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 2018 annual general meeting of shareholders, or (ii) the expiration of the period within which our 2018 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 and as are set forth in our constitution. 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, 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, 2018; 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 advisors 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 are, however, 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 challenge the allocation of income and deductions 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, the United Kingdom, and Ireland. As we grow our business, we expect to conduct increased operations through our subsidiaries in various jurisdictions. If two or more affiliated companies are located in different jurisdictions, the tax laws or regulations of each country generally will require transactions between those affiliated companies to be conducted on terms consistent with those between unrelated companies dealing at arms' length, and appropriate documentation generally must be 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 were to successfully challenge our transfer pricing, there could be an increase in our overall tax liability, which could adversely affect our financial condition, results of operations and cash flows. In addition, the tax laws in the jurisdictions in which we operate are subject to differing interpretations. Tax authorities may challenge our tax positions, and if successful, such challenges could increase our overall tax liability. In addition, the tax laws in the jurisdictions in which we operate are subject to change. We cannot predict the timing or content of such potential changes, and such changes could increase our overall 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. Our executive officers, our directors and their respective affiliates, and our other significant shareholders beneficially own a significant portion of our outstanding ordinary shares, and therefore, liquidity in our ordinary shares is limited. Due

to the limited liquidity in our ordinary shares, relatively small orders can have a disproportionate impact on the trading price of our shares. Further, the limited liquidity in our ordinary shares may also impair our ability to raise capital by conducting offerings of 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 experiences extreme price and volume fluctuations. In particular, the market prices of securities of pharmaceutical and biotechnology companies are extremely volatile, and experience fluctuations that are often unrelated or disproportionate to the operating performance of these companies. These broad and sector-specific market fluctuations can result in extreme fluctuations in the price of our ordinary shares, regardless of our operating performance, and can 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 continue to 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 continue 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 until December 31, 2020 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 as of the last business day of our second fiscal quarter, 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 a 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.

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.

Based on information publicly available to us as of December 31, 2017, our executive officers, our directors and their respective affiliates, and our other significant shareholders beneficially own a significant portion 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.

The estimates and judgments we make, or the assumptions on which we rely, in preparing our consolidated financial statements could prove inaccurate.

Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (U.S. GAAP). The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. We cannot assure, however, that our estimates, or the assumptions underlying them, will not change over time or otherwise prove inaccurate. For example, our estimates as they relate to anticipated timelines and milestones for our clinical trials or preclinical development may prove to be inaccurate. If this is the case, we may be required to restate our consolidated financial statements, which could, in turn, subject us to securities class action litigation. Defending against such potential litigation relating to a restatement of our consolidated financial statements would be expensive and would require significant attention and resources of our management. Moreover, our insurance to cover our obligations with respect to the ultimate resolution of any such litigation may be inadequate. As a result of these factors, any such potential litigation could have a material adverse effect on our financial results, harm our business, and cause our share price to decline.

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 stock. 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 use primarily for our current good manufacturing practice ("cGMP") manufacturing, as well as for additional laboratory and office space. In addition, we occupy laboratory space in 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

Market Information

Our ordinary shares are traded on the Nasdaq Global Market under the symbol "WVE." The following table sets forth, for the periods indicated, the high and low sales prices for our ordinary shares, as reported by Nasdaq:

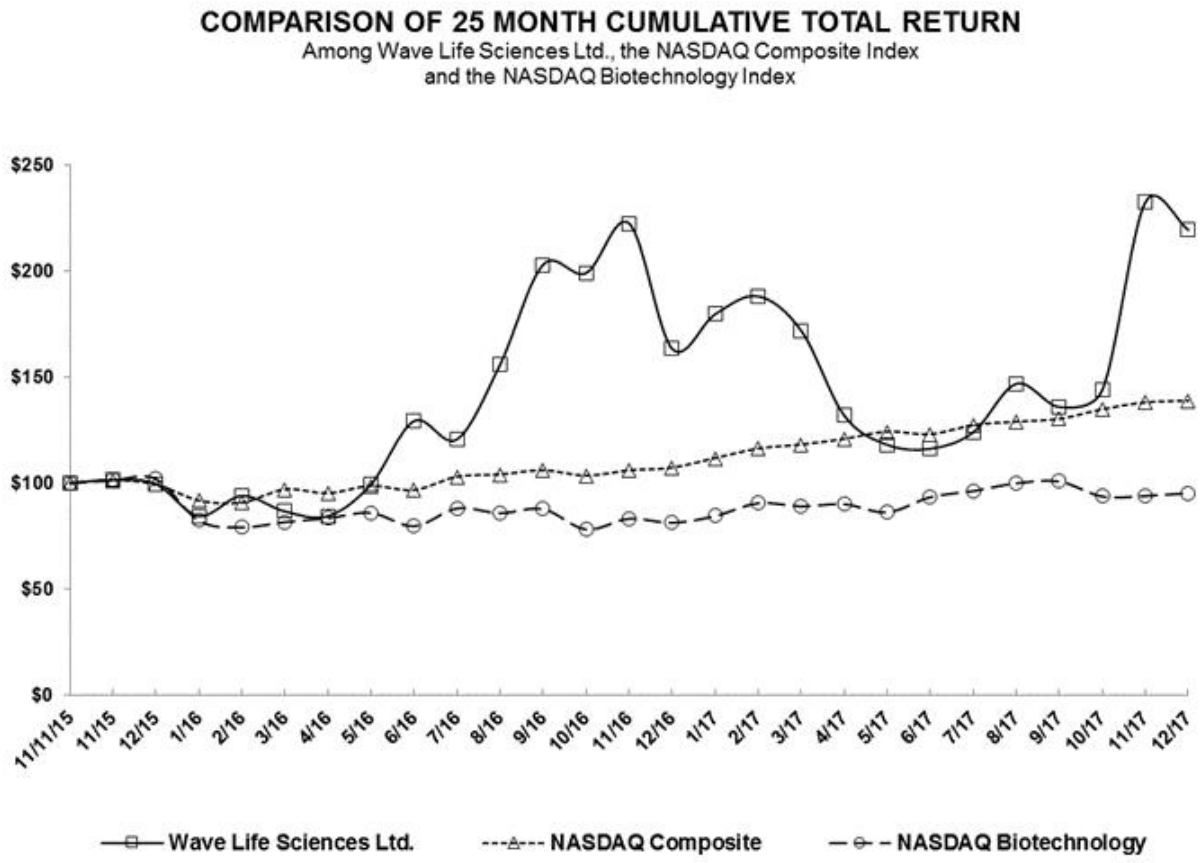
	High	Low
2016		
First Quarter 2016	$ 21.4899	$ 8.95
Second Quarter 2016	$ 23.059	$ 11.99
Third Quarter 2016	$ 37.30	$ 17.41
Fourth Quarter 2016	$ 40.15	$ 25.65
2017		
First Quarter 2017	$ 31.25	$ 24.975
Second Quarter 2017	$ 27.85	$ 18.50
Third Quarter 2017	$ 25.35	$ 15.15
Fourth Quarter 2017	$ 39.70	$ 21.00

Shareholders

As of March 1, 2018, there were approximately 12 shareholders of record of our ordinary shares.

Share Performance Graph

The following share performance graph compares our total share return with the total return for (i) the Nasdaq Composite Index and (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, 2017. 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.

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, 2017, 2016 and 2015 and the balance sheet data as of December 31, 2017 and 2016 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 years ended December 31, 2014 and 2013 and the balance sheet data as of December 31, 2015, 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,				
	2017	2016	2015	2014	2013
	(in thousands except share and per share data)				
Revenue	$ 3,704	$ 1,485	$ 152	$ —	$ —
Operating expenses:					
Research and development	79,309	40,818	9,057	2,395	1,920
General and administrative	26,975	15,994	10,393	2,999	1,654
Total operating expenses	106,284	56,812	19,450	5,394	3,574
Loss from operations	(102,580)	(55,327)	(19,298)	(5,394)	(3,574)
Other income (expense), net:					
Dividend income	1,578	255	—	—	—
Interest income (expense), net	6	337	86	(12)	(111)
Other income (expense), net	(331)	(50)	56	261	37
Total other income (expense), net	1,253	542	142	249	(74)
Loss before income taxes	(101,327)	(54,785)	(19,156)	(5,145)	(3,648)
Income tax benefit (provision)	(708)	(616)	(44)	(84)	330
Net loss	$ (102,035)	$ (55,401)	$ (19,200)	$ (5,229)	$ (3,318)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (3.85)	$ (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	26,513,382	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,				
	2017	2016	2015	2014	2013
	(in thousands)				
Cash and cash equivalents	$ 142,503	$ 150,293	$ 161,220	$ 1,048	$ 439
Working capital (deficit)	130,867	139,835	157,566	605	(9,270)
Total assets	181,843	164,811	165,424	2,938	2,323
Total liabilities	34,155	22,074	4,059	911	10,085
Series A preferred shares	7,874	7,874	7,874	—	—
Total shareholders' equity (deficit)	139,814	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 biotechnology company with an innovative and proprietary synthetic chemistry drug development platform that we are using to rationally 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. Nucleic acid therapeutics, or 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.

