WAVE™
LIFE SCIENCES

2024
Annual Report

June 23, 2025

Dear Wave Life Sciences Shareholders,

I am pleased to share our 2024 Annual Report, which highlights the progress we made over last year toward becoming the leading RNA medicines company and unlocking the broad potential of oligonucleotides to transform human health.

2024 was a year of tremendous progress for Wave, as we delivered multiple positive clinical datasets from our ongoing trials in alpha-1 antitrypsin deficiency (AATD), Duchenne muscular dystrophy (DMD), and Huntington's Disease (HD) which demonstrated the breadth and depth of our pipeline, unlocking the full potential of our PRISM® platform. In addition to achieving these meaningful clinical milestones, we continued to advance our earlier stage pipeline, and ended the year with our first Clinical Trial Application (CTA) submission for WVE-007, our GalNAc-INHBE siRNA for obesity. This target exemplifies how we are uniquely utilizing our proprietary toolkit based on a decade of chemistry innovation, and deep genetic insights to advance potential first-in-class therapies for common diseases, as well as rare diseases.

We continue to pioneer the field of RNA editing, led by WVE-006, our GalNAc RNA editing oligonucleotide, which is being investigated in the ongoing RestorAATion-2 trial for AATD. We began our RestorAATion clinical program with the dose escalation of WVE-006 in healthy volunteers in RestorAATion-1 and completed multidosing in the final cohort at dose levels greater than any planned for AATD patients in our RestorAATion-2 study. In 2024, we delivered a breakthrough in genomic medicine with the first-ever demonstration of successful RNA editing in humans with just a single dose of WVE-006 within the first two patients of the first 200 mg cohort. We observed mean 6.9 micromolar of circulating M-AAT and 10.8 micromolar of total AAT. We also observed increases in AAT from baseline as early as Day 3 and as late as Day 57, highlighting WVE-006's impressive durability. WVE-006 was also well-tolerated with a favorable safety profile.

These WVE-006 clinical data not only de-risked our RestorAATion-2 clinical trial, but served to validate the potential of our AIMer editing technology and pipeline of wholly owned programs across a range of potentially high-impact GalNAc hepatic and extra-hepatic targets. In 2024, we shared preclinical data from several of our RNA editing programs which are based on strong human genetics, leverage easily accessible biomarkers, offer efficient path to proof-of-concept in humans, address diseases of high unmet need, represent meaningful commercial opportunities, and build on the clinical experience of WVE-006 for AATD.

In 2024, we also brought a potentially transformative approach for obesity into the clinic with WVE-007, our GalNAc-siRNA candidate designed to silence INHBE mRNA, an obesity target with strong evidence from human genetics. At our annual Research Day, we shared preclinical data which corroborated the strong genetic evidence for the INHBE target and demonstrated WVE-007's potential in multiple obesity treatment settings, including as a single agent, as an add-on to semaglutide, and as an off-ramp and maintenance treatment following semaglutide treatment. We have continued our positive momentum in 2025 with the advancement of our INLIGHT clinical trial of WVE-007 in obesity and continue to make progress with the first two cohorts fully dosed and progressing ahead with great momentum.

In DMD, we delivered positive 48-week data in March 2025 from our Phase 2 open-label FORWARD-53 trial of WVE-N531 in boys with DMD amenable to exon 53 skipping. These results build on the positive data we shared last year from our interim analysis, including industry-leading muscle tissue concentrations supporting monthly dosing intervals, evidence of myogenic stem cell uptake and high and consistent dystrophin levels. At 48 weeks, we observed statistically significant and clinically meaningful improvement of 3.8 seconds in Time-to-Rise vs. natural history, which is the largest effect on Time-to-Rise at 48 weeks relative to any approved dystrophin restoration therapy. We also

observed additional functional benefits in other outcome measures including NSAA, and delivered the first-ever demonstration of substantial improvements in muscle health with exon skipping, as evidenced by less inflammation, necrosis and a statistically significant reduction in fibrosis. WVE-N531 was safe and well-tolerated and no serious adverse events were observed.

In HD, we delivered positive clinical data from our SELECT-HD study of WVE-003 in 2024. Results from the multi-dose portion of this study showed clear translation of target engagement to clinic with statistically significant, potent, durable and allele-selective reductions in CSF mHTT of up to 46% and preservation of healthy protein. Within this cohort, we also observed a statistically significant correlation between mHTT reductions and slowing of caudate atrophy on brain MRI, indicating a potential benefit of allele-selective mHTT reductions, which is particularly encouraging as caudate atrophy is a well-characterized measure of disease progression and neurodegeneration in HD. In 2024, we received supportive initial feedback from FDA, who recognize the severity of HD and are receptive to and engaged with us regarding a potential pathway to accelerated approval.

We carried the strong momentum into 2025 and as we look to the remainder of the year, we are focused on the following priorities:

- **Delivering data from RestorAATion-2 in AATD and advancing our wholly owned RNA editing pipeline**

  There remains a major unmet need in AATD as other investigational treatment approaches are often confined to either lung or liver manifestations, rely on exogenously delivered enzymes, and/or utilize complex delivery systems such as lipid nanoparticles. Weekly intravenous augmentation therapy is the only current treatment option for AATD in those with the lung pathology and there are currently no approved therapies to address the liver pathology. By correcting the single RNA base mutation that causes a majority of AATD cases with the Pi*ZZ genotype (approximately 200,000 in the United States and Europe), WVE-006 may provide an ideal approach for increasing circulating levels of wild-type AAT protein and reducing mutant protein aggregation in the liver, thus simultaneously addressing both the lung and liver manifestations of the disease.

  We are advancing WVE-006 in both the multidose portion of the first cohort of RestorAATion-2 where patients are receiving 200 mg of WVE-006 every other week, and in the second single dose cohort at 400 mg. As we look to the remainder of 2025, we are on track to deliver two comprehensive updates, with data from the complete 200 mg multidose and single dose cohorts expected in the third quarter 2025, and data from the complete 400 mg single dose cohort expected in the fall of 2025. We believe this higher single dose cohort coupled with the multi-dose 200 mg data will give us meaningful insights into extending the dosing interval and inform the therapeutic potential of WVE-006, as well as our pipeline of additional RNA editing programs.

  Behind WVE-006, we are continuing to advance a wholly owned pipeline of RNA editing candidates which utilize our proprietary chemistry in a variety of hepatic and extrahepatic tissues. We plan to share new preclinical data from these programs in 2025 and to initiate clinical development of additional RNA editing programs in 2026.

- **Delivering initial clinical data with WVE-007 from our INLIGHT clinical trial in obesity**

  WVE-007 is our first siRNA candidate in clinical development using our potential best-in-class proprietary oligonucleotide chemistry. WVE-007 is designed to drive healthy weight reduction through a unique mechanism of action that induces lipolysis (fat burning) without impacting muscle mass. By using GalNAc-siRNA silencing, we aim to recapitulate the protective phenotype of INHBE loss-of-function heterozygous carriers, as individuals who have a protective loss-of-function mutation in the INHBE gene have a healthier cardiometabolic profile, including less unhealthy visceral fat, lower triglycerides, and lower risk of type 2 diabetes and cardiovascular disease.

  Despite the rapid ascension of GLP-1s as standard of care, their use is often limited by frequent dosing, loss of muscle mass, poor tolerability, including gastrointestinal side effects, and high discontinuation rates. With WVE-007's orthogonal mechanism from GLP-1s, focusing on

peripheral action directly on fat tissue, rather than centrally-acting appetite regulation, we see an opportunity to use WVE-007 across multiple treatment settings. Our preclinical data support WVE-007's potential to disrupt the obesity treatment paradigm by delivering durable, healthy weight loss, with preservation of muscle mass and once or twice a year dosing.

We continue to advance WVE-007 in our INLIGHT clinical trial and expect to deliver clinical data from INLIGHT in the second half of 2025, including safety, tolerability and biomarkers reflective of healthy weight loss.

- **Advancing our late-stage pipeline in DMD and HD**

  DMD is a devastating disease that impacts individuals early in life. Each year there are approximately 20,000 new cases of DMD with up to 10% amenable to exon 53 skipping. Notably, up to half of exon 53, 51, and 45 patients remain untreated with current exon-skipping therapies, due in part to the burden of weekly dosing and limited evidence of benefit. Despite the limitations of currently marketed therapies, sales of exon-skipping therapies were about $1.1 billion in 2024.

  All participants in FORWARD-53 have elected to advance to the extension portion of the clinical trial, which is currently ongoing with boys receiving monthly doses of WVE-N531. To augment monthly data and ensure a monthly regimen at a potential launch, we are also expanding FORWARD-53 to include additional boys who will be dosed monthly. We plan to file a New Drug Application (NDA) in 2026 to support accelerated approval of WVE-N531 with monthly dosing. We also expect to submit clinical trial applications for other exon skipping programs in 2026.

  There are currently no disease modifying therapies for HD, which affects over 200,000 individuals across pre-symptomatic and symptomatic disease stages in the United States and Europe. Following our positive SELECT-HD data in 2024, we are preparing for a potentially registrational, global Phase 2/3 study of WVE-003 in adults with SNP3 and HD using caudate atrophy as a primary endpoint. We expect to submit an Investigational New Drug (IND) application for WVE-003 in the second half of 2025.

With the delivery of four positive clinical data sets across modalities, we are seeing the continued translation of our potential best-in-class chemistry to the clinic. We are excited to build on our progress as we look forward to multiple key data readouts in the second half of 2025. We remain focused and driven to deliver on our ambitious goal of unlocking the broad potential of RNA medicines to transform human health for the patients, families, and caregivers who drive the work we do each day. They remain our strongest source of inspiration, and we extend our deepest gratitude to them.

On behalf of everyone at Wave, we thank you for your continued support and are grateful to be sharing this journey with you.

Sincerely,

PAUL B. BOLNO, MD, MBA
President and Chief Executive Officer

WAVE™
LIFE SCIENCES

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, 2024

☐ **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	**98-1356880**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
7 Straits View #12-00, Marina One East Tower Singapore	
(Address of principal executive offices)	**018936 (Zip code)**

Registrant's telephone number, including area code: +65 6236 3388

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

Title of each class	Trading symbol	Name of each exchange on which registered
$0 Par Value Ordinary Shares	WVE	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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

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

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

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

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

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

The aggregate market value of 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 28, 2024) was $488,707,919.

The number of outstanding ordinary shares of the registrant as of February 24, 2025 was 153,486,021.

DOCUMENTS INCORPORATED BY REFERENCE

If the Registrant's Definitive Proxy Statement relating to the 2025 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 Registrant 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.

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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 (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), that relate to future events or to our future operations or financial performance. Any forward-looking statement involves known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by such forward-looking statement. 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, although not all forward-looking statements contain these identifying words. Forward-looking statements include statements, other than statements of historical fact, about, among other things: our ability to fund our future operations; our financial position, revenues, costs, expenses, uses of cash and capital requirements; our need for additional financing or the period for which our existing cash resources will be sufficient to meet our operating requirements; the success, progress, number, scope, cost, duration, timing or results of our research and development activities, preclinical studies and clinical trials, including the timing for initiation or completion of or availability of results from any preclinical studies and clinical trials or for submission, review or approval of any regulatory filing; the timing of, and our ability to, obtain and maintain regulatory approvals for any of our product candidates; the potential benefits that may be derived from any of our product candidates; our strategies, prospects, plans, goals, expectations, forecasts or objectives; the success of our collaborations with third parties; any payment that our collaboration partners may make to us; 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; developments and projections relating to our competitors in the industry; our liquidity and working capital requirements; the expected impact of new accounting standards; and our expectations regarding the impact of any local and global health epidemics on our business, including our research and development activities, preclinical studies and clinical trials, supply of drug product, and workforce.

Although we believe that we have a reasonable basis for each forward-looking statement contained in this report, we caution you that these statements are based on our estimates or projections of the future that are subject to known and unknown risks and uncertainties and other important factors that may cause our actual results, level of activity, performance or achievements expressed or implied by any forward-looking statement to differ. These risks, uncertainties and other factors include, among other things, our critical accounting policies; the ability of our preclinical studies to produce data sufficient to support the filing of global clinical trial applications and the timing thereof; our ability to continue to build and maintain the company infrastructure and personnel needed to achieve our goals; the clinical results and timing of our programs, which may not support further development of our product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; our effectiveness in managing current and future clinical trials and regulatory processes; the success of our platform in identifying viable candidates; the continued development and acceptance of nucleic acid therapeutics as a class of drugs; our ability to demonstrate the therapeutic benefits of our stereopure candidates in clinical trials, including our ability to develop candidates across multiple therapeutic modalities; our ability to obtain, maintain and protect intellectual property; our ability to enforce our patents against infringers and defend our patent portfolio against challenges from third parties; our ability to fund our operations and to raise additional capital as needed; competition from others developing therapies for similar uses; and any impacts on our business as a result of or related to any local and global health epidemics, the conflict involving Russia and Ukraine, the conflict in the Middle East, global economic uncertainty, volatility in inflation, volatility in interest rates or market disruptions on our business, as well as other risks and uncertainties under the "Risk Factors" section of this Annual Report on Form 10-K and in other filings we make with the Securities and Exchange Commission ("SEC").