Our goal is to develop and commercialize 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. Our initial focus for our clinical development programs is in neurology, which we broadly define as genetic diseases within the central nervous system ("CNS") and neuromuscular system. We have initiated clinical trials of our two lead programs in Huntington's disease ("HD") and our lead program in Duchenne muscular dystrophy ("DMD") targeting exon 51. In 2018, we expect to initiate three additional development programs, targeting exon 53 in DMD and *C9ORF72* in amyotrophic lateral sclerosis ("ALS") and frontotemporal dementia ("FTD"). In addition to neurology, we continue to advance discovery research in ophthalmologic and hepatic diseases. 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 that we are well positioned to achieve our goals and attain our objective of becoming a fully integrated biotechnology company because our team is comprised of leaders in the field of nucleic acid therapeutics, including world renowned scientists, leading researchers and executives with proven track records in drug discovery, development and commercialization of innovative therapeutics.

Additional details regarding our programs are set forth below.

Neurology: CNS

- In HD, we are advancing two separate programs, WVE-120101 and WVE-120102, each targeting a disease-associated single nucleotide polymorphism ("SNP") within the huntingtin gene ("HTT"): rs362307 ("HTT SNP1") and rs362331 ("HTT SNP2"), respectively. 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 associated with the expression of a disease-causing protein. We have shown that by targeting HTT SNP1 and HTT SNP2 in preclinical models, the production of disease-causing proteins associated with HD can be reduced. In July 2017, we initiated PRECISION-HD1 and PRECISION-HD2, global Phase 1b/2a clinical trials for WVE-120101 and WVE-120102, respectively. We expect top-line data from these trials in H1 2019.
- In ALS and FTD, we are advancing WVE-3972-01, which targets the transcript containing the GGGGCC ("G4C2") expansion in the C9ORF72 gene. The G4C2 expansion in the C9ORF72 gene is the most common cause of familial ALS and FTD and is a strong genetic risk factor for non-inherited (sporadic) forms of ALS and FTD. We expect to initiate clinical trials of WVE-3972-01 in ALS and FTD in Q4 2018.
- In SCA3, we expect to have a candidate targeting ATXN3 identified by the end of 2018.

Neurology: Muscle

- In DMD, we are advancing WVE-210201, which targets exon 51, a region within the precursor messenger RNA ("pre-mRNA") that is transcribed from the *dystrophin* gene (also referred to as the "*DMD*" gene). DMD is a genetic disorder caused by mutations in the *DMD* gene that results in dysfunctional dystrophin protein. In November 2017, we initiated a global Phase 1 clinical trial of WVE-210201 administered intravenously. Safety data from the Phase 1 clinical trial are anticipated in Q3 2018.

- We also are advancing programs targeting additional *DMD* exons. In September 2017, we announced that our next DMD development program will target exon 53, and we expect to initiate clinical trials in Q1 2019. In addition, we are exploring subcutaneous administration for all of our DMD programs.
- We have initiated research to identify potential targets for additional neuromuscular diseases.

Ophthalmology

- In genetic ophthalmologic diseases, we have conducted preclinical research into the development of stereopure compounds and tested the hypothesis that controlling the chirality of PS linkages in the backbones of oligonucleotides will provide benefits in potency, distribution and duration of effect in the eye. In these studies, we have employed *MALAT1* as a surrogate target. We have evaluated lead stereopure oligonucleotides *in vivo* following single intravitreal injection in mouse and non-human primate ("NHP") eyes.

Hepatic

- We are collaborating with Pfizer to advance 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. Under the terms of the agreement, Pfizer may select, and we will advance, up to five targets from discovery through 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 ("APOC3"). In Q3 2016, Pfizer nominated its third target. Per the terms of the agreement amended in November 2017, Pfizer is entitled to nominate up to two additional targets by May 2018.

We have never been profitable, and since our inception, we have incurred significant operating losses. Our net losses were $102.0 million in 2017, $55.4 million in 2016, and $19.2 million in 2015. As of December 31, 2017 and 2016, we had an accumulated deficit of $192.5 million and $90.5 million, respectively. We expect to incur significant expenses and increasing operating losses for the foreseeable future.

Recent Developments

In February 2018, we entered into a global strategic collaboration (the "Takeda Collaboration") that provides Takeda Pharmaceutical Company Limited ("Takeda") with the option to co-develop and co-commercialize our CNS development programs in HD, ALS and FTD, as well as a discovery-stage program targeting ATXN3 for the treatment of spinocerebellar ataxia type 3 ("SCA3"). In addition, Takeda has the right to license multiple preclinical programs for CNS indications including Alzheimer's disease ("AD") and Parkinson's disease ("PD"). Subject to customary closing conditions, including the expiration or early termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 (the "HSR Act"), the Takeda Collaboration is expected to become effective during Q1 2018. A description of the Takeda Collaboration is included under "*Business – Licensing Arrangements and Research Collaborations – Our Partnerships.*"

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 years ended December 31, 2017 and 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, 2017.

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:

- compensation-related expenses, including employee salaries, bonuses, share-based compensation expense and other related benefits expenses for personnel in our research and development organization;
- expenses incurred under agreements with third parties, including contract research organizations (“CROs”) that conduct research, preclinical and clinical activities on our behalf, as well as contract manufacturing organizations (“CMOs”) that manufacture drug product for use in our preclinical and clinical trials;
- expenses incurred related to our internal manufacturing of drug product for use in our preclinical and clinical trials;
- costs of third-party consultants, including fees, share based-compensation and certain 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 expenses.

Our primary research and development focus since inception has been the development of our innovative and proprietary 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 direct expenses related to our CROs, CMOs, consultants, other external vendors and fees paid to global regulatory agencies, in addition to compensation-related expenses, facility-related expenses and other general operating expenses. These expenses are incurred in connection with research and development efforts and our preclinical and clinical studies. We track certain external expenses on a program-by-program basis, however, we do not allocate the cost of sponsored research on a program-by-program basis, because these costs are deployed across multiple product programs under research and development and, as such, are classified as costs of our research. The cost of sponsored research includes compensation-related expenses, laboratory supplies, equipment repairs and maintenance, facility-related expenses and other operating costs. This cost is included in the “Other discovery programs, platform development and identification of potential drug discovery candidates” category.

The table below summarizes our research and development expenses incurred for the years ended December 31, 2017, 2016 and 2015.

	For the Year Ended December 31,		
	2017	2016	2015
	(in thousands)		
HD programs	$ 8,968	$ 6,190	$ 376
DMD programs	13,762	2,087	410
ALS and FTD programs	1,658	39	—
Other discovery programs, platform development and identification of potential drug discovery candidates	54,921	32,502	8,271
Total research and development expenses	$ 79,309	$ 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 continue to manage our existing clinical trials, initiate additional clinical trials for certain product candidates, pursue later stages of clinical development for certain product candidates, further develop our manufacturing capabilities and continue to discover and develop additional product candidates in areas including neurology, ophthalmology and hepatic. 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 current good manufacturing practices ("cGMP") manufacturing, as well as for additional laboratory and office space.

General and Administrative Expenses

General and administrative expenses consist primarily of compensation-related expenses, including salaries, bonuses, share-based compensation and other related benefits costs for personnel in our executive, finance, corporate, legal and administrative functions as well as compensation-related expenses for our board of directors. General and administrative expenses also include legal fees; 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-related expenses, 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.

Other Income (Expense), net

Other income (expense), net consists primarily of dividend and interest income earned on cash and cash equivalents balances for the years ended December 31, 2017 and 2016, respectively. For the year ended December 31, 2015, other income (expense), net was comprised of interest income earned on cash balances and reimbursement of research and development costs under a research and development grant awarded by the Japanese Ministry of Economy, Trade and Industry.

Income Taxes

We are a Singapore multi-national company subject to taxation in the United States and various other jurisdictions.

In 2017, 2016 and 2015, our provision for income taxes was $0.7 million, $0.6 million and less than $0.1 million, respectively, on pre-tax loss of $101.3 million, $54.8 million and $19.2 million, respectively. As of December 31, 2017 and 2016, we had U.S. federal research and development tax credit carryforwards of approximately $2.8 million and $0.2 million, respectively, available to offset future U.S. federal income taxes. As of December 31, 2017 and 2016, we had state research and development tax credit carryforwards of approximately $1.1 million and $0.3 million, respectively, available to offset future state income taxes. The U.S. federal and state research and development tax credits will begin to expire in 2032. As of December 31, 2017, we had a U.S. orphan drug credit carryforward of $0.4 million, which will begin to expire in 2037. As of December 31, 2017 and 2016, we had net operating loss carryforwards in Japan of $4.1 million and $5.3 million, respectively, which may be available to offset future income tax liabilities and which will begin to expire in 2021. As of December 31, 2017 and 2016, we also had net operating loss carryforwards in Singapore of $149.2 million and $84.0 million, respectively, which may be available to offset future income tax liabilities and can be carried forward indefinitely. As of December 31, 2017, we also had net operating loss carryforwards in the UK of $10.5 million, which may be available to offset future income tax liabilities and which can be carried forward indefinitely. As of December 31, 2017, we have recorded a full valuation allowance against our net operating loss carryforwards due to uncertainty regarding future taxable income.

On October 1, 2017, we made changes to our corporate entity operating structure, including transferring our intellectual property from our Japanese subsidiary to our Singapore parent company and from our Singapore parent company to our U.S. and UK subsidiaries, primarily to align our intellectual property holding and management structure with our business functions. The transfer of assets occurred between wholly-owned legal entities within the Wave group that are all based in different tax jurisdictions. As the impact of the transfer was the result of an intra-entity transaction, any resulting gain or loss and immediate tax impact on the transfer is eliminated and not recognized in the consolidated financial statements under U.S. GAAP. The recipient entities will receive a tax benefit associated with the future amortization of the intellectual property received in accordance with the applicable tax laws. As discussed in Note 2 of our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we will adopt ASU 2016-16 in the first quarter of 2018 and we estimate that there will be a cumulative-effect increase of approximately $0.4 million to our accumulated deficit.

The Tax Cuts and Jobs Act (the "Tax Act") was enacted on December 22, 2017 and includes significant changes to the U.S. corporate tax system. Effective January 1, 2018, the Tax Act reduced the U.S. federal corporate tax rate from 35% to 21% and transitioned the U.S. federal tax system from a worldwide tax system to a territorial tax system. On December 22, 2017, the SEC issued Staff Accounting Bulletin 118 ("SAB 118") that provides additional guidance allowing companies to apply a measurement period of up to twelve months to account for the impacts of the Tax Act in our financial statements. As of December 31, 2017, we have accounted for the impacts of the Tax Act to the extent a reasonable estimate could be made. We recognized a $0.8 million provisional charge related to the remeasurement of our deferred tax assets and liabilities, which was included as a component of our provision for income taxes and was fully offset by a corresponding amount in our valuation allowance. We will continue to refine our estimates throughout the measurement period or until the accounting is complete as allowed under SAB 118.

Comparison of the Year Ended December 31, 2017 to the Year Ended December 31, 2016

The following table summarizes our results of operations for 2017 and 2016:

	For the Year Ended December 31,		
	2017	2016	Change
	(in thousands)		
Revenue	$ 3,704	$ 1,485	$ 2,219
Operating expenses:			
Research and development	79,309	40,818	38,491
General and administrative	26,975	15,994	10,981
Total operating expenses	106,284	56,812	49,472
Loss from operations	(102,580)	(55,327)	(47,253)
Total other income (expense), net	1,253	542	711
Loss before income taxes	(101,327)	(54,785)	(46,542)
Income tax provision	(708)	(616)	(92)
Net loss	$ (102,035)	$ (55,401)	$ (46,634)

Revenue

Revenue of $3.7 million and $1.5 million for the years ended December 31, 2017 and 2016, respectively, was earned under the Pfizer Collaboration Agreement. This increase is due to the fact that in 2017 there was a full year of revenue earned for all three of the nominated hepatic targets as well as the achievement of a milestone, whereas in 2016 revenue was earned on the first two hepatic targets from May 5, 2016, the effective date of the Pfizer Collaboration Agreement, through December 31, 2016, and revenue was earned on the third hepatic target from its nomination in August 2016 through December 31, 2016.

Research and Development Expenses

The table below summarizes our research and development expenses incurred for the years ended December 31, 2017 and 2016:

	For the Year Ended December 31,		
	2017	2016	Change
	(in thousands)		
HD programs	$ 8,968	$ 6,190	$ 2,778
DMD programs	13,762	2,087	11,675
ALS and FTD programs	1,658	39	1,619
Other discovery programs, platform development and identification of potential drug discovery candidates	54,921	32,502	22,419
Total research and development expenses	$ 79,309	$ 40,818	$ 38,491

Research and development expenses were $79.3 million for the year ended December 31, 2017, compared to approximately $40.8 million for the year ended December 31, 2016. The increase of $38.5 million was due primarily to the following:

- an increase of $2.8 million in preclinical and clinical external expenses related to our two HD programs;
- an increase of $11.7 million in preclinical and clinical external expenses related to our DMD programs, mainly driven by activities related to WVE-210201;
- an increase of $1.6 million in preclinical external expenses related to our ALS program and our FTD program, each of which targets *C9ORF72*; and
- an increase of $22.4 million in internal and external research and development expenses, including costs related to our sponsored research, our other discovery programs, platform development and identification of potential drug discovery candidates, due to an increase of $14.3 million in internal compensation-related expenses, which is the result of an increase in employee headcount, and an increase of $8.1 million in external research and development supplies and services expenses and facility-related expenses.

General and Administrative Expenses

General and administrative expenses were $27.0 million for the year ended December 31, 2017 compared to $16.0 million for the year ended December 31, 2016. The increase of $11.0 million was primarily due to the $4.9 million increase in compensation-related costs resulting from an increase in employee headcount. Increased facility-related expenses and other general and administrative expenses account for the remaining $6.1 million increase.

Total Other Income (Expense), net

Total other income (expense), net for the years ended December 31, 2017 and 2016 was $1.3 million and $0.5 million, respectively. The increase in total other income (expense), net is primarily due to increased dividend income earned in 2017 on our cash equivalents.

Income Tax Provision

During the year ended December 31, 2017 and 2016, we recorded a tax provision of $0.7 million and $0.6 million, respectively. The 2017 tax provision was due to our establishment of a valuation allowance against our U.S. deferred tax assets, as well as income earned under research and management services arrangements between our U.S. and Singapore entities, which is taxed in the U.S. The 2016 tax provision is a result of income earned under research and management services arrangements between our U.S. and Singapore entities, which is taxed in the U.S. During the years ended December 31, 2017 and 2016, we did not record any income tax benefit for the net operating losses incurred in Japan and Singapore due to uncertainty regarding future taxable income in those jurisdictions. In May 2016, we established a wholly-owned subsidiary in Ireland, however no income tax expense or benefit has been recorded during the years ended December 31, 2017 and 2016. In April 2017, we established a wholly-owned subsidiary in the UK and during the year ended December 31, 2017, we did not record any income tax benefit for the net operating losses incurred in the UK due to uncertainty regarding future taxable income in that jurisdiction.

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,		
	2016	2015	Change
	(in thousands)		
Revenue	$ 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 expenses	56,812	19,450	37,362
Loss from operations	(55,327)	(19,298)	(36,029)
Total other income (expense), net	542	142	400
Loss before income taxes	(54,785)	(19,156)	(35,629)
Income tax 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. 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 which was terminated in May 2015.

Research and Development Expenses

The table below summarizes our research and development expenses incurred by program and on our platform for 2016 and 2015:

	For the Year Ended December 31,		
	2016	2015	Change
	(in thousands)		
HD programs	$ 6,190	$ 376	$ 5,814
DMD programs	2,087	410	1,677
ALS and FTD programs	39	—	39
Other discovery programs, platform development and identification of potential drug discovery candidates	32,502	8,271	24,231
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 in 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.

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 other general and administrative expenses account for the remaining $2.8 million increase.

Total Other Income (Expense), net

Total other income (expense), net for the years ended December 31, 2016 and 2015 was $0.5 million and $0.1 million, respectively. The increase in total 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 years 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 earned under research and management services arrangements between our U.S. and Singapore entities, which is taxed in the U.S. During the years ended December 31, 2016 and 2015, we did not record any income tax benefit for the net operating losses incurred in Japan and Singapore due to uncertainty regarding future taxable income in those jurisdictions. In May 2016, we established a wholly-owned subsidiary in Ireland, however no income tax expense or benefit has been recorded during the year ended December 31, 2016.

Liquidity and Capital Resources

To date, we have primarily funded our operations through private placements of debt and equity securities, public offerings of our ordinary shares and collaborations with third parties. Through December 31, 2017, we have received an aggregate of approximately $323.2 million in net proceeds from these transactions. We received $89.3 million in net proceeds from private placements of our debt and equity securities, $100.4 million in net proceeds ($111.9 million gross proceeds) from our initial public offering, inclusive of the over-allotment exercise, $40.0 million under the Pfizer Agreements, including $10.0 million as an upfront payment under the Pfizer Collaboration Agreement and $30.0 million in the form of an equity investment, and $93.5 million in net proceeds ($100.0 million gross proceeds) from our April 2017 follow-on underwritten public offering.

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

As of December 31, 2017, we had cash and cash equivalents of $142.5 million, restricted cash of $3.6 million and an accumulated deficit of $192.5 million.

We believe that our existing cash and cash equivalents will be sufficient to fund our operations for at least the next twelve months.

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 or private 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. On April 18, 2017, we closed a follow-on underwritten public offering of 4,166,667 ordinary shares for gross proceeds of $100.0 million under this shelf registration. After the closing of our follow-on underwritten public offering, approximately $400.0 million of securities remain available for issuance under our universal shelf registration. This shelf 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 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,		
	2017	2016	2015
	(in thousands)		
Cash used in operating activities	$ (83,671)	$ (31,872)	$ (12,527)
Cash used in investing activities	(18,896)	(8,162)	(2,909)
Cash provided by financing activities	94,374	29,121	175,593
Effect of foreign exchange rates of cash	403	(14)	15
Net increase (decrease) in cash and cash equivalents	$ (7,790)	$ (10,927)	$ 160,172

Operating Activities

During 2017, operating activities used $83.7 million of cash, primarily resulting from our net loss of $102.0 million offset by non-cash charges of $18.7 million. The non-cash charges for 2017 related mainly to share-based compensation expense of $12.1 million, an increase in deferred rent of $3.6 million and $2.2 million of depreciation expense.