Each forward-looking statement contained in this report is based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain.

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 caution you not to place undue reliance on any forward-looking statement.

In addition, any forward-looking statement in this report represents our views only as of the date of this report and should not be relied upon as representing our views as of any subsequent date. We anticipate that subsequent events and developments may cause our views to change. Although we may elect to update these forward-looking statements publicly at some point in the future, 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 applicable law. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

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.

The Wave Life Sciences Ltd. and Wave Life Sciences Pte. Ltd. names, the Wave Life Sciences mark, PRISM and the other registered and pending trademarks, trade names and service marks of Wave Life Sciences Ltd. appearing in this Annual Report on Form 10-K are the property of Wave Life Sciences Ltd. This Annual Report on Form 10-K also contains additional trade names, trademarks and service marks belonging to Wave Life Sciences Ltd. and to other companies. We do not intend our use or display of other parties' trademarks, trade names or service marks to imply, and such use or display should not be construed to imply, a relationship with, or endorsement or sponsorship of us by, these other parties. Solely for convenience, the trademarks and trade names in this Annual Report on Form 10-K are referred to without the ® and ™ symbols, but such reference should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Summary of Risk Factors

We are providing the following summary of the risk factors contained in this Annual Report on Form 10-K to enhance the readability and accessibility of our risk factor disclosures. We encourage you to carefully review the full risk factors contained in this Annual Report on Form 10-K in their entirety for additional information regarding the material factors that make an investment in our securities speculative or risky. These risks and uncertainties include, but are not limited to, the following:

- 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 will require substantial additional funding, which may not be available on acceptable terms, or at all.
- 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 operating history as a clinical-stage biotechnology company may make it difficult for shareholders to evaluate the success of our business to date and to assess our future viability.
- We, or third parties upon whom we depend, may face risks related to local and global health epidemics, which may delay our ability to complete our ongoing clinical trials, initiate additional clinical trials, delay regulatory activities and have other adverse effects on our business and operations.
- The approach we are taking to discover and develop RNA medicines is novel and may never lead to marketable products.
- We may not be able to conduct clinical trials successfully due to various process-related factors that could negatively impact our business plans.
- 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.
- Results of preclinical studies and early clinical trials may not be predictive of results of subsequent clinical trials.
- 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.
- 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.
- Even if we obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory oversight. If we or our collaborators fail to comply with continuing U.S. and foreign requirements, our approvals, if obtained, could be limited or withdrawn, we could be subject to other penalties, and our business would be seriously harmed.
- The pharmaceutical industry is intensely competitive. If we are unable to compete effectively with existing drugs, new treatment methods and new technologies, we may be unable to successfully commercialize any drugs that we develop.
- Risks associated with our operations outside of the United States and developments in international trade by the U.S. and foreign governments could adversely affect our business.
- 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 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.
- 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.
- 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.
- If we are not able to obtain and enforce market exclusivity for our technologies or product candidates, development and commercialization of our product candidates may be adversely affected.
- 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.
- 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.
- 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, or at all.
- 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.
- We are subject to the laws of Singapore, which differ in certain material respects from the laws of the United States.
- The public market may not be liquid enough for our shareholders to sell their ordinary shares quickly or at market price, or at all.
- The market price of our ordinary shares is likely to be highly volatile, and our shareholders may lose some or all of their investment.

PART I

Item 1. Business

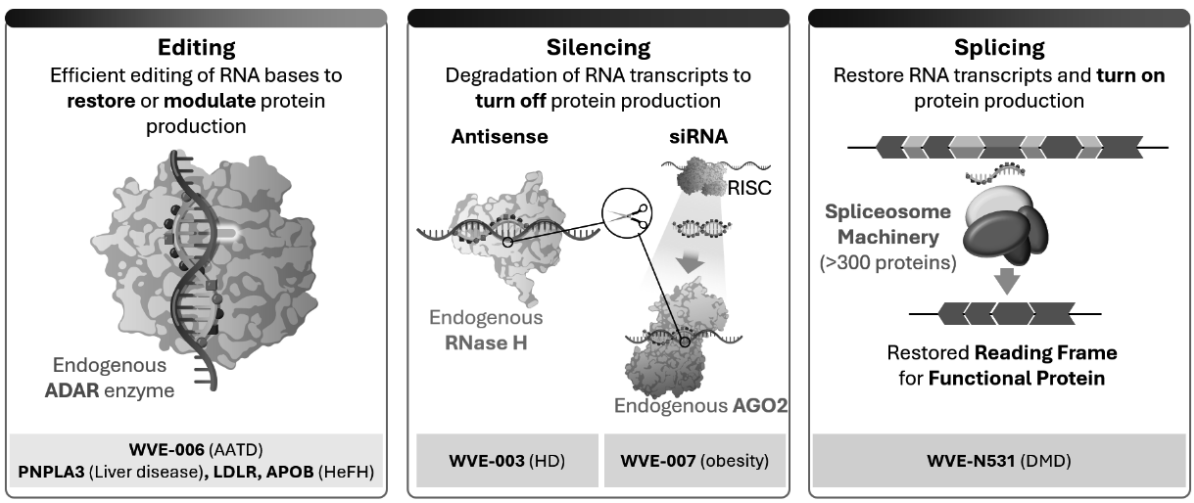
Overview

We are a clinical-stage biotechnology company focused on unlocking the broad potential of ribonucleic acid ("RNA") medicines (also known as oligonucleotides), or those targeting RNA, to transform human health. Our RNA medicines platform, PRISM®, combines multiple modalities, chemistry innovation and deep insights into human genetics to deliver scientific breakthroughs that treat both rare and common disorders. Our toolkit of RNA-targeting modalities includes RNA editing, splicing, silencing using RNA interference ("siRNA") and antisense silencing, providing us with unique capabilities for designing and sustainably delivering candidates that optimally address disease biology. Our diversified pipeline includes clinical programs in obesity, alpha-1 antitrypsin deficiency ("AATD"), Duchenne muscular dystrophy ("DMD"), and Huntington's disease ("HD"), as well as several preclinical programs utilizing our versatile RNA medicines platform.

We were founded on the recognition that there was a significant, untapped opportunity to use chemistry innovation to tune the pharmacological properties of oligonucleotides. We have more than a decade of experience challenging convention related to oligonucleotide design and pioneering novel chemistry modifications to optimize the pharmacological properties of our molecules. We have seen in clinical trials that these chemistry modifications enhance potency, distribution, and durability of effect of our molecules. Our novel chemistry also allows us to avoid using complex delivery vehicles, such as lipid nanoparticles and viruses, and instead use clinically proven conjugates (*e.g., N*-acetylgalactosamine or ("GalNAc")) or free uptake for delivery to a variety of cell and tissue types. We maintain strong and broad intellectual property, including for our novel chemistry modifications.

Our best-in-class chemistry capabilities have also unlocked new areas of biology, such as harnessing adenosine deaminases acting on RNA ("ADAR") enzymes for messenger RNA ("mRNA") correction and upregulation, selectively silencing a mutant allele, and more. By opening up new areas of biology, we have also opened up new opportunities to slow, stop or reverse disease and have expanded the possibilities offered through our platform.

The inspiration for our multimodal platform is based on the recognition that the biological machinery *(i.e.,* enzymes) needed to address human disease already exists within our cells and can be harnessed for therapeutic purposes with the right tools. We believe that we have built the most versatile toolkit of RNA-targeting modalities in the industry, with multiple means of repairing, restoring, or reducing proteins and designing best-fit solutions based on the unique biology of a given disease target. We are actively advancing programs using four distinct modalities, including novel A-to-I RNA editing oligonucleotides ("AIMers").



These modalities include:

- **RNA editing,** which uses AIMers that are designed to target single bases on an RNA transcript and recruit endogenous ADAR enzymes that naturally possess the ability to change an adenine (A) to an inosine (I), which cells read as guanine (G). This approach enables both the correction of G-to-A point mutations and the modulation of RNA to either upregulate protein expression, modify protein-protein interactions, or alter RNA folding and processing. AIMers are short in length, fully chemically modified, and use our novel chemistry, which make them distinct from other ADAR-mediated editing approaches.

- **Antisense (silencing)**, which uses our oligonucleotide designed to bind to a specific sequence in a target RNA strand that encodes a disease-associated protein or pathogenic RNA. The resulting double-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) (silencing)**, which uses our double-stranded RNAs called siRNAs to engage the RNAi machinery known as the RNA-induced silencing complex ("RISC") and 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 / exon skipping**, which is the processing of a nascent pre-mRNA transcript into mRNA by removing introns and joining exons together. Exon skipping uses our oligonucleotide designed to bind to a particular sequence within a target pre-mRNA and direct the cellular machinery to alter the final composition of exons in mature mRNA by deleting, or splicing out, certain specific regions of that RNA.

We intentionally focus on targeting the transcriptome using oligonucleotides rather than other nucleic acid modalities such as gene therapy and DNA editing. This focus enables us to:

- Leverage diversity of expression across cell types by modulating the many regulatory pathways that impact gene expression, including transcription, endogenous RNAi pathways, splicing, and translation;

- Address diseases that have historically been difficult to treat with small molecules or biologics;

- Access a variety of tissue types or cell types throughout the body and modulate the frequency of dosing for broad distribution in tissues over time;

- Avoid the risk of permanent off-target genetic changes and other challenges associated with DNA editing or gene therapy approaches; and

- Leverage well-established industry manufacturing processes and regulatory, access, and reimbursement pathways.

We have a robust and diverse pipeline of potential first-or best-in-class programs addressing both rare and common diseases::

- GalNAc-conjugated oligonucleotides for hepatic and metabolic diseases including:

    - Obesity: WVE-007 is a GalNAc-conjugated siRNA targeting inhibin βE ("INHBE");

    - Alpha-1 antitrypsin deficiency ("AATD"): WVE-006 is a GalNAc-conjugated SERPINA1 AIMer;

    - Liver disease: GalNAc-conjugated AIMer targeting PNPLA3 I148M for correction; and

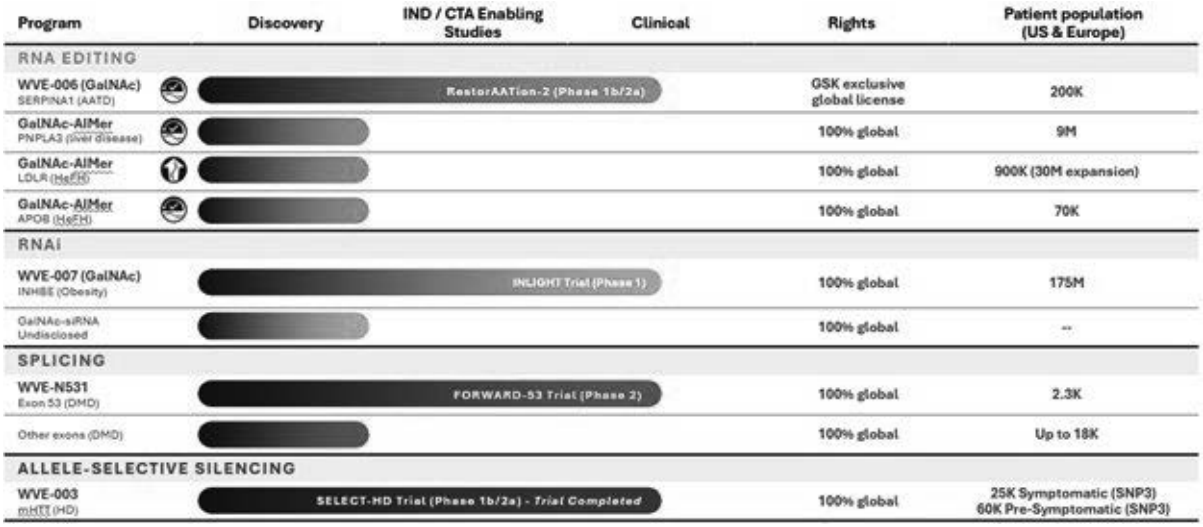
    - Heterozygous Familial Hypercholesterolemia ("HeFH"): GalNAc-conjugated AIMer targeting low-density lipoprotein receptor ("LDLR") for upregulation and GalNAc-conjugated AIMer targeting apolipoprotein B ("APOB") for correction.

- Unconjugated oligonucleotides for muscle, CNS and other disease areas including:

    - Duchenne muscular dystrophy ("DMD"): WVE-N531 is an exon 53 splicing oligonucleotide; and

    - Huntington's disease ("HD"): WVE-003 is an allele-selective oligonucleotide designed to lower mutant huntingtin ("mHTT") protein and preserve healthy, wild-type huntingtin ("wtHTT") protein.