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.

Investing Activities

During 2017, investing activities used $18.9 million of cash, consisting primarily of purchases of property and equipment of $18.9 million.

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 manufacturing, laboratory and office 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.

Financing Activities

During 2017, net cash provided by financing activities was $94.4 million, which was primarily due to the $93.5 million in net proceeds from the April 2017 follow-on underwritten public offering of 4,166,667 ordinary shares as well as the $0.9 million in proceeds from the exercise of share options.

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. These payments were partially offset by the $0.3 million in 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.

Effect of Foreign Exchange Rates on Cash

During 2017, the effect of changes in foreign exchange rates on cash was $0.4 million due to changes in the Japanese yen related primarily to the translation of intercompany accounts denominated in Japanese yen in 2017.

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.

Funding Requirements

We expect our expenses will continue to increase in connection with our ongoing research and development activities and the expansion of our internal cGMP manufacturing capabilities. Furthermore, we anticipate that our expenses will continue to increase if and as we:

- continue to conduct our two Phase 1b/2a clinical trials evaluating our product candidates WVE-120101 and WVE-120102 in patients with HD and our Phase 1 clinical trial evaluating our product candidate WVE-210201 in patients with DMD;
- conduct research and preclinical development of discovery targets and advance additional programs into clinical development;
- file clinical trial applications with global regulatory agencies and conduct clinical trials for our programs;
- make strategic investments in expanding our research and development platform capabilities and in optimizing our manufacturing processes and formulations;
- further expand our manufacturing capabilities through our internal facility and our CMOs;
- 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, distribute and sell 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 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 continued preclinical and clinical development within our therapeutic programs and with respect to future potential pipeline candidates;
- the cost of manufacturing clinical supplies of our product candidates;
- the costs, timing and outcome of regulatory review of 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 of 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 and committed funds and possible future milestones and payments from our collaboration with Takeda that we expect will take effect following the satisfaction of customary closing conditions, including the expiration or early termination of the applicable waiting period under the HSR Act. 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. On April 18, 2017, we closed a follow-on underwritten public offering of 4,166,667 ordinary shares for gross proceeds of $100.0 million under this shelf registration. After the closing of our follow-on underwritten public offering, approximately $400.0 million of securities remain available for issuance under the aforementioned universal shelf registration. 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 as of December 31, 2017 and the effect such obligations are expected to have on our liquidity and cash flows in future periods:

	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years	Total
Operating lease commitments	$ 4,666	$ 17,542	$ 6,201	$ 26,163	$ 54,572
Capital lease obligation	16	—	—	—	16
Total	$ 4,682	$ 17,542	$ 6,201	$ 26,163	$ 54,588

We enter into contracts in the normal course of business with CROs and CMOs 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, 2017 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 consolidated 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 of our significant accounting policies included in Note 2 "Significant Accounting Policies" in the notes to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, the estimates and assumptions involved in our revenue recognition policy, particularly the period over which revenue is recognized, involve a greater degree of judgement, and therefore we consider it our critical accounting policy. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions and conditions.

Revenue Recognition

As of December 31, 2017, the Company's only significant source of revenue is derived from the Pfizer Collaboration Agreement (as defined in Note 5 " Pfizer Collaboration and Share Purchase Agreement" in the notes to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, "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, 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 in May 2016. The Pfizer 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. In August 2016, Pfizer nominated the third hepatic target under the Collaboration and pursuant to the terms of the Pfizer Collaboration Agreement, Pfizer had the option to nominate two additional targets by November 5, 2017. On November 5, 2017, the Company amended its Pfizer Collaboration Agreement to extend the target nomination period from November 5, 2017 to May 5, 2018. This amendment provides Pfizer with an additional six months to nominate the two remaining hepatic targets under the Pfizer Collaboration Agreement.

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, 2017.

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 and capital market risk.

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

Due to our operations outside of the Unites States, we are exposed to market risk, related to changes in foreign currency exchange rates. Historically, we have not hedged our foreign currency exposure. Changes in the relative values of currencies occur regularly and, in some instances, could materially adversely affect our business, our financial condition, the results of our operations or our cash flows. For the years ended December 31, 2017, 2016 and 2015, changes in foreign currency exchange rates did not have a material impact on our historical financial position, our business, our financial condition, the results of our operations or our cash flows.

A hypothetical 10% change in foreign currency rates would not have a material impact on our historical financial position or results of operations. However, there can be no assurance that changes in foreign currency exchange rates will not have a material adverse impact on us in the future.

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.

Capital Market Risk

We currently have no product revenues and depend on funds raised through other sources. One possible source of funding is through further equity offerings. Our ability to raise funds in this manner depends upon capital market forces affecting our share price.

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, 2017. 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, 2017, 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.

Changes in Internal Control over Financial Reporting

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, 2017 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, 2017. 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, 2017, 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, 2017.

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 2018 Annual General Meeting of Shareholders, or the Proxy Statement, if the Proxy Statement is filed not later than 120 days after the end of our fiscal year ended December 31, 2017, 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, 2017, 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, 2017, 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, 2017, 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 Accounting 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, 2017, 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
10.9.1†	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
10.9.2	Amendment No. 1 to Research, License and Option Agreement by and between the Registrant and Pfizer Inc., dated as of November 5, 2017	X			
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		Form 10-Q (Exhibit 10.1)	11/09/2017	001-37627
10.20+	Form of Non-qualified Share Option Agreement under the 2014 Equity Incentive Plan, as amended		Form 10-Q (Exhibit 10.2)	11/09/2017	001-37627
10.21+	Form of Incentive Share Option Agreement under the 2014 Equity Incentive Plan, as amended		Form 10-Q (Exhibit 10.3)	11/09/2017	001-37627
10.22+	Form of Restricted Share Unit Agreement under the 2014 Equity Incentive Plan, as amended		Form 10-Q (Exhibit 10.4)	11/09/2017	001-37627

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
10.23+	Form of Non-qualified Share Option Agreement for UK Participants under the 2014 Equity Incentive Plan, as amended		Form 10-Q (Exhibit 10.5)	11/09/2017	001-37627
21.1	List of Subsidiaries of the Registrant	X			
23.1	Consent of Independent Registered Public Accounting Firm	X			
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 that accompanies this Annual Report on Form 10-K 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 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 12, 2018

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 12, 2018
/s/ Keith C. Regnante Keith C. Regnante	Chief Financial Officer (*principal financial officer and principal accounting officer*)	March 12, 2018
/s/ Christian Henry Christian Henry	Chairman of the Board of Directors	March 12, 2018
Gregory L. Verdine, Ph.D.	Director	March 12, 2018
/s/ Peter Kolchinsky, Ph.D. Peter Kolchinsky, Ph.D.	Director	March 12, 2018
/s/ Koji Miura Koji Miura	Director	March 12, 2018
/s/ Adrian Rawcliffe Adrian Rawcliffe	Director	March 12, 2018
/s/ Ken Takanashi Ken Takanashi	Director	March 12, 2018

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and Board of Directors
Wave Life Sciences Ltd.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Wave Life Sciences Ltd. and subsidiaries (the "Company") as of December 31, 2017 and 2016, 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, 2017, and the related notes (collectively, the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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 are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

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

Cambridge, Massachusetts
March 12, 2018

WAVE LIFE SCIENCES LTD.
CONSOLIDATED BALANCE SHEETS

(In thousands, except share amounts)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 142,503	$ 150,293
Prepaid expenses and other current assets	7,985	1,483
Deferred tax assets	—	214
Total current assets	150,488	151,990
Long-term assets:		
Property and equipment, net	27,334	8,607
Deferred tax assets	—	560
Restricted cash	3,610	3,601
Other assets	411	53
Total long-term assets	31,355	12,821
Total assets	$ 181,843	$ 164,811
Liabilities, Series A preferred shares and shareholders' equity		
Current liabilities:		
Accounts payable	$ 7,598	$ 4,943
Accrued expenses and other current liabilities	8,898	4,434
Current portion of capital lease obligation	16	62
Current portion of deferred rent	60	—
Current portion of deferred revenue	2,705	2,705
Current portion of lease incentive obligation	344	11
Total current liabilities	19,621	12,155
Long-term liabilities:		
Capital lease obligation, net of current portion	—	16
Deferred rent, net of current portion	4,214	680
Deferred revenue, net of current portion	5,607	8,311
Lease incentive obligation, net of current portion	3,094	116
Other liabilities	1,619	796
Total long-term liabilities	14,534	9,919
Total liabilities	$ 34,155	$ 22,074
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; 27,829,079 and 23,502,169 shares issued and outstanding at December 31, 2017 and 2016, respectively	310,038	215,602
Additional paid-in capital	22,172	10,029
Accumulated other comprehensive income (loss)	116	(291)
Accumulated deficit	(192,512)	(90,477)
Total shareholders' equity	139,814	134,863
Total liabilities, Series A preferred shares and shareholders' equity	$ 181,843	$ 164,811

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,		
	2017	2016	2015
Revenue	$ 3,704	$ 1,485	$ 152
Operating expenses:			
Research and development	79,309	40,818	9,057
General and administrative	26,975	15,994	10,393
Total operating expenses	106,284	56,812	19,450
Loss from operations	(102,580)	(55,327)	(19,298)
Other income (expense), net:			
Dividend income	1,578	255	—
Interest income (expense), net	6	337	86
Other income (expense), net	(331)	(50)	56
Total other income (expense), net	1,253	542	142
Loss before income taxes	(101,327)	(54,785)	(19,156)
Income tax provision	(708)	(616)	(44)
Net loss	$ (102,035)	$ (55,401)	$ (19,200)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (3.85)	$ (2.43)	$ (1.83)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	26,513,382	22,800,628	10,501,455

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,		
	2017	**2016**	**2015**
Net loss	$ (102,035)	$ (55,401)	$ (19,200)
Other comprehensive loss:			
Foreign currency translation	407	(332)	(15)
Comprehensive loss	$ (101,628)	$ (55,733)	$ (19,215)

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

WAVE LIFE SCIENCES LTD.
CONSOLIDATED STATEMENTS 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 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 December 31, 2016	3,901,348	$ 7,874	—	$ —	—	$ —	23,502,169	$ 215,602	$ 10,029	$ (291)	$ (90,477)	$ 134,863
Issuance of ordinary shares, net of issuance costs of $491	—	—	—	—	—	—	4,166,667	93,509	—	—	—	93,509
Share-based compensation	—	—	—	—	—	—	—	—	12,143	—	—	12,143
Vesting of RSUs	—	—	—	—	—	—	22,750	—	—	—	—	—
Option exercises	—	—	—	—	—	—	137,493	927	—	—	—	927
Other comprehensive loss	—	—	—	—	—	—	—	—	—	407	—	407
Net loss	—	—	—	—	—	—	—	—	—	—	(102,035)	(102,035)
Balance at December 31, 2017	3,901,348	$ 7,874	—	$ —	—	$ —	27,829,079	$ 310,038	$ 22,172	$ 116	$ (192,512)	$ 139,814

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,		
	2017	**2016**	**2015**
Cash flows from operating activities			
Net loss	$ (102,035)	$ (55,401)	$ (19,200)
Adjustments to reconcile net loss to net cash flows used in operating activities:			
Amortization of lease incentive obligation	(208)	—	—
Depreciation and amortization	2,155	784	594
Share-based compensation expense	12,143	6,847	4,024
Deferred rent	3,594	565	88
Loss on disposal of property and equipment	205	—	—
Deferred income taxes	774	(564)	36
Tax benefit related to share-based compensation	—	(310)	—
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(6,502)	(1,337)	130
Other non-current assets	(358)	—	—
Accounts payable	3,892	3,369	1,648
Accrued expenses and other current liabilities	4,550	2,296	267
Deferred revenue	(2,704)	11,015	(152)
Other non-current liabilities	823	864	38
Net cash used in operating activities	(83,671)	(31,872)	(12,527)
Cash flows from investing activities			
Increase in restricted cash	(9)	(2,599)	(1,055)
Proceeds from government grant reimbursements for property and equipment	—	—	3
Proceeds from the sale of property and equipment	—	4	—
Purchases of property and equipment	(18,887)	(5,567)	(1,857)
Net cash used in investing activities	(18,896)	(8,162)	(2,909)
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	93,509	30,000	11,631
Proceeds from issuance of Series B preferred shares, net of offering costs	—	—	62,532
Proceeds from government grant	—	—	112
Payments on capital lease obligation	(62)	(62)	(126)
Proceeds from the exercise of share options	927	258	—
Net cash provided by financing activities	94,374	29,121	175,593
Effect of foreign exchange rates on cash	403	(14)	15
Net increase (decrease) in cash and cash equivalents	(7,790)	(10,927)	160,172
Cash and cash equivalents at beginning of period	150,293	161,220	1,048
Cash and cash equivalents at end of period	$ 142,503	$ 150,293	$ 161,220
Supplemental disclosure of cash flow information:			
Deferred offering costs in accounts payable and accrued expenses at period end	$ —	$ —	$ 1,075
Cash paid for interest	$ 37	$ 29	$ —
Cash paid for taxes, net of refunds	$ (11)	$ 554	$ —
Equipment acquired for capital lease obligation	$ —	$ —	$ 268
Property and equipment purchases in accounts payable and accrued expenses at period end	$ 339	$ 1,653	$ 306
Tenant improvements paid for by the landlord during the period	$ 2,774	$ 128	$ —
Tenant improvements to be reimbursed by the landlord	$ 745	$ —	$ —

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" or the "Company") is a biotechnology company with an innovative and proprietary synthetic chemistry drug development platform that the Company is using to rationally 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. Nucleic acid therapeutics, or oligonucleotides, are comprised of a sequence of nucleotides that are linked together by a backbone of chemical bonds. The Company is 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 13, 2012. On May 31, 2016, Wave Life Sciences Ireland Limited ("Wave Ireland") was formed as a wholly-owned subsidiary of Wave Life Sciences Ltd. On April 3, 2017, Wave Life Sciences UK Limited ("Wave UK") was formed as a wholly-owned subsidiary of Wave Life Sciences Ltd.

The Company's primary activities since inception have been developing an innovative and proprietary 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 into additional therapeutic areas including ophthalmology and hepatic, advancing programs into the clinic, furthering clinical development of such clinical-stage programs, building the Company's intellectual property, recruiting personnel and assuring adequate 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. 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.

The Company has never been profitable, and since its inception has incurred recurring operating losses. The Company expects to incur significant expenses and increasing operating losses for the foreseeable future. To date, the Company has primarily funded its operations through private placements of debt and equity securities, public offerings of its ordinary shares and collaborations with third parties. As of December 31, 2017, the Company has received an aggregate of approximately $323.2 million in net proceeds from these transactions. The Company received $89.3 million in net proceeds from private placements of its debt and equity securities, $100.4 million in net proceeds ($111.9 million gross proceeds) from its initial public offering, inclusive of the over-allotment exercise, $40.0 million under the Pfizer Agreements, including $10.0 million as an upfront payment under the Pfizer Collaboration Agreement and $30.0 million in the form of an equity investment, and $93.5 million in net proceeds ($100.0 million gross proceeds) from its April 2017 follow-on underwritten public offering.

Basis of Presentation

The Company has prepared the accompanying consolidated financial statements in conformity with generally accepted accounting principles in the United States of America ("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 the Company's 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 in November 2015, the assumptions used to determine the fair value of share-based awards, the period over which revenue is recognized under the Pfizer Collaboration Agreement (as defined in Note 5), the evaluation of progress to completion of external research and development costs which can result in prepaid or accrued expenses related to the Company's contract research organizations and contract manufacturing organizations and 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 is the U.S. dollar for all of the Company's entities aside from Wave Japan, which has the Japanese Yen as its functional currency. 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. Prior to 2017, Wave Japan had intercompany loans payable to Wave that were not expected to be settled in the foreseeable future which were therefore translated at the historical rate for the date of each capital transaction. In 2017, Wave Japan repaid the intercompany loans which resulted in a foreign exchange loss which is included in the consolidated statements of operations within other income (expense), net. 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.

Cash and cash equivalents are Level 1 assets which are comprised of funds held in readily available checking and money market accounts. Cash and cash equivalents were recorded at fair value as of December 31, 2017 and 2016, totaling $142.5 million and $150.3 million, respectively. 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 and Lexington, Massachusetts facilities (refer to Note 8). As of December 31, 2017 and 2016, the Company had $3.6 million of restricted cash, of which $2.6 million related to the Lexington facility and the remaining $1.0 million 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, 2017, the Company has not recognized any impairment charges.

Revenue Recognition

As of December 31, 2017, 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, 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 in May 2016. The Pfizer 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. In August 2016, Pfizer nominated the third hepatic target under the Collaboration and pursuant to the terms of the Pfizer Collaboration Agreement, Pfizer had the option to nominate two additional targets by November 5, 2017. On November 5, 2017, the Company amended its Pfizer Collaboration Agreement to extend the target nomination period from November 5, 2017 to May 5, 2018. This amendment provides Pfizer with an additional six months to nominate the two remaining hepatic targets under the Pfizer Collaboration Agreement.

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, 2017.

Product Revenue

The Company has had no product revenue to date.

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 unit 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 accounts for the expense from share-based awards to non-employees by re-measuring the awards at fair value over the vesting 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 the Company's IPO, the fair value of the ordinary shares underlying the Company's share-based awards is 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 the Company's IPO, the fair value of the Company's ordinary shares underlying the Company's share options was historically determined by the board of directors. Because prior to the Company's IPO, there was no public market for the Company's ordinary shares, the board of directors determined the fair value of the Company's 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 the Company's IPO, the fair value of the ordinary shares underlying the Company's share-based awards is 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 its U.S., Japan, UK 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 its service arrangements for changes in its 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.