Our Current Programs



Additional details regarding our lead therapeutic programs are set forth below.

Obesity

Background and Market Opportunity

Obesity is increasingly being recognized as a growing global epidemic. In the United States, an estimated 42% of the adult population is living with obesity, and there are an estimated 175 million adults with obesity in the United States and Europe. Adults with obesity have higher risk for many serious health conditions, including heart disease, type 2 diabetes, and some forms of cancer; and obesity is estimated to cost the U.S. healthcare system almost $173 billion annually.

Current Treatments

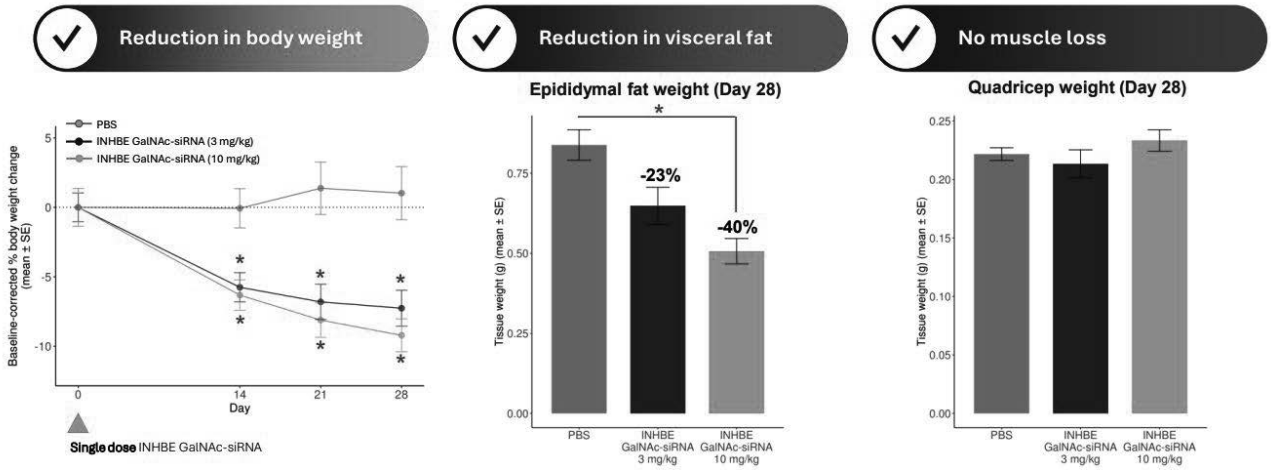
There are two GLP-1 receptor agonists approved in the United States and the European Union ("EU") for the treatment of obesity: Saxenda (liraglutide, Novo Nordisk) and Wegovy (semaglutide, Novo Nordisk). Tirzepatide (Eli Lilly), approved as Zepbound by the U.S. Food and Drug Administration ("FDA") and as Mounjaro by the European Medicines Agency ("EMA") in November 2023, is a GLP-1/GIP receptor agonist. Other FDA-approved therapies for obesity include Xenical (H2-Pharma, approved in the United States in 1999), Qsymia (Vivus, approved in the United States in 2012), and Contrave (Currax Pharmaceuticals, approved in the United States in 2014).

Although GLP-1 receptor agonists induce weight loss, there remains a substantial unmet need in obesity, as GLP-1 receptors lead to weight loss at the expense of muscle mass. For instance, in a Phase 3 study of semaglutide, 34% of total weight loss was from loss of lean mass (King 2021), and in a Phase 3 study of tirzepatide, treatment led to an approximately 34% loss in fat mass and an approximately 11% loss in lean mass (Jastreboff 2022). GLP-1s have also been shown to suppress the general reward system and are associated with a poor tolerability profile, frequent (weekly) administration, and discontinuation rates up to 68%.

Our Obesity Program

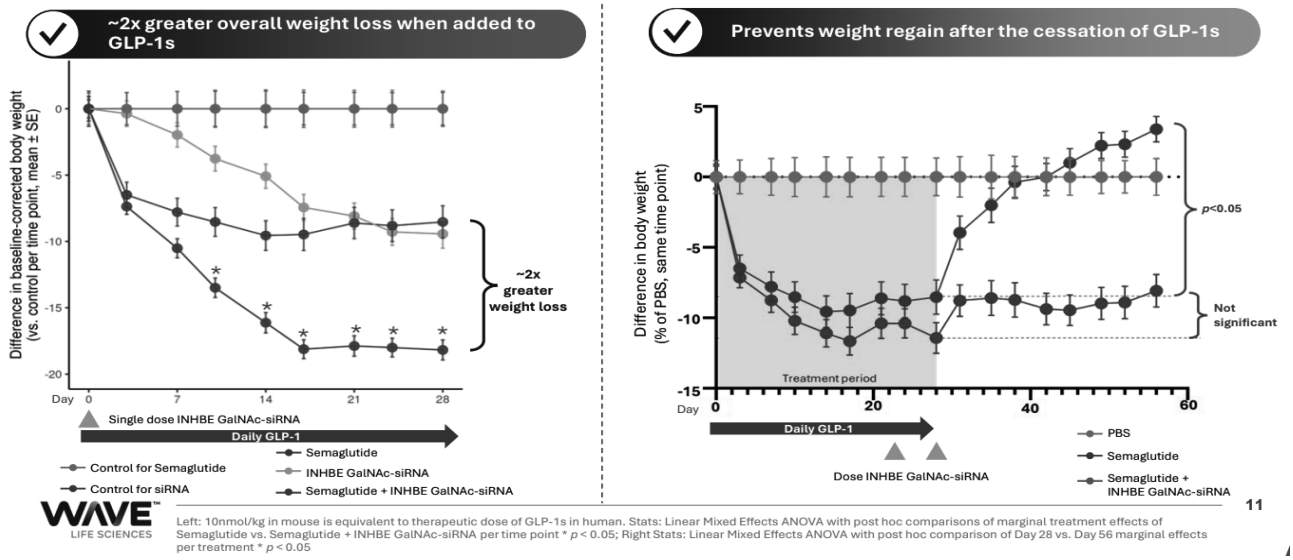
WVE-007 is a GalNAc-siRNA that is designed to silence the INHBE gene to induce lipolysis (fat-burning) while preserving muscle mass to restore and maintain a healthy metabolic profile. Heterozygous INHBE loss-of-function ("LoF") human carriers exhibit a healthy metabolic profile, including reduced waist-to-hip ratio and reduced odds of developing type 2 diabetes or coronary artery disease, and reduction of INHBE by 50% or more is expected to restore a healthy metabolic profile. In connection with our 2023 Research and Development Day, we shared *in vivo* proof-of-concept data in diet-induced obesity ("DIO") mice demonstrating INHBE silencing well beyond the anticipated 50% therapeutic threshold, which led to substantially lower body weight and reduction of visceral fat as compared to controls. These are the first data to demonstrate INHBE silencing *in vivo* in an animal model is consistent with the phenotypes of heterozygous loss-of-function carriers.

WVE-007 utilizes our next generation GalNAc-siRNA format. In preclinical diet-induced obesity ("DIO") mouse models, our INHBE GalNAc-siRNA has demonstrated highly potent INHBE silencing (ED50 < 1 mg/kg), durable silencing following one, low-single digit dose supporting every-six-month or annual subcutaneous dosing in humans, weight loss with no loss of muscle mass and reduction in fat mass, with preferential effect to the visceral fat, consistent with the profile of INHBE LoF in human genetics.



*Stats: (left, middle, right) Linear Mixed Effects ANOVA with post hoc comparisons of marginal treatment effects vs. PBS per timepoint (left) or per tissue (middle, right) * $p < 0.05$*

In a head-to-head study in DIO mice, we have observed a weight loss effect from a single dose of our INHBE GalNAc-siRNA similar to semaglutide. In addition, treatment with our INHBE GalNAc-siRNA prior to cessation of semaglutide treatment curtailed expected rebound weight gain. Additionally, in a separate ongoing study in DIO mice, when administered as an add-on to semaglutide, a single dose of our INHBE GalNAc-siRNA doubled the weight loss observed with semaglutide alone, and this effect was sustained throughout the duration of the study.



*Left: 10nmol/kg in mouse is equivalent to therapeutic dose of GLP-1s in human. Stats: Linear Mixed Effects ANOVA with post hoc comparisons of marginal treatment effects of Semaglutide vs. Semaglutide + INHBE GalNAc-siRNA per time point * $p < 0.05$; Right Stats: Linear Mixed Effects ANOVA with post hoc comparison of Day 28 vs. Day 56 marginal effects per treatment * $p < 0.05$*

In February 2025, we announced that we had initiated INLIGHT, the first-in-human Phase 1 clinical trial of WVE-007 in obesity. INLIGHT is enrolling adults living with overweight or obesity to assess safety, tolerability, pharmacokinetics ("PK"), biomarkers for target engagement, body weight and composition, and metabolic health. Dosing in INLIGHT is underway and we expect to deliver clinical data from INLIGHT in the second half of 2025.

Alpha-1 antitrypsin deficiency ("AATD")

Background and Market Opportunity

We are leveraging our RNA editing platform capability to develop a first-in-class treatment for AATD. AATD is a rare, inherited genetic disorder that is commonly caused by a G-to-A point mutation in the *SERPINA1* gene; this mutant allele is termed the *Z* allele. This mutation leads to misfolding and aggregation of Z-AAT protein in hepatocytes and a lack of functional Alpha-1 antitrypsin ("AAT") in the lungs. People with AATD typically exhibit progressive lung damage, liver damage or both, leading to frequent hospitalizations and potentially terminal lung disease and/or liver disease. Weekly intravenous augmentation therapy is the only treatment option for AATD in those with the lung pathology; there are currently no approved therapies to address the liver pathology. Approximately 200,000 people in the United States and Europe are homozygous for the Z allele, which is the most common form of severe disease.

Current Treatments

There are five treatments currently approved in the United States for chronic augmentation and maintenance therapy in adults with emphysema due to congenital deficiency of alpha1-proteinase inhibitor ("Alpha1-PI"). Per FDA labeling for each, the effect of augmentation therapy with any Alpha1-PI on pulmonary exacerbations and on the progression of emphysema in Alpha1-PI deficiency has not been demonstrated in randomized, controlled clinical trials. Augmentation therapy is also approved in the EU, but reimbursement and accessibility vary by country. Patients with AATD can also be treated with therapies used in other lung diseases including bronchodilators to open airways and corticosteroids to reduce chronic inflammation common in the lungs of patients with AATD.

There are currently no approved therapies to prevent the accumulation of the misfolded AAT protein in the liver. Treatments are available to help deal with intestinal bleeding, fluid in the abdomen, nutritional issues, and other complications from scarring of the liver, but ultimately many patients will progress towards requiring a liver transplant.

Our AATD Program

Our AATD program uses our novel GalNAc-conjugated AIMers (RNA editing oligonucleotides) and endogenous ADAR enzymes to correct a single base in the mutant SERPINA1 mRNA. By correcting the single RNA base mutation that causes a majority of AATD cases with the Pi*ZZ genotype (approximately 200,000 in the United States and Europe), RNA editing may provide an ideal approach for increasing circulating levels of wild-type AAT protein and reducing mutant protein aggregation in the liver, thus simultaneously addressing both the lung and liver manifestations of the disease.

WVE-006 is first-in-class in AATD and is the most advanced program currently in clinical development using an oligonucleotide to harness an endogenous enzyme for RNA editing. Our RestorAATion clinical program investigating WVE-006 as a treatment for AATD is comprised of two parts: RestorAATion-1, a study of healthy volunteers; and RestorAATion-2, a study in patients with AATD who have the homozygous Pi*ZZ mutation. We have completed multi-dosing in healthy volunteers in the top cohort of RestorAATion-1 at a dose level greater than those planned for any cohort in RestorAATion-2. RestorAATion-2 is a Phase 1b/2a open label study designed to evaluate the safety, tolerability, pharmacodynamics ("PD") and PK of WVE-006 in individuals with AATD who have the homozygous Pi*ZZ mutation. The trial includes both single ascending dose ("SAD") and multiple ascending dose ("MAD") portions.

In October 2024, we announced positive proof-of-mechanism data from the ongoing Phase 1b/2a RestorAATion-2 study: Following a single subcutaneous dose of 200 mg of WVE-006 in the study's first two patients, circulating wild-type M-AAT protein in plasma reached a mean of 6.9 micromolar at day 15, representing more than 60% of total AAT. Increases in neutrophil elastase inhibition from baseline were consistent with production of functional M-AAT. Mean total AAT protein increased from below the level of quantification at baseline to 10.8 micromolar at day 15, meeting the level that has historically been the basis for regulatory approval for AAT augmentation therapies. Increases in total AAT from baseline and M-AAT protein were observed as early as day 3 and through day 57. WVE-006 was well-tolerated with a favorable safety profile. All adverse events in RestorAATion-2, as well as in the RestorAATion-1 trial of healthy volunteers, were mild to moderate, with no serious adverse events ("SAEs") reported. These data were the first-ever clinical demonstration of RNA editing in humans.