Recently Issued Accounting Pronouncements

In May 2014, the FASB issued Accounting Standards Update (“ASU”) No. 2014-09, Revenue from Contracts with Customers (Topic 606) (“ASU 2014-09”), which supersedes the revenue recognition requirements in ASC 605-25, *Multiple-Element Arrangements* and most industry-specific guidance. In addition, the FASB recently issued ASUs 2016-10 and 2016-12, which provide clarifying amendments to ASU 2014-09. ASU 2014-09 and its related amendments will be effective for the Company for interim and annual periods beginning after December 15, 2017. The new standard requires that an entity recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. The update also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. Companies have the option of applying this new guidance retrospectively to each prior reporting period presented (the full retrospective method) or retrospectively with the cumulative effect of initially applying this update recognized at the date of initial application (the modified retrospective method). The Company will adopt the new standard effective January 1, 2018 under the full retrospective method.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. ASC 606 also impacts certain other areas, such as the accounting for costs to obtain or fulfill a contract. The standard also requires disclosure of the nature, amount, timing, and uncertainty of revenue and cash flows arising from contracts with customers.

The Company is assessing but has not yet completed its assessment of the impact of the adoption of this standard on its consolidated financial statements. Therefore, the Company does not know and cannot reasonably estimate the impact that adoption of ASC 606 is expected to have on the consolidated financial statements. Currently, the Company anticipates a potential impact on the revenue recognition method used to recognize revenue for the identified performance obligations under the Pfizer Collaboration Agreement as well as the recognition of milestone revenue prior to achievement. The expected impact is further described below. Estimated impacts from the adoption of this standard could differ upon the final adoption and implementation of the standard.

With respect to the Pfizer Collaboration Agreement, the Company currently expects the five performance obligations identified under the provisions of ASC 606 will be consistent with the five units of accounting identified under the provisions of ASC 605. However, as previously described, it currently expects that the timing and pattern of revenue recognition under step (v) above will differ from the pattern of revenue recognition under ASC 605. Under ASC 606, the revenues will be recognized over time. As of December 31, 2017, the Company had recognized $5.2 million of revenue under the Pfizer Collaboration Agreement. Deferred revenue related to the Pfizer Collaboration Agreement amounted to $8.3 million as of December 31, 2017, of which $2.7 million is included in current liabilities. The Company expects a change in the timing and pattern of revenue recognition upon adoption of ASC 606 to impact the Company’s revenue, deferred revenue and net loss.

The Company expects the accounting for contingent milestone payments under its collaboration agreements to change under ASC 606. ASC 606 does not contain guidance specific to milestone payments, thereby requiring contingent milestone payments to be considered in accordance with the overall model of ASC 606. Revenue from contingent milestone payments may be recognized earlier under ASC 606 than under ASC 605, based on an assessment of the probability of achievement of the milestone event and the likelihood of a significant reversal of such milestone revenue at each reporting date. This assessment may result in the recognition of revenue related to a contingent milestone payment before the milestone event has been achieved.

ASC 606 requires more robust disclosures than required by previous guidance, including disclosures related to disaggregation of revenue into appropriate categories, performance obligations, the judgments made in revenue recognition determinations, adjustments to revenue which relate to activities from previous quarters or years, any significant reversals of revenue, and costs to obtain or fulfill contracts.

In connection with the adoption of these standards, the Company is implementing several new internal controls, including controls to monitor the probability of achievement of contingent milestone payments and the timing and pattern of performance of the performance obligation.

In February 2016, the FASB issued Accounting Standards Update No. 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 Accounting Standards Update No. 2016-16, Income Taxes (Topic 740): Intra-Entity Transfers of Assets Other Than Inventory (“ASU 2016-16”), which requires an entity to recognize the income tax consequences of an intra-entity transfer of an asset, other than inventory, when the transfer occurs, even though the pre-tax effects of that transaction are eliminated in consolidation. The amendments are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2017. These amendments should be applied on a modified retrospective basis through a cumulative-effect adjustment directly to retained earnings at the beginning of the period adopted. The Company will adopt ASU 2016-16 in the first quarter of 2018 and the Company estimates that there will be a cumulative-effect increase of approximately $0.4 million to the Company’s accumulated deficit.

In November 2016, the FASB issued Accounting Standards Update No. 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.

Recently Adopted Accounting Pronouncements

In November 2015, the FASB issued Accounting Standards Update No. 2015-17, Balance Sheet Classification of Deferred Taxes (“ASU 2015-17”), which requires entities to present deferred tax assets and liabilities, along with any related valuation allowance, as noncurrent on the balance sheet. The new standard is effective for annual and interim periods beginning after December 15, 2016. During the three months ended March 31, 2017, the Company elected to adopt ASU 2015-17 on a prospective basis. The adoption of this standard resulted in the reclassification of short-term deferred tax assets to long-term deferred tax assets.

3. PROPERTY AND EQUIPMENT, NET

Property and equipment, net, consists of the following

	December 31,	
	2017	2016
	(in thousands)	
Furniture and equipment	$ 13,626	$ 7,231
Software	108	43
Leasehold improvements	16,029	1,964
Fixed assets in progress	1,988	1,863
Total	31,751	11,101
Less accumulated depreciation and amortization	(4,417)	(2,494)
Property and equipment, net	$ 27,334	$ 8,607

Leasehold improvements made during the years ended December 31, 2017 and 2016 consisted of costs related to the Company's leased facilities in Cambridge, Massachusetts and Lexington, Massachusetts.

Depreciation and amortization expense was $2.2 million, $0.8 million and $0.6 million for the years ended December 31, 2017, 2016 and 2015, respectively.

4. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

Accrued expenses and other current liabilities consist of the following:

	December 31,	
	2017	2016
	(in thousands)	
Accrued compensation	$ 5,428	$ 2,480
Accrued professional fees	3,281	417
Accrued vacation	33	589
Other current liabilities	156	948
Total accrued expenses and other current liabilities	$ 8,898	$ 4,434

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 "Pfizer Collaboration"). The Company received $10.0 million as an upfront license fee under the Pfizer Collaboration Agreement. Subject to option exercises by Pfizer, the Company may earn 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 Pfizer 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 Pfizer 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 Pfizer Collaboration in May 2016. In August 2016, Pfizer nominated the third hepatic target under the Pfizer Collaboration for which the Company received a $2.5 million milestone payment in 2016. On November 5, 2017, the Company amended its Pfizer Collaboration Agreement to extend the target nomination period from November 5, 2017 to May 5, 2018. This amendment provides Pfizer with an additional six months to nominate the two remaining hepatic targets under the Pfizer Collaboration Agreement.

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 was allocated to the options to nominate the three remaining targets upon inception. The amount allocated to the three options will be recognized as the research and development services 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. In November 2017, the Company achieved a milestone under the Pfizer Collaboration Agreement, the revenue related to this milestone was recognized in full during the year ended December 31, 2017.

The Pfizer 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 Pfizer Collaboration Agreement by the other party.

During the year ended December 31, 2017, the Company recognized revenue of $3.7 million under the Pfizer Collaboration Agreement. Deferred revenue amounted to $8.3 million as of December 31, 2017, 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, 2017:

- 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 connection with this financing, the Company's 5,334,892 Series B preferred shares automatically converted into 5,334,892 of the Company's ordinary shares.
- 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.

- In April 2017, the Company closed a follow-on underwritten public offering of 4,166,667 ordinary shares for gross proceeds of $100.0 million. The net proceeds from this issuance were $93.5 million after deducting underwriting discounts and commissions and other estimated offering expenses.

Features of the Ordinary Shares

The ordinary shares have no par value and there is no concept of 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.

Dividends

All dividends, if any, 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, 2017:

- 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 $0.002 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 concept of 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 was increased to 5,064,544 in 2015 and to 6,064,544 in 2017. 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 and non-employees of the Company.

As of December 31, 2017, 1,716,110 ordinary shares remained available for future grant under the 2014 Plan.

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)
Outstanding as of January 1, 2017	3,577,766	$ 10.58		
Granted	522,750	26.33		
Exercised	(137,493)	6.74		
Forfeited or cancelled	(195,893)	14.71		
Outstanding as of December 31, 2017	3,767,130	$ 12.69	7.81	$ 84,675
Options exercisable as of December 31, 2017	2,257,455	$ 7.64	7.43	$ 62,060
Options unvested as of December 31, 2017	1,509,675	$ 20.23	8.37	$ 22,614

(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.

Options generally vest over a period of three or four years, and options that are forfeited or cancelled are available to be granted again. The contractual life of options is generally five or ten years from the grant date. Share-based compensation expense related to options is included in research and development expenses or general and administrative expenses on the consolidated statements of operations.

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,		
	2017	2016	2015
Risk-free interest rate	1.49% – 2.23%	1.15% – 2.18%	1.56% - 1.89%
Expected term (in years)	3.00 – 6.25	3.00 – 6.25	5.52 - 6.12
Expected volatility	68.95% – 72.24%	60.89% – 68.76%	62.14% - 71.02%
Expected dividend yield	0%	0%	0%

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%

There were no options granted to non-employees in 2017 or 2016.