In the first quarter of 2025, we initiated multi-dosing in the first cohort of RestorAATion-2, where patients are receiving 200 mg subcutaneous doses every two weeks, and initiated the second single dose cohort of RestorAATion-2 at 400 mg. We expect to share multi-dose data from RestoraAATion-2 in 2025.

GSK has an exclusive global license for WVE-006, with clinical development and commercial responsibilities transitioning to GSK after we complete the RestorAATion trial. Under the terms of the collaboration, we are eligible to receive up to $525 million in development, launch, and commercial milestone payments, as well as double-digit tiered royalties up to the high teens, as a percentage of net sales for WVE-006. In December 2023, we announced that we achieved the first WVE-006 milestone in our collaboration with GSK, resulting in a $20 million payment.

Preclinical data show that treatment with WVE-006 resulted in serum AAT protein levels of up to 30 micromolar in an established AATD mouse model (NSG-PiZ). WVE-006 also led to restoration of approximately 50% wild-type M-AAT protein in serum and a 3-fold increase in neutrophil elastase inhibition activity, indicating that the restored M-AAT protein was functional. Our AATD AIMers are highly specific to SERPINA1 RNA *in vitro* and *in vivo* based on transcriptome-wide analyses.

Duchenne muscular dystrophy ("DMD")

Background and Market Opportunity

DMD is a rare, genetic progressive neuromuscular disorder caused by mutations in the dystrophin gene on the X chromosome that affects approximately one in 5,000 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, patients with DMD 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 2017, Emflaza (deflazacort) became the first corticosteroid approved by the FDA as a treatment for patients with DMD. Santhera Pharmaceuticals' Agamree (vamorolone), an alternative steroid, was approved in the United States and EU in 2023. In 2024, FDA granted approval to Italfarmaco/ITF Therapeutics' Duvyzat (givinostat), a histone deacetylase inhibitor.

Four exon skipping therapies have been approved in the United States, all under the accelerated approval pathway. They include three products from Sarepta Therapeutics: Exondys 51 (eteplirsen) for exon 51 skipping, approved in 2016; Vyondys 53 (golodirsen) for exon 53 skipping, approved in 2019; and Amondys 45 (casimersen) for exon 45 skipping, approved in 2021. NS Pharma's Viltepso (viltolarsen) was approved for exon 53 skipping in 2020. All of these products require weekly IV infusion, and to date, none of these products has demonstrated clinical benefit in a confirmatory trial.

Sarepta Therapeutics' Elevidys, a microdystrophin gene therapy, is available in the United States and select ex-EU markets. The labeled indication in the United States is currently for ambulatory and non-ambulatory DMD patients aged at least four years who have a confirmed mutation in the DMD gene. The indication that includes ambulatory DMD patients was granted under a traditional approval, and the indication that includes non-ambulatory DMD patients was approved under accelerated approval based on expression of Elevidys microdystrophin. Continued approval for non-ambulatory DMD patients may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

In 2014, PTC Therapeutics' Translarna (ataluren) was the first disease-modifying treatment to receive conditional approval by the EMA for patients with DMD who have a nonsense mutation (12% of DMD cases) in the dystrophin gene. However, in 2023, the Committee for Medicinal Products for Human Use ("CHMP") of the EMA issued a negative opinion on the renewal of the conditional marketing authorization, and in 2024, CHMP re-confirmed this negative opinion. Once adopted by the European Commission, this ruling will result in the withdrawal of Translarna from the EU market.

Our DMD Program

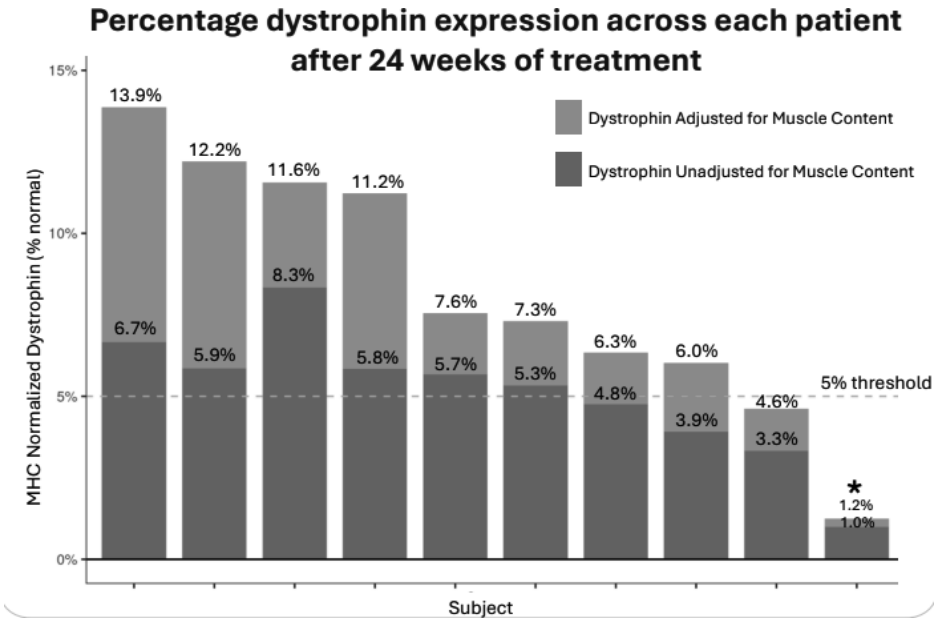
In DMD, we are advancing WVE-N531, which is designed to skip exon 53 within the dystrophin gene – a therapeutic approach that would address approximately 8-10% of DMD cases. WVE-N531 is designed to cause the cellular splicing machinery to skip over exon 53 during pre-mRNA processing, which restores the dystrophin mRNA reading frame and enables production of a truncated, but functional, dystrophin protein. Exon skipping produces dystrophin from the endogenous dystrophin gene (not micro or mini dystrophin expressed from a foreign vector), under the control of native gene-regulatory elements, resulting in physiological control over its expression. WVE-N531 is our first splicing candidate incorporating PN backbone ("PN") chemistry to be assessed in the clinic. In the third quarter of 2024, the FDA granted Rare Pediatric Disease Designation and Orphan Drug Designation to WVE-N531.

In December 2022, we announced a positive update from Part A of the Phase 1b/2a proof-of-concept, open label trial of WVE-N531 in three boys with DMD amenable to exon 53 skipping. High muscle concentrations of WVE-N531 and exon skipping were observed six weeks after initiating multi-dosing at 10 mg/kg every other week, achieving proof-of-concept in the trial. WVE-N531 also appeared safe and well-tolerated.

In September 2023, we shared an analysis of muscle biopsy data from the Part A proof-of-concept trial indicating that WVE-N531 was present in myogenic stem cells, which are integral to muscle regeneration. This is the first demonstration of uptake in myogenic stem cells in a clinical study and supports the potential differentiation of WVE-N531 from other therapeutics, including gene therapies.

In December 2023, we initiated dosing of WVE-N531 in FORWARD-53, the Phase 2 portion of the open-label trial ("Part B"). The study is designed to administer 10 mg/kg infusions of WVE-N531 every two weeks ("Q2W"), and muscle biopsies are taken after 24 and 48 weeks of dosing. The primary endpoint will be dystrophin protein levels, and the trial will also evaluate PK, digital and functional endpoints, and safety and tolerability.

In September 2024, we announced positive interim data from the ongoing Phase 2 FORWARD-53 study. Eleven boys amenable to exon 53 skipping (age 5-11; 10 ambulatory and 1 non-ambulatory) are enrolled. The interim analysis was conducted after 24 weeks of 10 mg/kg dosing Q2W. WVE-N531 appeared safe and well tolerated. We observed mean muscle content-adjusted dystrophin expression of 9.0% and unadjusted dystrophin of 5.5%, with high consistency across participants, in a prespecified analysis of ambulatory participants.



**Excluded from prespecified mean analysis of ambulatory patients; Muscle content adjustment was done using the formula: MHC-normalized dystrophin/(total myofiber area/total area of biopsy section); Graph shows all patients (including non-ambulatory) with appropriate biopsy sample; dystrophin measured by Western Blot (AB15277)*

Dystrophin expression was quantified from two isoforms consistent with those observed in Becker muscular dystrophy patients who display milder disease. In addition, we observed meaningful improvements in serum biomarkers for muscle health, with localization of WVE-N531 in myogenic stem cells and in myofibers. Mean skeletal muscle concentrations of ~41,000 ng/g and a 61-day tissue half-life support monthly dosing going forward.

The FORWARD-53 trial is ongoing and all patients have elected to continue treatment in the planned extension portion of the study with monthly doses of WVE-N531. In the first quarter of 2025, we expect to deliver the 48-week FORWARD-53 data and feedback from regulators on a pathway to accelerated approval. Pending positive results from this trial, we are planning to advance a broader DMD pipeline with PN-modified splicing oligonucleotides designed to skip other exons, with the goal of providing new treatment options for a larger population of boys with DMD.

Huntington's disease ("HD")

Background and Market Opportunity

HD is a rare hereditary neurodegenerative disease that results in early death and for which there is no cure. In patients with HD, there is a progressive loss of neurons in the brain leading to cognitive, psychiatric, and motor disabilities. HD is caused by a mutation (an expanded cytosine-adenine-guanine ("CAG") triplet repeat) in the Huntingtin ("*HTT")* gene, which results in production of mHTT protein and decreases the amount of wtHTT protein that is expressed. Patients with HD still express some wtHTT protein, which is important for neuronal function, and which may be neuroprotective in an adult brain. Studies suggest a multifaceted mechanism by which gain of mHTT protein and a concurrent loss of wtHTT protein may drive the pathophysiology of HD.

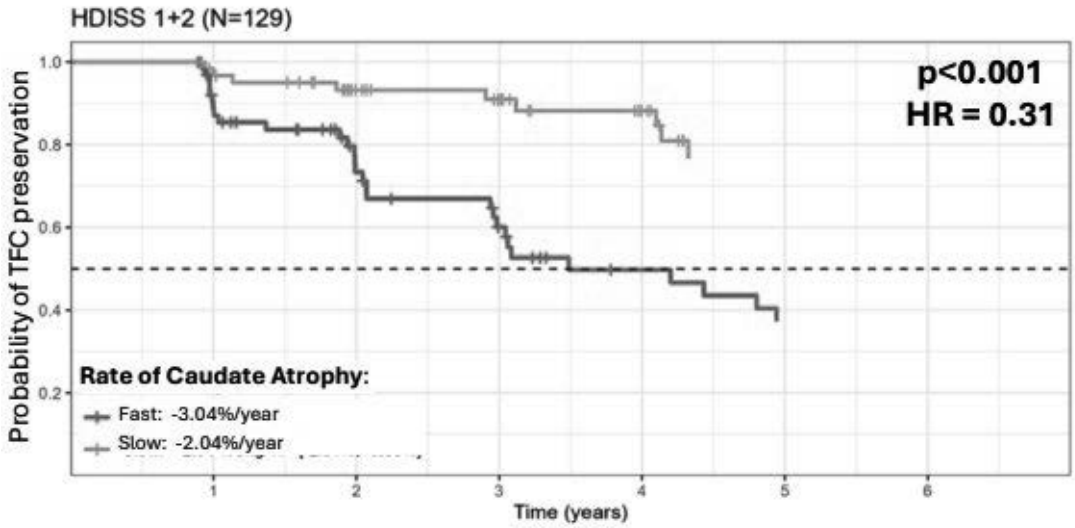
Accordingly, therapeutic approaches for HD that aim to lower mHTT but that also suppress wtHTT may have detrimental long-term consequences. Wild-type HTT is important both for normal neuronal function in the adult CNS and for protection against HD. It can protect against stress-induced neurodegeneration in multiple model systems: in cultured neurons, wtHTT is protective against stress-induced apoptosis; in mice, postnatal deletion of wtHTT leads to progressive neurological phenotypes, neurodegeneration, and premature death, whereas overexpression of wtHTT conveys neural protection during stress, including ischemia and other types of CNS injury, as well as NMDA-induced excitotoxicity. In the YAC128 mouse model of HD, overexpression of wtHTT ameliorates striatal neuropathology, whereas loss of the wild-type mouse Htt worsens motor performance, survival, and striatal neuronal size.

In patients with HD, a variant in a regulatory element impacts expression of the associated HTT gene. An A variant decreases expression relative to a G variant at this position. Accordingly, when the A variant associates with mHTT, expression of mHTT is reduced and disease onset is delayed (on average, 10 years). By contrast, when the A variant associates with wtHTT, expression of wtHTT is reduced and disease onset is earlier (on average, four years), indicating that increased expression of wtHTT can be protective against HD in patients. Together, these studies provide evidence that wtHTT is both neural protective during stress and is specifically protective against HD; thus, we believe an allele-selective therapeutic, one that can diminish the production of mHTT while sparing wtHTT, may be ideal.