RSU activity for the years ended December 31, 2017 and 2016 is summarized as follows:

	RSUs	Average Grant Date Fair Value (in dollars per share)
Outstanding as of January 1, 2017	22,750	21.69
Granted	170,859	29.05
Vested	(22,750)	21.69
Forfeited	(16,400)	29.05
RSUs Outstanding at December 31, 2017	154,459	$ 29.05

There were no RSUs granted in 2015. The RSUs granted in 2016 fully vested upon the first anniversary of the grant date and the RSUs granted in 2017 vest annually over a period four years. RSUs that are forfeited are available to be granted again. Share-based

compensation expense related to the RSUs is included in research and development expenses or general and administrative expenses on the consolidated statements of operations.

As of December 31, 2017, the unrecognized compensation cost related to outstanding options was $16.9 million for employees and $1.0 million for non-employees. The unrecognized compensation cost related to outstanding options for employees and non-employees is expected to be recognized over a weighted-average period of approximately 2.6 years. For the years ended December 31, 2017 and 2016, the weighted-average grant date fair value per granted option was $16.58 and $30.23, respectively. The aggregate fair value of options that vested during the year ended December 31, 2017 was $11.5 million. The unrecognized compensation costs related to outstanding RSUs was $3.5 million as of December 31, 2017, and is expected to be recognized over a weighted-average period of approximately 3.11 years.

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 related to these fully-vested ordinary shares is included in general and administrative expenses on the consolidated statements of operations.

Share-based compensation expense for the years ended December 31, 2017, 2016 and 2015 is classified in the consolidated statements of operations as follows:

	For the Year Ended December 31,		
	2017	2016	2015
	(in thousands)		
Research and development expenses	$ 7,670	$ 4,936	$ 2,268
General and administrative expenses	4,473	1,911	1,756
Total share-based compensation expense	$ 12,143	$ 6,847	$ 4,024

Of the total share-based compensation expense recorded for the years ended December 31, 2017, 2016 and 2015, $2.9 million, $2.7 million and $1.6 million related to options granted to non-employees, respectively, all of which is included in research and development expenses on the consolidated statements of operations.

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 facility in Lexington, Massachusetts, which the Company uses primarily for its cGMP manufacturing, as well as for additional laboratory and office space. 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, 2017.

In connection with the lease agreement, the Company is entitled to receive $11.5 million of tenant improvement allowances. The Company has received $3.6 million as of December 31, 2017, which is amortized over the period from the commencement of tenant improvement construction through to the end of the lease term.

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, 2017 and 2016.

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 guarantee 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, 2017, are as follows:

For the Year Ended December 31,	Amount (in thousands)
2018	4,666
2019	5,675
2020	5,846
2021	6,021
2022	6,201
Thereafter	26,163
	54,572

The Company recorded rent expense of $5.6 million, $1.5 million and $0.5 million for the years ended December 31, 2017, 2016 and 2015, respectively.

Capital Lease

In April 2015, the Company entered into 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 as of December 31, 2017 and 2016.

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 and other 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,		
	2017	2016	2015
	(in thousands except share and per share data)		
Numerator:			
Net loss attributable to ordinary shareholders	$ (102,035)	$ (55,401)	$ (19,200)
Denominator:			
Weighted-average ordinary shares outstanding	26,513,382	22,800,628	10,501,455
Net loss per share, basic and diluted	$ (3.85)	$ (2.43)	$ (1.83)

The Company's potentially dilutive shares, which include outstanding share options to purchase ordinary shares and restricted share units, 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,	
	2017	2016
Options to purchase ordinary shares	3,767,130	3,577,766
Restricted share units	154,459	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,		
	2017	2016	2015
	(in thousands)		
Singapore	$ (76,885)	$ (53,387)	$ (16,534)
Rest of world	(24,442)	(1,398)	(2,622)
Loss before income taxes	$ (101,327)	$ (54,785)	$ (19,156)

During the years ended December 31, 2017, 2016, and 2015, the Company recorded a tax provision of $0.7 million, $0.6 million and less than $0.1 million, respectively. The 2017 tax provision was due to the Company's establishment of a valuation allowance against the Company's U.S. deferred tax assets and U.S. income generated under research and management services arrangements between the Company's U.S. and Singapore entities which is taxed in the U.S. The 2016 and 2015 tax provisions were primarily the result of U.S. income generated under research and management services arrangements between the Company's U.S. and Singapore entities which is taxed in the U.S.

On October 1, 2017, the Company made changes to its corporate entity operating structure, including transferring intellectual property from the Japanese subsidiary to the Singapore parent company, as well as transferring intellectual property from the Singapore parent company to the U.S. and UK subsidiaries, primarily to align the Company's intellectual property holding and management structure with its business functions. The transfer of assets occurred between wholly-owned legal entities within the Wave group that are all based in different tax jurisdictions. As the impact of the transfer was the result of an intra-entity transaction, any resulting gain or loss and immediate tax impact on the transfer is eliminated and not recognized in the consolidated financial statements under U.S. GAAP. The recipient entities will receive a tax benefit associated with the future amortization of the intellectual property received in accordance with the applicable tax laws. As discussed in Note 2, the Company will adopt ASU 2016-16 in the first quarter of 2018 and the Company estimates that there will be a cumulative-effect increase of approximately $0.4 million to the Company's accumulated deficit.

During the years ended December 31, 2017, 2016 and 2015, the Company recorded no income tax benefit for the net operating losses incurred in Singapore and Japan, due to uncertainty regarding future taxable income in those jurisdictions. In May 2016, the Company established a wholly-owned subsidiary in Ireland, however no income tax expense or benefit has been recorded during the years ended December 31, 2017 and 2016. In April 2017, the Company established a wholly-owned subsidiary in the UK, however, during the year ended December 31, 2017 no income tax benefit was recorded related to the net operating losses incurred in the UK due to uncertainty regarding future taxable income in that jurisdiction.

The Tax Cuts and Jobs Act (the "Tax Act") was enacted on December 22, 2017 and includes significant changes to the U.S. corporate tax system. Effective January 1, 2018, the Tax Act reduced the U.S. federal corporate tax rate from 35% to 21% and transitioned the U.S. federal tax system from a worldwide tax system to a territorial tax system. On December 22, 2017, the SEC issued Staff Accounting Bulletin 118 ("SAB 118") that provides additional guidance allowing companies to apply a measurement period of up to twelve months to account for the impacts of the Tax Act in their financial statements. As of December 31, 2017, the Company has accounted for the impacts of the Tax Act to the extent a reasonable estimate could be made. The Company recognized a $0.8 million provisional charge related to the remeasurement of the Company's deferred tax assets and liabilities, which was included as a component of the Company's provision for income taxes and was fully offset by a corresponding amount in the Company's valuation allowance. The Company will continue to refine its estimates throughout the measurement period or until the accounting is complete as allowed under SAB 118.

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

	Year Ended December 31,		
	2017	2016	2015
	(in thousands)		
Current benefit (provision) for income taxes:			
Singapore taxes	$ 199	$ —	$ —
Rest of world taxes	(133)	(1,180)	(8)
Total current benefit (provision) for income taxes	$ 66	$ (1,180)	$ (8)
Deferred benefit (provision) for income taxes:			
Singapore taxes	$ —	$ —	$ —
Rest of world taxes	(774)	564	(36)
Total deferred benefit (provision) for income taxes	$ (774)	$ 564	$ (36)
Total benefit (provision) for income taxes	$ (708)	$ (616)	$ (44)

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

	Year Ended December 31,		
	2017	2016	2015
Singapore statutory income tax rate	17.0%	17.0%	17.0%
Federal and state tax credits	5.7	3.1	2.3
Permanent differences	(2.6)	(0.9)	5.5
Changes in reserves for uncertain tax positions	(3.5)	(3.6)	(1.2)
Foreign rate differential	2.8	(0.1)	1.2
Tax rate change	(0.9)	—	—
Other	0.5	(0.9)	0.2
Change in deferred tax asset valuation allowance	(19.7)	(15.7)	(25.2)
Effective income tax rate	(0.7)%	(1.1)%	(0.2)%

The components of the Company's deferred tax assets as of December 31, 2017 and 2016 are as follows:

	December 31,	
	2017	2016
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 28,913	$ 16,046
Federal and state tax credits	4,522	449
Accrued expenses	1,903	242
Share-based compensation	1,921	1,024
Other	176	102
Total deferred tax assets	37,435	17,863
Valuation allowance	(36,069)	(15,999)
Net deferred tax assets	1,366	1,864
Deferred tax liabilities:		
Depreciation	(1,366)	(1,090)
Total deferred tax liabilities	(1,366)	(1,090)
Net deferred tax assets (liabilities)	$ —	$ 774

A roll-forward of the valuation allowance for the years ended December 31, 2017 and 2016 is as follows:

	Year Ended December 31,	
	2017	2016
	(in thousands)	
Balance at beginning of year	$ 15,999	$ 7,466
Increase in valuation allowance	20,595	8,774
Reversal of valuation allowance	(598)	(282)
Effect of foreign currency translation	73	41
Balance at end of year	$ 36,069	$ 15,999

As of December 31, 2017 and 2016, the Company has U.S. federal research and development tax credit carryforwards of approximately $2.8 million and $0.2 million, respectively, available to offset future U.S. federal income taxes. As of December 31, 2017 and 2016, the Company has state research and development tax credit carryforwards of approximately $1.1 million and $0.3 million, respectively, available to offset future state income taxes. The U.S. federal and state research and development tax credits will begin to expire in 2032. As of December 31, 2017, the Company had a U.S. orphan drug credit carryforward of $0.4 million, which will begin to expire in 2037.