In patients with HD, a variant in a regulatory element impacts expression of the associated HTT gene. Accordingly, the variant that decreases expression of mHTT associates with delayed onset of disease (on average by 10 years compared with the variant that increases mHTT expression). By contrast, the same variant that decreases expression of wtHTT associates with earlier onset (on average four years compared with increased wtHTT expression), indicating that increased expression of wtHTT can be protective against HD in patients. Together, these studies provide evidence that wtHTT is both neural protective during stress and is specifically protective against HD; thus, we believe an allele-selective therapeutic, one that can diminish the production of mHTT while sparing wtHTT, may be ideal.

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 amyotrophic lateral sclerosis, Parkinson's Disease and Alzheimer's Disease simultaneously. Patients experience a reduction in motor function and psychological disturbances. Life expectancy after symptom onset is approximately 20 years. In the most symptomatic stages, often lasting over 10 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, and often require premature placement in a long-term care facility. It is estimated that there are over 200,000 individuals with HD across all disease stages in the United States and Europe; ~160,000 are pre-symptomatic and ~65,000 are symptomatic. Our allele-selective approach may enable us to address both the symptomatic and pre-symptomatic populations.

Medium spiny neurons in a deep brain region called the striatum, which is composed of caudate and putamen, are particularly sensitive to death in HD. Caudate volume, as measured by magnetic resonance imaging ("MRI"), is an imaging biomarker that consistently shows atrophy at the earliest stages of disease, and it is one of the biomarkers that serves as a landmark for disease progression (Tabrizi et al., 2022 Lancet Neurol). Our evaluation of longitudinal natural history data from TRACK-HD and PREDICT-HD demonstrate that an absolute reduction of 1% in the rate of caudate atrophy is associated with a delay of onset of disability for individuals with HD of at least 7.5 years.



TRACK-HD (n=366) and PREDICT-HD (n=1,078) are longitudinal HD natural history studies that include MRI brain imaging, clinical outcome assessments. Paulson et al., Neurosci.2014, Tabrizi et al., Lancet Neurol 2009, Tabrizi et al., Lancet Neurol 2012, Tabrizi et al., Lancet Neurol. 2013

Current Treatments

There are currently 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), Austedo (deutetrabenazine), and as of August 2023, Ingrezza (valbenazine) are the only therapies approved for the treatment of chorea associated with HD in the United States. In the EU, Xenazine, Haldol (haloperidol), and Tiapridal (tiapride) are approved for the treatment of chorea associated with HD.

Our HD Program

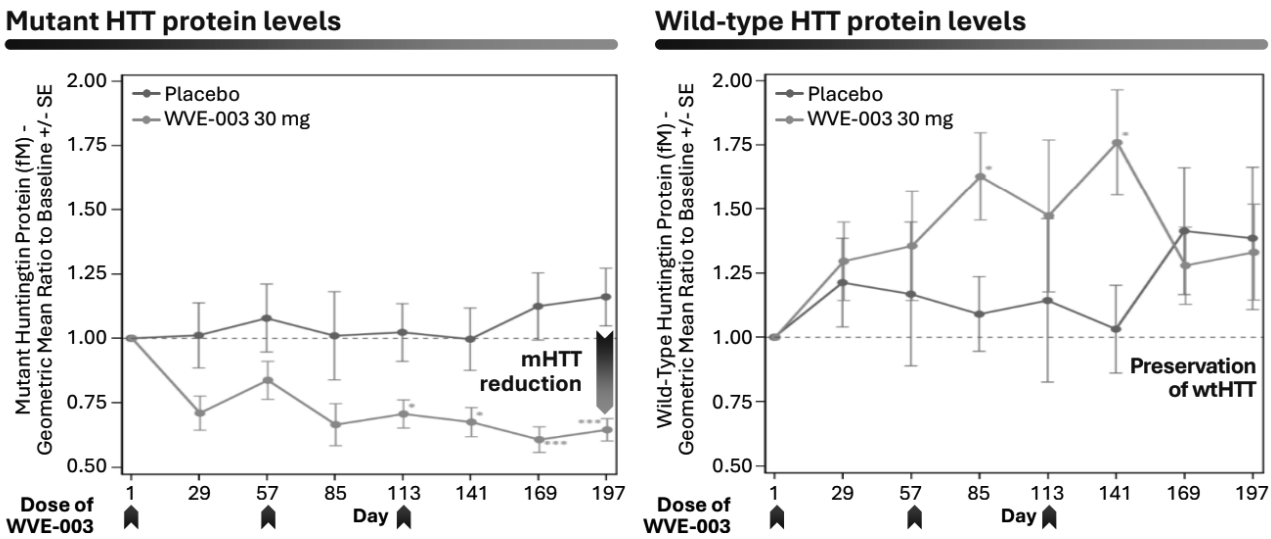
In HD, we are currently advancing WVE-003, a stereopure allele-selective oligonucleotide designed to selectively target rs362273, a variant of the single nucleotide polymorphism ("SNP"), "mHTT SNP3", associated with the disease-causing mHTT mRNA transcript within the HTT gene (Iwamoto et al., MTNA). Approximately 40% of the HD population carries SNP3 according to published literature (Carroll et al., Molecular Therapy, 2011), and up to 80% of HD may be addressed in the future with other SNP-targeted candidates.

WVE-003 incorporates our proprietary PN chemistry. Targeting mRNA through SNP3 allows us to lower expression of transcript from the mutant allele, while leaving the healthy transcript relatively intact, thereby preserving wild-type (healthy) huntingtin ("wtHTT") protein, which is important for neuronal function. Only an allele-selective approach to mHTT lowering has the potential to both protect the reservoir of wtHTT protein and decrease the mHTT to wtHTT ratio in neurons, potentially releasing wtHTT from the inhibitory actions of mHTT. In preclinical studies, WVE-003 showed dose-dependent and selective reduction of mHTT mRNA *in vitro*, as well as potent and durable knockdown of mHTT mRNA and protein *in vivo* in mouse models.

In the third quarter of 2023, we achieved a milestone in our collaboration with Takeda Pharmaceutical Company Limited ("Takeda"), which pertained to the positive results from a non-clinical study of WVE-003 in non-human primates and resulted in a payment of $7.0 million to us. This study showed significant tissue exposure levels of WVE-003 in the deep brain regions, including striatum and bolstered our existing datasets that confirm the ability of our oligonucleotides to distribute to the areas of the CNS important for HD.

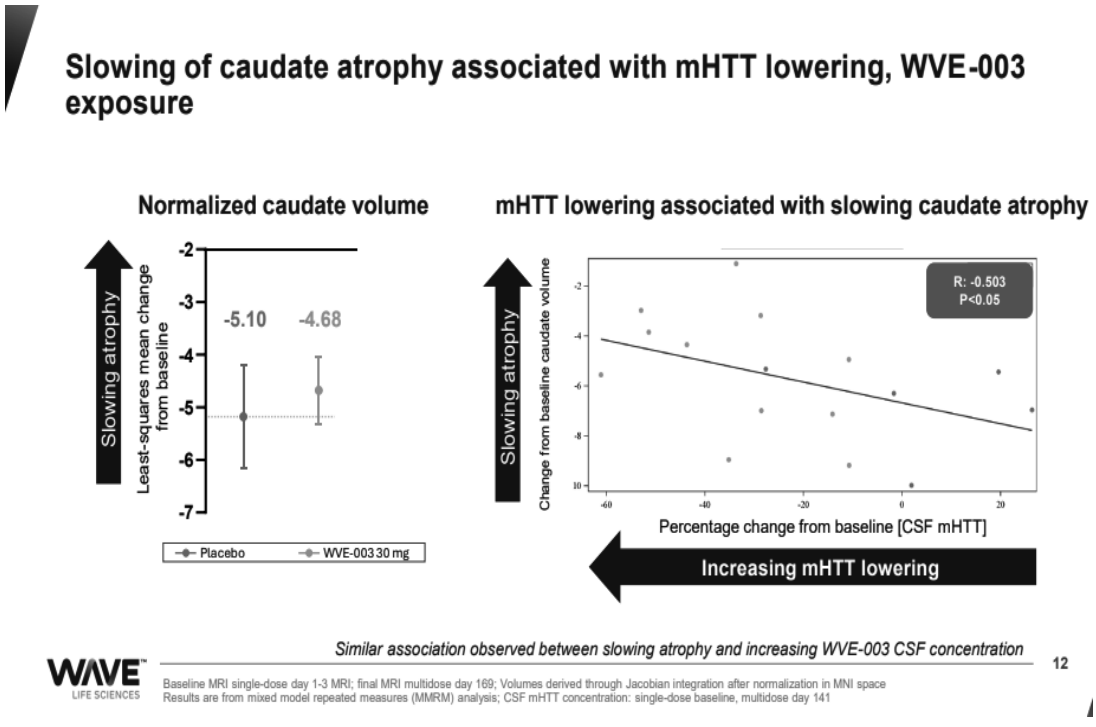
SELECT-HD was a global, multicenter, randomized, double-blind, placebo-controlled Phase 1b/2a clinical trial to assess the safety and tolerability of WVE-003 in people with a confirmed diagnosis of HD who are in the early stages of the disease and carry SNP3 in association with their CAG expansion. Additional objectives included assessing PK and exploratory PD and clinical endpoints.

In June 2024, we announced positive clinical data from the Phase 1b/2a SELECT-HD study of WVE-003. Results from the multi-dose portion of the trial, which evaluated three doses of 30 mg WVE-003 administered every eight weeks, showed clear translation of target engagement to clinic with statistically significant, potent, durable and allele-selective reductions in cerebrospinal fluid ("CSF") mHTT of up to a mean 46% with preservation of wtHTT protein.



** p<0.05, **p<0.01, ***p<0.001, ****p<0.0001*

The multi-dose cohort also revealed a statistically significant correlation between mHTT reduction and slowing of caudate atrophy, indicating a potential benefit of allele-selective mHTT reductions. Caudate atrophy, as measured by MRI, is a well-characterized measures of disease progression in HD.



Baseline MRI single-dose day 1-3 MRI; final MRI multi-dose day 169; Volumes derived through Jacobian integration after normalization in MNI space. Results are from mixed model repeated measures (MMRM) analysis; CSF mHTT concentration: single-dose baseline, multi-dose day 141

In the multi-dose cohort, WVE-003 was generally safe and well-tolerated, with mild-to-moderate adverse events ("AEs") and no SAEs. In November 2024, five months after a patient completed their final safety visit, an SAE was reported that we assessed to be not related to WVE-003.

Following our positive clinical results, we initiated engagement with the FDA. In November 2024, we received supportive initial feedback from the FDA, who recognize the severity of HD and are receptive to and engaged with us regarding a potential pathway to accelerated approval. The FDA is open to our plan to evaluate biomarkers, including caudate atrophy, as an endpoint to assess HD progression with the potential to predict clinical outcome. Also in November 2024, the FDA granted Orphan Drug Designation to WVE-003.

Preparation is ongoing for a global, potentially registrational Phase 2/3 study of WVE-003 with caudate atrophy as a primary endpoint. We expect to submit an Investigational New Drug ("IND") application for WVE-003 in the second half of 2025.

Discovery Pipeline

We are advancing new targets across multiple disease areas to expand our pipeline of wholly owned programs. Our compelling preclinical data indicates our oligonucleotides can distribute to various tissues and cells without complex delivery vehicles, enabling us to address a wide variety of diseases, including pulmonary and renal diseases. Within RNA editing, we have demonstrated preclinically that we can edit to correct monogenic diseases by restoring or correcting protein function for the treatment of AATD. Building on our work in AATD, we have demonstrated our ability to address more prevalent diseases by editing RNA to upregulate or increase the stability of the mRNA transcript, thereby increasing endogenous protein production. Utilizing our proprietary "edit-verse," which is powered by genetic datasets and deep learning models, we have identified several RNA editing targets in indications that leverage easily accessible biomarkers, offer efficient paths to proof-of-concept in humans, and represent meaningful commercial opportunities.

Our wholly owned discovery-stage pipeline includes hepatic and extra hepatic targets, including three RNA editing programs in liver that leverage GalNAc conjugates and have efficient clinical paths to proof-of-concept.

- PNPLA3, which uses mRNA correction to restore the heterozygous phenotype for those at high risk for genetically defined liver disease. Homozygous PNPLA3-I148M patients are at high risk for a variety of liver diseases and there are more than nine million impacted individuals in the United States and Europe.
- LDLR and APOB, which utilize first-in-class mRNA upregulation and mRNA correction approaches, respectively, to achieve target low-density lipoprotein cholesterol (LDL-c) levels in people with heterozygous familial hypercholesterolemia. Combined, LDLR and APOB AIMers could address approximately one million HeFH patients in the United States and Europe. LDLR upregulation also offers significant expansion opportunities in patients with statin intolerance or prior cardiovascular events which represent approximately 30 million patients in the United States and Europe.

Through our collaboration with GSK, we are also leveraging GSK's novel genetic insights to expand our wholly owned pipeline. In addition, we and GSK are actively working on multiple target validation programs as GSK-partnered programs, for which all of our costs and expenses are prepaid by GSK. In April 2024, GSK selected its first two programs to advance to development candidates following achievement of target validation, triggering an aggregate initiation payment to us of $12.0 million from GSK. These programs utilize our next generation GalNAc-siRNA format and are in hepatology.

We plan to share new preclinical data from our wholly owned hepatic and extra-hepatic RNA editing programs in 2025. In 2026, we expect to initiate clinical development of additional RNA editing programs, including PNPLA3, LDLR, and APOB.

Our Strategy

We are building a leading RNA medicines company by leveraging PRISM to design, develop and commercialize optimized disease-modifying medicines for indications with a high degree of unmet medical need. We have a robust and diverse pipeline of first- or best-in-class RNA medicines using our RNA editing, splicing, silencing using siRNA, and antisense silencing modalities. Our lead programs aim to address both rare and common diseases, including obesity, AATD, DMD, and HD, as well as preclinical programs for liver diseases and HeFH. In addition to driving clinical and preclinical programs, we are continuously investing in PRISM to fully unlock the potential of our unique and expanding platform capabilities.

The key components of our strategy are as follows:

- ***Extend our leadership in RNA medicines***. We intend to establish a dominant position in the field of oligonucleotides, advancing basic research and pharmacology using stereochemistry and other novel modifications across multiple therapeutic modalities and target classes. Our work has already led to the development of AIMers for RNA editing, as well as the introduction of PN backbone chemistry modifications for potential therapeutic use and novel base modifications such as N3U. Through PRISM, our efforts continue to reveal structure-activity relationships among base modifications and sequence, chemistry and backbone stereochemistry that may allow us to further tune the activity of our oligonucleotides in a previously unexplored, modality-specific manner.

- ***Rapidly advance and sustainably grow our differentiated portfolio of RNA medicines.*** We are committed to transforming the care of devastating diseases where patients have limited treatment options. Our current and future portfolio is focused on novel therapeutic approaches that optimally address disease biology, that offer biomarkers for target engagement, and that inform on clinical effects early in development. We are currently advancing multiple clinical programs: WVE-007 (obesity), WVE-006 (AATD), WVE-N531 (DMD), and WVE-003 (HD), which were all designed with novel PN backbone chemistry modifications and developed from our PRISM platform. We continue to conduct discovery-stage research on novel therapeutic approaches, and have the opportunity, through our GSK collaboration, to advance programs leveraging GSK's novel genetic insights. We expect these activities will add multiple first-in-class therapeutics to our pipeline over the next several years.
- ***Expand our pipeline of high-value programs.*** In 2024, we made meaningful progress in advancing preclinical programs utilizing our versatile PRISM platform. With multiple modalities at our disposal, we are positioned to unlock new biology and develop first-in-class therapeutics. To build on our demonstration of first-ever RNA editing in humans with WVE-006 (AATD), we announced three wholly owned GalNAc-AIMer programs that offer first-in-class approaches to address unmet needs in cardiometabolic diseases. These new programs include PNPLA3, which uses mRNA correction for those at high risk for a genetically defined liver disease, and LDLR and APOB, which utilize first-in-class mRNA upregulation and mRNA correction, respectively, to achieve target LDL-c levels in people with heterozygous familial hypercholesterolemia.
- ***Leverage manufacturing leadership in oligonucleotides.*** We have built a hybrid internal / external manufacturing model that gives us the capability to produce stereopure oligonucleotides at scales from one micromole to potential commercial scale. Through our internal manufacturing, based in our Lexington, Massachusetts facility, we have the capacity to support multiple discovery, preclinical, and early clinical-stage programs, and we have the expertise to conduct manufacturing runs for oligonucleotides spanning multiple modalities. We believe that leveraging our internal manufacturing capabilities along with expertise from contract manufacturing organizations ("CMOs") facilitates our growth and enhances our ability to secure drug substance for current and future development activities.

PRISM: Our proprietary discovery and drug development platform

Our PRISM platform demonstrates the powerful convergence of best-in-class chemistry with human genetics. The platform was built on the recognition that a significant opportunity exists to tune the pharmacological properties of oligonucleotides by leveraging three key features of these molecules: base modifications and sequence, chemistry, and stereochemistry. Our unique ability to control stereochemistry provides the resolution necessary to optimize pharmacological profiles and develop and manufacture stereopure oligonucleotides. Stereopure oligonucleotides are comprised of molecules with atoms precisely and purposefully arranged in three-dimensional orientations at each linkage. Our stereopure oligonucleotides are distinct from the chiral backbone-modified or "mixture-based" oligonucleotides currently on the market or in development by others, which we believe are not optimized for stability, catalytic activity, efficacy or toxicity. We believe that PRISM has the potential to set a new industry standard for the molecular characterization of complex oligonucleotide mixtures. Our rational process for designing stereopure oligonucleotides allows us to selectively optimize chemical modifications to a specific therapeutic modality in order to generate best-in-class oligonucleotides.

Advantages of PRISM

We believe that PRISM is a significant advancement in the development of oligonucleotides. The advantages of our approach include:

- ***Ability to rationally design product candidates with optimized pharmacological properties***. Our platform combines our unique ability to construct stereopure oligonucleotides with a deep understanding of how the interplay among oligonucleotide base modifications and sequence, chemistry and backbone stereochemistry impacts key pharmacological properties. By exploring these interactions through iterative analysis of *in vitro* and *in vivo* outcomes and machine learning-driven predictive modeling, we continue to define design principles that we deploy across programs to rapidly develop and manufacture clinical candidates that meet pre-defined product profiles. PRISM has also enabled us to further innovate our chemistry, including the application of novel PN backbone chemistry modifications to our pipeline programs.
- ***Broad applicability***. PRISM is applicable to oligonucleotides acting via multiple therapeutic modalities, including RNA editing, splicing, and silencing (including siRNA and antisense). It is also compatible with a broad range of chemical modifications and targeting moieties.
- ***Simplified delivery***. We can take advantage of simplified delivery strategies, such as free-uptake or GalNAc conjugation, to reach the site of action in the right tissue. This approach avoids the need, and certain limitations, for complex delivery vehicles such as lipid nanoparticles ("LNPs") or adeno-associated viruses ("AAV").

- ***Proprietary production of stereopure oligonucleotides and scalable manufacturing***. Our scientists have developed expertise in the techniques required to produce adequate supplies of chemically modified stereopure oligonucleotide materials for our preclinical and 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. We believe that our scalable synthesis processes will allow us to meet demand for current good manufacturing practices ("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 stereorandom oligonucleotides.

Our Proprietary Chemistry

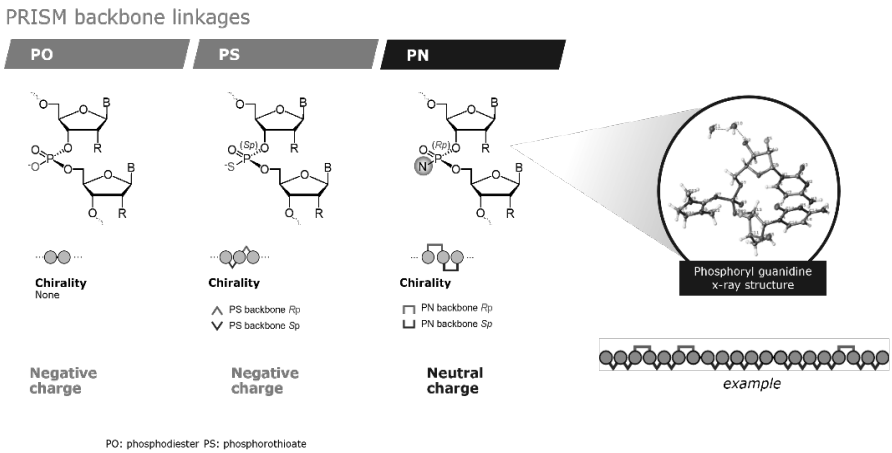
Backbone Stereochemistry

In our foundational *Nature Biotechnology* paper (Iwamoto N, et al. Nature Biotechnol. 2017;35(9):845-851), we described our studies using our proprietary chemistry to design and synthesize stereopure oligonucleotides and oligonucleotide mixtures based on mipomersen. Mipomersen, an oligonucleotide containing 20 nucleotides and 19 PS modifications, is synthesized by traditional oligonucleotide chemistry; thus, it is 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. These and other preclinical studies have demonstrated that stereochemistry impacts pharmacology, and that by controlling stereochemistry, we can tune multiple aspects of pharmacology, including stability, catalytic activity, and efficacy.

We have subsequently published multiple additional manuscripts that provide evidence that stereopure oligonucleotides can be developed to have superior pharmacology to stereorandom oligonucleotides.

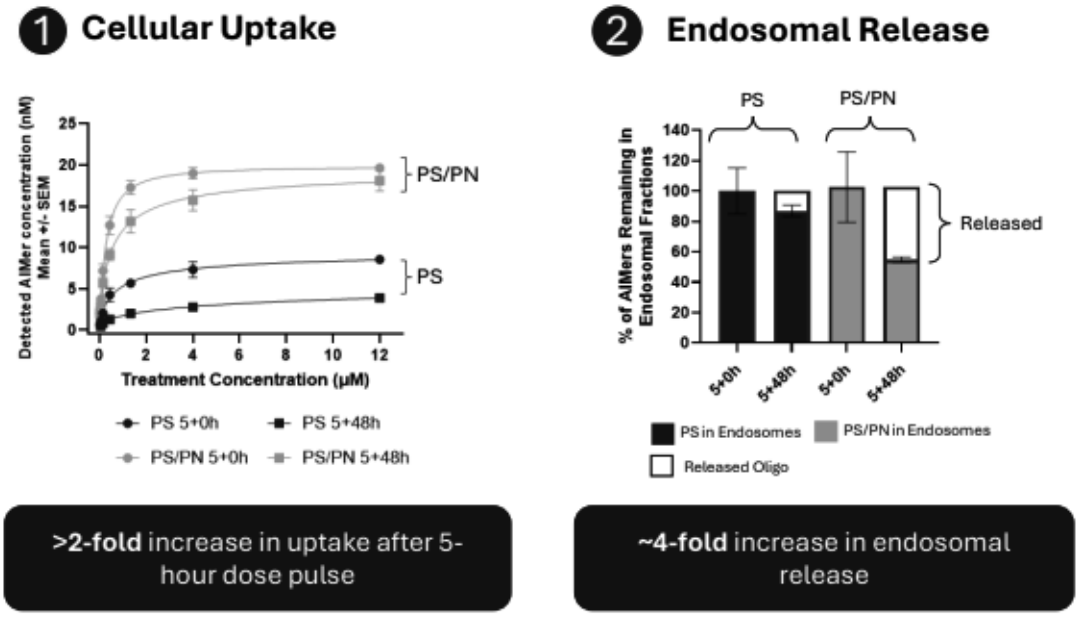
PN Backbone Chemistry Modifications

Our initial investigations into the impact of backbone chemistry and stereochemistry on oligonucleotide pharmacology focused on the widely used phosphodiester ("PO") and phosphorothioate ("PS") backbones because they are amenable to all oligonucleotide modalities. In 2020, we introduced PN chemistry to our repertoire of backbone modifications; this backbone modification replaces a non-bridging oxygen atom in a phosphodiester linkage with a nitrogen-containing moiety, as shown below.