As of December 31, 2017 and 2016, the Company has net operating loss carryforwards in Japan of $4.1 million and $5.3 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2021.

As of December 31, 2017 and 2016, the Company has net operating loss carryforwards in Singapore of $149.2 million and $84.0 million, respectively, which may be available to offset future income tax liabilities and can be carried forward indefinitely.

As of December 31, 2017, the Company has net operating loss carryforwards in the UK of $10.5 million, 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. As of December 31, 2016, 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. Additionally as of December 31, 2016, management has considered the Company's expected utilization of U.S. 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 tax credit carryforward. As of December 31, 2016, there was a $0.8 million deferred tax asset in the U.S. As of December 31, 2017, 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, as well as the corporate entity restructuring, and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets in Singapore, the U.S., Japan and the UK. Accordingly, a full valuation allowance has been established against those deferred tax assets as of December 31, 2017.

The valuation allowance increased by approximately $20.1 million in 2017, $8.5 million in 2016 and $4.8 million in 2015 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 either increasing net income or decreasing net loss.

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:

	2017	2016	2015
		(in thousands)	
Unrecognized tax benefit at the beginning of the year	$ 2,343	$ 1,280	$ 1,025
Tax positions released related to prior years	—	(1,066)	—
Tax positions related to the current year	3,864	2,129	255
Unrecognized tax benefit at the end of the year	$ 6,207	$ 2,343	$ 1,280

As of December 31, 2017, 2016 and 2015, the total amount of gross unrecognized tax benefits, which excludes interest and penalties, was $6.2 million, $2.3 million and $1.3 million, respectively. At December 31, 2017, $4.2 million of the net unrecognized tax benefits would affect the Company's annual effective tax rate if recognized.

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 uncertain tax positions as part of its income tax provision. As of December 31, 2017 and 2016, the Company had incurred less than $0.1 million and zero, respectively, of interest or penalties related to uncertain tax positions.

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 U.S., 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 U.S., 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, 2017 and 2016, $48.8 million and $1.7 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 U.S. 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. Based on the results of the study, 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. Should an ownership change have occurred after December 31, 2015 or occur in the future, the Company’s ability to utilize research and development tax credit carryforwards may be limited.

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 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 made contributions of $0.4 million in the year ended December 31, 2017. The Company did not make contributions to the 401(k) Plan during the years ended December 31, 2016 or 2015.

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 held cash of $0.1 million in depository accounts with Kagoshima Bank, Ltd., an affiliate of one of the Company's shareholders, Kagoshima Shinsangyo Sousei Investment Limited Partnership, as of December 31, 2017 and 2016.
- Pursuant to the terms of various service agreements with SNBL, the Company paid SNBL $0.5 million, $0.4 million and $0.1 million for the years ended December 31, 2017, 2016 and 2015, respectively, for contract research services provided to the Company and its affiliates.
- In 2012, the Company entered into a consulting agreement for scientific services with Dr. Gregory L. Verdine, one of the Company's founders and a member of the Company's board of directors. 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.

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, 2017	December 31, 2016
	(in thousands)	
Japan	$ 14	$ 136
United States	27,320	8,471
Total long-lived assets	$ 27,334	$ 8,607

14. SELECTED QUARTERLY FINANCIAL INFORMATION (UNAUDITED)

Selected quarterly results from operations for the years ended December 31, 2017 and 2016 are as follows:

	2017 Quarter Ended			
	March 31	June 30	September 30	December 31
	(in thousands, except for per share data)			
Revenues	$ 676	$ 676	$ 676	$ 1,676
Operating expenses	20,590	25,770	27,668	32,256
Loss from operations	(19,914)	(25,094)	(26,992)	(30,580)
Net loss	(20,996)	(24,693)	(26,135)	(30,211)
Basic and diluted net loss per ordinary share	$ (0.89)	$ (0.92)	$ (0.94)	$ (1.09)

	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)

15. SUBSEQUENT EVENTS

Takeda Collaboration and License Agreement

In February 2018, two of the Company's subsidiaries entered into a global strategic collaboration (the "Takeda Collaboration") that provides Takeda Pharmaceutical Company Limited ("Takeda") with the option to co-develop and co-commercialize the Company's CNS development programs in Huntington's disease, amyotrophic lateral sclerosis and frontotemporal dementia, as well as a discovery stage program targeting ATXN3 for the treatment of spinocerebellar ataxia type 3. In addition, Takeda has the right to license multiple preclinical programs for CNS indications including Alzheimer's disease and Parkinson's disease. Subject to customary closing conditions, including the expiration or early termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 (the "HSR Act"), the Takeda Collaboration is expected to become effective during the first quarter of 2018.

Simultaneously with the Company's entry into the Takeda Collaboration Agreement, the Company entered into a share purchase agreement with Takeda pursuant to which the Company agreed to sell to Takeda 1,096,892 of its ordinary shares at a purchase price of $54.70 per share, for an aggregate purchase price of approximately $60.0 million (the "Takeda Equity Investment"). Subject to customary closing conditions, including the expiration or early termination of the applicable waiting period under the HSR Act, the Takeda Equity Investment is expected to close during the first quarter of 2018.

Amendment No. 1 to
Research, License and Option Agreement
("Amendment No. 1")

Amendment No. 1	**Date: November 5, 2017**
Name of Original Agreement:	Research, License and Option Agreement (the "Original Agreement," and together with any previous amendments which may be described below, the "Agreement")
Effective Date of Original Agreement:	May 5th, 2016 ("Effective Date")
Parties:	Pfizer Inc. ("Pfizer") and Wave Life Sciences Ltd. ("Wave")
Dates of Previous Amendment(s):	None.

WHEREAS, the parties hereto desire to amend certain terms of the Agreement in order to provide for an extension of the period of time to nominate the Additional Programs,

NOW, THEREFORE, in order to accommodate the desired amendment(s), the parties hereby agree as follows:

1. Defined Terms. Capitalized terms used but not defined herein shall have the respective meanings ascribed to such terms in the Agreement.

2. Amendment(s) to the Agreement.

2.1. Section 4.1.2 of the Agreement is hereby revised and replaced to read, in its entirety, as follows:

"Additional (3) Programs. Pfizer will have the right (but not the obligation) to designate up to three (3) additional therapeutic targets, all three (3) of which will be hepatic targets directed toward hepatic therapeutic conditions (each, an "**Additional Program**"). The total of up to three (3) Additional Programs will be designated by Pfizer by written notice to Wave within **twenty four (24) months** after the Effective Date. The Additional Programs may be against any hepatic target directed toward hepatic therapeutic conditions of Pfizer's choosing, provided that such hepatic target is not a Wave Reserved Target listed in Exhibit D and is not at the time of designation either: (1) the subject of a *bona fide* on-going Wave internal research program; or (2) the subject of a *bona fide* existing collaboration, license, option or asset purchase agreement between Wave and a Third Party. Each such Additional Program may include Pfizer Technology or Wave Hepatic Targeting Technology, at Pfizer's election"

3. Ratification of the Agreement. Except as expressly set forth in Article 2 above, the Agreement shall remain unmodified and in full force and effect. The execution, delivery and effectiveness of this Amendment No. 1 shall not, except as expressly provided herein, operate as a waiver of any right, power or remedy of the parties to the Agreement, nor constitute a waiver of any provision of the Agreement.

4. Counterparts. This Amendment No. 1 may be executed in any number of counterparts, each of which shall be an original instrument and all of which, when taken together, shall constitute one and the same agreement.

IN WITNESS WHEREOF, the duly authorized representatives of Pfizer andWave have executed this Amendment No. 1 as of the date first above written.

Wave Life Sciences Ltd.		**Pfizer Inc.**	
By:	/s/ Paul Bolno	By:	/s/ Morris J. Birnbaum
Print Name:	Paul Bolno	Print Name:	Morris J. Birnbaum
Title:	President and CEO (Duly authorized)	Title:	SVP, CSO, Internal Medicine (Duly authorized)

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
Wave Life Sciences UK Limited	100%	United Kingdom

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 and No. 333-221480) on Form S-8 and (No. 333-215428) on Form S-3, as amended, of Wave Life Sciences Ltd., of our report dated March 12, 2018, with respect to the consolidated balance sheets of Wave Life Sciences Ltd. as of December 31, 2017 and 2016 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, 2017, and the related notes (collectively, the "consolidated financial statements"), which report appears in the December 31, 2017 annual report on Form 10-K of Wave Life Sciences Ltd.

/s/ KPMG LLP

Cambridge, Massachusetts
March 12, 2018

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 12, 2018

/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 12, 2018

/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, 2017, 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 12, 2018

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

March 12, 2018

/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.