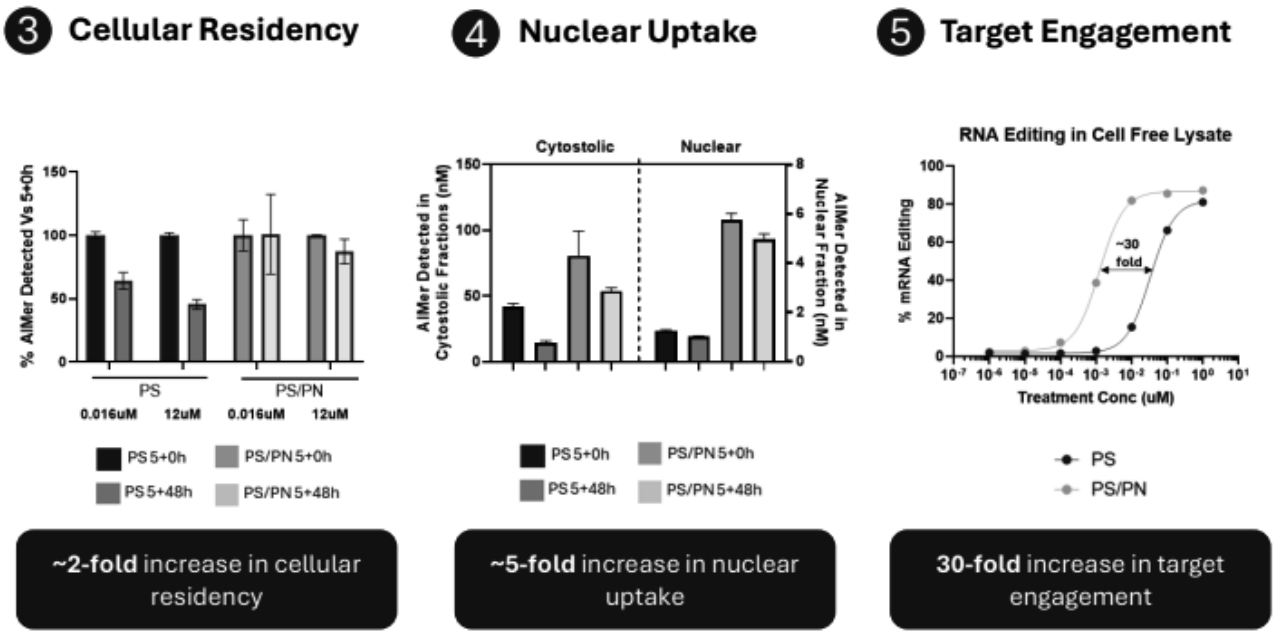


We have incorporated these PN modifications – specifically phosphoryl guanidine – into oligonucleotide compounds. As with PS modifications, PN modifications are chiral, and we have the capacity to control PN backbone stereochemistry. Unlike PS modifications, PN modifications are neutral, meaning that the negative charge of the oligonucleotide is reduced with every PN modification added to the backbone. In preclinical experiments, we have demonstrated that judicious use of PN backbone chemistry modifications in stereopure oligonucleotides have generally increased potency, tissue exposure and durability of effect across our RNA editing, siRNA, splicing, and antisense modalities.

We have also investigated the impact of PN chemistry and performed experiments under gymnotic or free uptake conditions. In the graph labeled one below, the data demonstrate the contrast between AIMer uptake in cells, depending on whether it incorporates PN chemistry, shown in light blue, or not, shown in dark blue. To the right, in the graph labeled two, the data demonstrate the proportion of AIMer released from endosomes inside the cell. The addition of PN chemistry drove a greater than 2-fold increase in cellular uptake and an over 4-fold increase in endosomal release compared with PS chemistry.



Below, we also demonstrated the benefits of PN chemistry on cellular residency, with a higher percentage of PN-containing molecules persisting within the cell, a 5-fold benefit on nuclear uptake, and ultimately, evidence this modification leads to a dramatic 30-fold improvement in target engagement in a cell free lysate system.



Base Modifications

In 2023, we introduced base modifications (*e.g.,* N-3-uridine, N3U) to our repertoire of chemical modifications that allow us to tune the activity of oligonucleotides to the biological modality. For example, we have shown that the introduction of an N3U at the "orphan position" of an RNA editing oligonucleotide, which is across from the edit site in the transcript, enhances RNA editing across a diversity of sequences in preclinical studies.

In our 2024 *Nucleic Acids Research* paper (Lu et al., 2024 Nuc Acid Res; doi.org/10.1093/nar/gkae681 N), we described the development of new AIMer designs with base modifications and sequence, sugar and backbone modifications that improve RNA editing efficiency over our previous design. AIMers incorporating a novel pattern of backbone and 2′ sugar modifications support enhanced editing efficiency across multiple sequences. Further efficiency gains were achieved through incorporation of N3U in place of cytidine (C) in the orphan position. Molecular modeling suggested that N3U might enhance ADAR catalytic activity by stabilizing the AIMer-ADAR interaction and potentially reducing the energy required to flip the target base into the active site. Supporting this hypothesis, AIMers containing N3U consistently enhanced RNA editing over those containing C across multiple sequences and multiple nearest neighbor sequence combinations. These modifications to AIMers improved RNA editing both *in vitro* and in *vivo*.

We continuously explore how new modifications and new combinations of modifications from our expansive repertoire can redefine what's possible with oligonucleotide therapeutics.

PRISM Supports Multiple Therapeutic Modalities

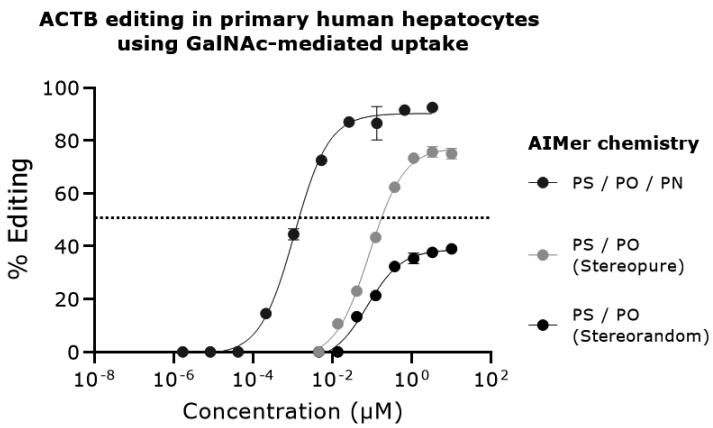
Using PRISM, we have designed and optimized diverse sets of stereopure oligonucleotides, which allows us to characterize and compare the impact of various chemical modifications on key properties that impact a specific modality.

In the next section, we describe different therapeutic modalities for which we have used PRISM to optimize stereopure oligonucleotides and develop built-for-purpose candidates to optimally address disease biology.

RNA editing

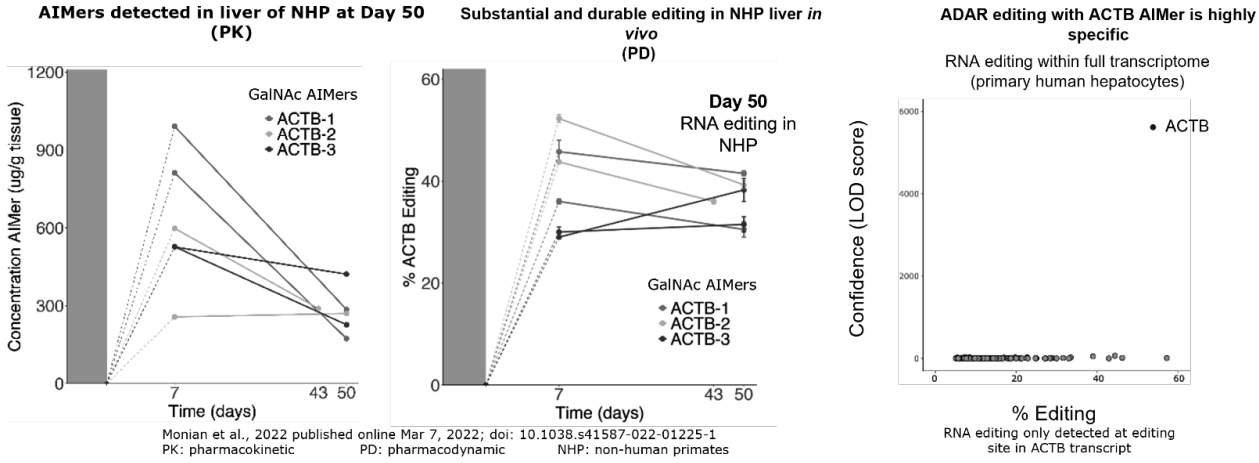
We have applied our PRISM platform to the generation of short, single-stranded, highly specific A-to-I (G) RNA editing oligonucleotides – called "AIMers". Because our AIMers are relatively short and stable (fully chemically modified), we can leverage clinically proven GalNAc-mediated delivery to hepatocytes with subcutaneous dosing. We are developing fully chemically modified AIMers with and without GalNAc conjugation. In preclinical studies, we have evaluated thousands of AIMers, assessing a variety of sugar and base modifications, backbone chemistry and stereochemistry, and other parameters such as AIMer length to produce insight into the relationship between an AIMer's structure and its ability to elicit RNA editing activity.

With PRISM, we have generated stereopure AIMers, optimized for chemistry and stereochemistry, which promote RNA editing with endogenous ADAR enzymes in cellular models. As shown in the figure below, we show the activity of beta-actin-editing stereopure AIMers, with and without PN linkages, compared to a matched stereorandom AIMer (shown in black) in primary human hepatocytes. These AIMers are GalNAc conjugated to increase uptake in hepatocytes. The addition of PN chemistry substantially improves both potency and editing efficiency.

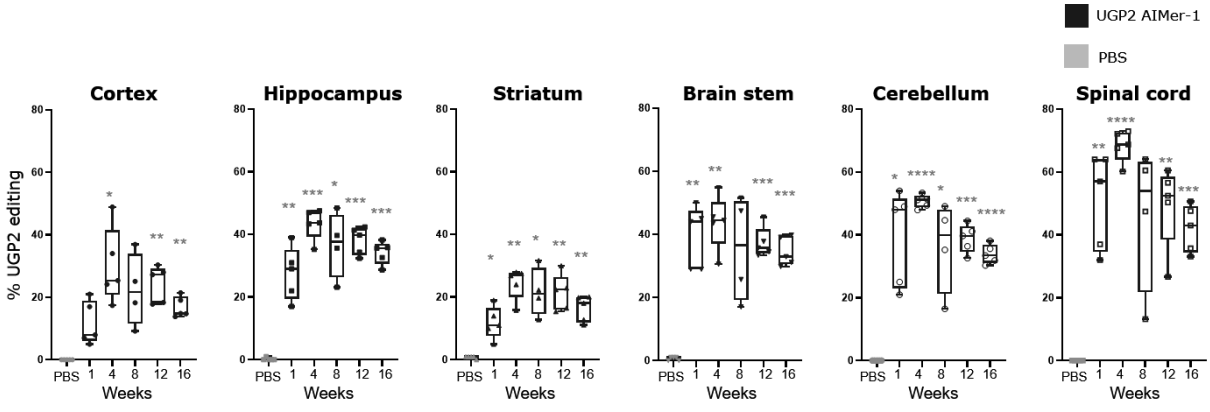


In our foundational RNA editing paper published in *Nature Biotechnology* (Monian P, et. Al., 2022; doi.org/10.1038/s41587-022-01225-1), we demonstrated efficient RNA editing *in vitro* with our AIMers across a variety of cell lines, including non-human primate ("NHP") and human primary hepatocytes, as shown in the figures below. We observed potent, dose-dependent RNA editing with three chemically distinct stereopure AIMers (ACTB 1, ACTB 2, ACTB 3) via GalNAc-mediated uptake.

We next evaluated these same ACTB-editing AIMers *in vivo* in NHPs, and the results are shown in the figures below. For this study, we dosed NHPs subcutaneously once a day for five days. We took liver biopsy samples at baseline at two days and 45 days after the last dose to evaluate editing. We detected up to 50% editing two days after the last dose as compared to a baseline of 0% editing, as shown in the figure below in the middle. These editing results were durable: we continued to see significant editing 45 days after the last dose. The PK data, shown in the figure below on the left, confirmed that a significant amount of AIMer was still detectable in the liver at that time. To assess off-target editing for the whole transcriptome, a mutation-calling software was used to call edit sites. From this analysis, we observed nominal off-target editing across the transcriptome. Sites where potential off-target editing occurred mapped predominantly to non-coding regions of the transcriptome and had either low read coverage in the analysis or occurred at low percentages of less than 10%, indicating that these are relatively rare events, as shown in the figure below on the right.

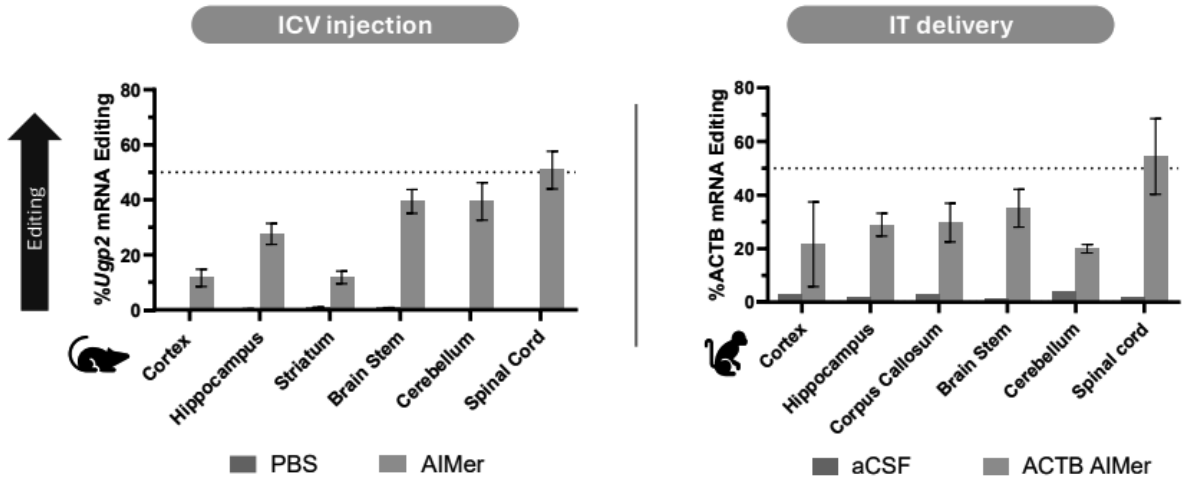


We have demonstrated potent (up to 65%) and durable (out to at least four months) editing of UGP2 mRNA *in vivo* in multiple regions of the CNS following a single unconjugated AIMer dose in a mouse model with human ADAR, as shown in the figure below.

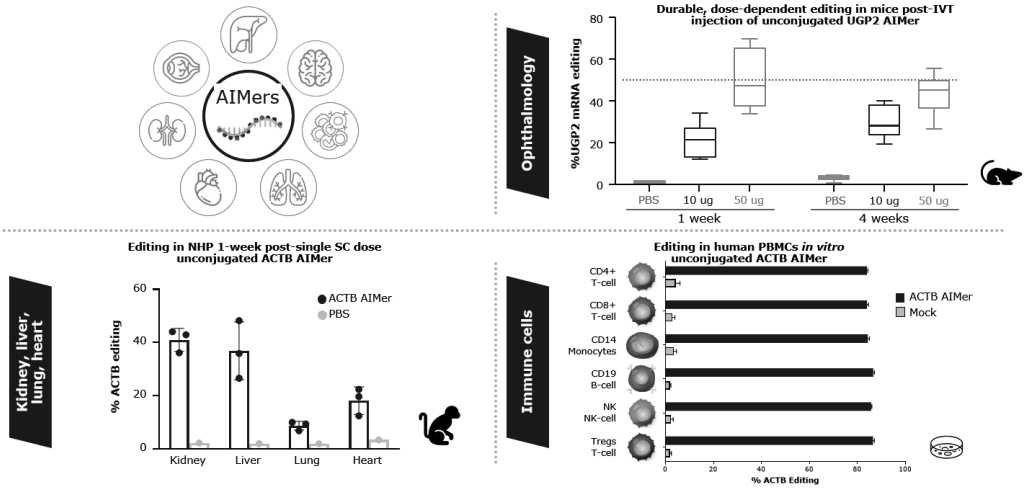


Peak editing	30%	>40%	25%	>40%	50%	>65%

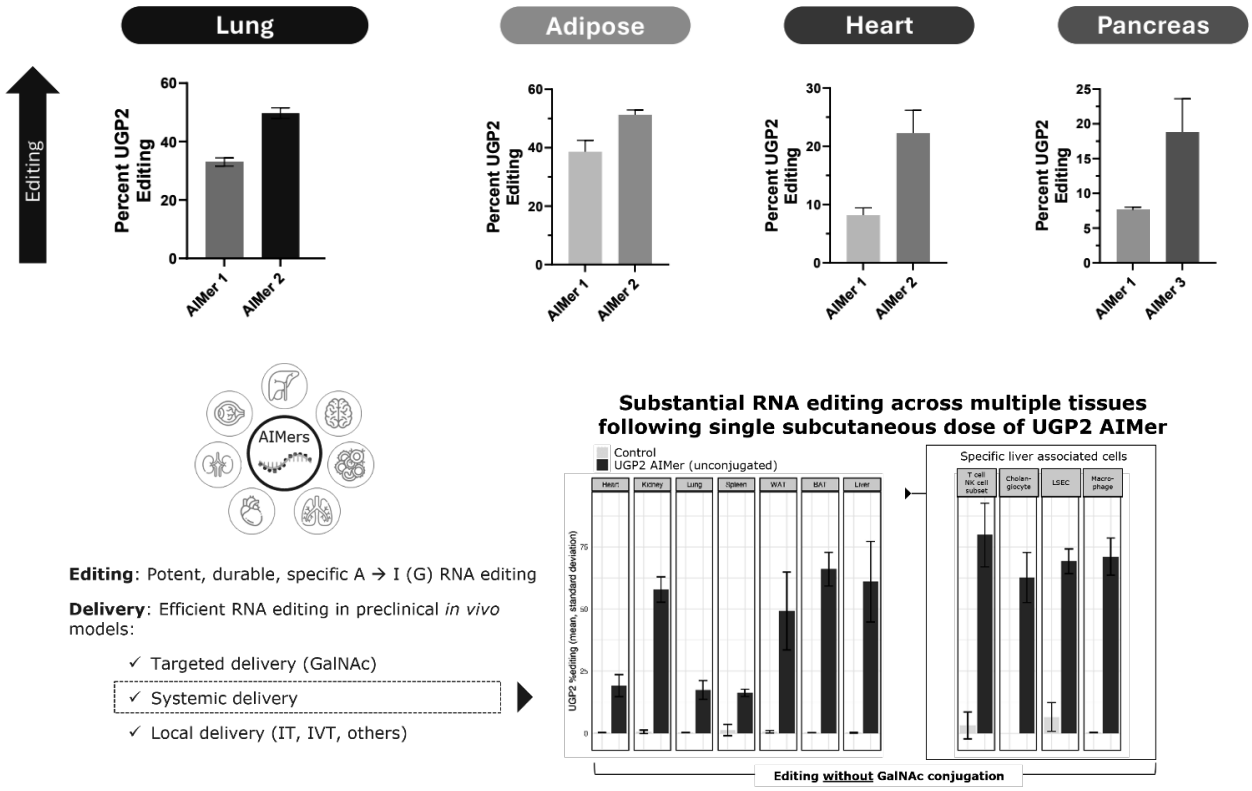
We have also demonstrated that RNA editing observed in mice translates when moving to non-human primates. As shown in the figure below on the left, we observed editing of UGP2 mRNA *in vivo* in multiple regions of CNS following a single unconjugated AIMer dose in a mouse model with human ADAR. As shown in the figure below on the right, we observed editing of ACTB mRNA in multiple regions of CNS following a single, intrathecal unconjugated AIMer dose in non-human primates.



We have also observed productive editing beyond liver and CNS with unconjugated AIMers in multiple tissue types including the retina in mice (below top right), kidney, liver, lung and heart of NHPs (below bottom left), and human PBMCs *in vitro* (below bottom right).

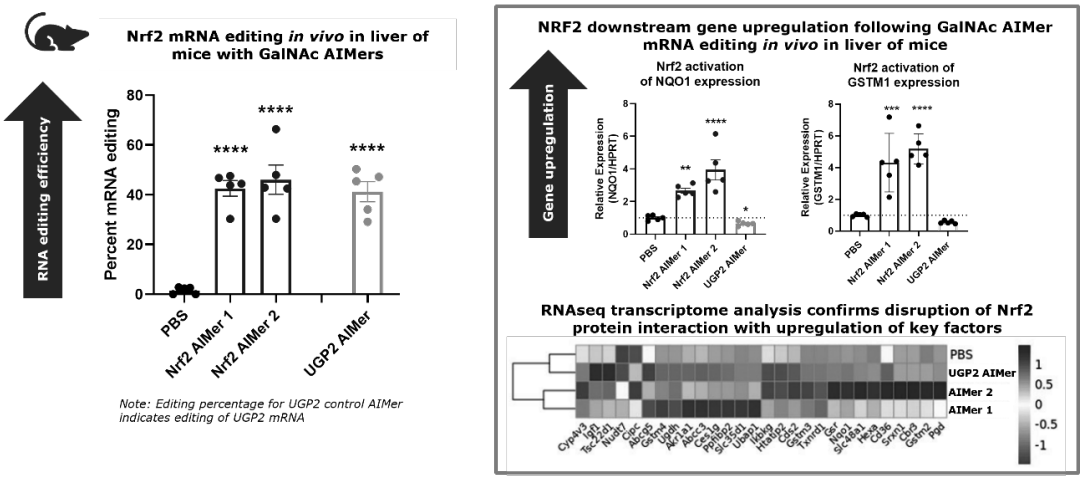


We also observed potent, durable, and specific editing across multiple additional tissues following systemic administration of a single dose of an unconjugated UGP2 AIMer in mice. These additional tissues in mice include heart, kidney, lung, pancreas and spleen, as well as liver cells beyond hepatocytes.



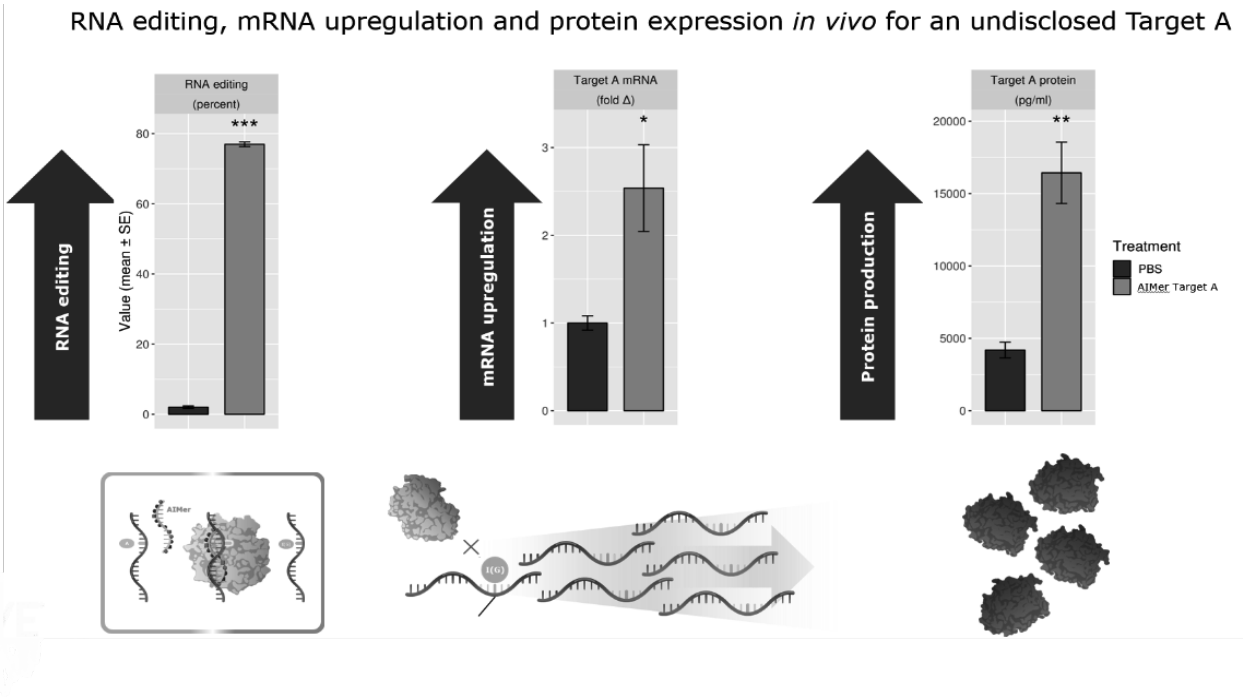
The application of PRISM to RNA editing opens the door to therapeutic applications extending beyond precise correction of genetic mutations, including upregulation of expression, modification of protein function, or alteration of protein stability. To date, we have achieved *in vivo* proof-of-concept modulating protein-protein interactions and upregulating protein expression.

To exemplify our ability to modulate protein-protein interactions using ADAR, we evaluated the well characterized KEAP1/NRF2 system. Through direct protein-protein interactions, KEAP1 negatively regulates the activity of NRF2 as an inducer of antioxidant gene expression. As a proof-of-concept experiment, we investigated if we could mimic the cellular stress response by using ADAR to edit individual amino acids at the protein-protein interaction interface between NRF2 and KEAP1 *in vivo* in mice. If these edits work as designed, we would expect to see downstream upregulation of the NRF2-dependent gene expression program even in the absence of cellular stressors. As shown below, treatment with AIMers resulted in increased expression of known downstream NRF2-dependent genes involved in the antioxidant response. Control treatment did not increase expression of any of the NRF2-dependent genes, indicating that AIMer treatment did not lead to NRF2-dependent gene expression changes through non-specific mechanisms such as increased cellular stress.



Methods: hADAR C57BL/6 mice dosed subQ (days 0, 2, 4) at 10mg/kg GalNAc-conjugated AIMers. Livers harvested (day 7), analyzed for editing and NQO1 expression via Sanger sequencing or qPCR, respectively. Data analyzed via One-way ANOVA with Tukey's multiple comparison test. Asterisks indicate statistical significance to PBS-treated animals as follows: * = p<0.05; ** = p<0.01; *** = p<0.001; **** = p<0.0001

To exemplify our ability to upregulate protein expression levels using ADAR, we evaluated AIMers designed to modify regulatory elements in RNA that mediate protein-RNA or RNA-RNA interactions. Specific structural or sequence motifs that mediate these intermolecular interactions impact RNA processing and stability. In the figures below, we demonstrate *in vivo* proof-of-concept for this application of AIMers using an undisclosed target. Moving from left to right, we first demonstrate over 75% RNA editing of the target, which leads to >2-fold upregulation of that mRNA, and, ultimately, an increase in protein expression (as shown on the far right).



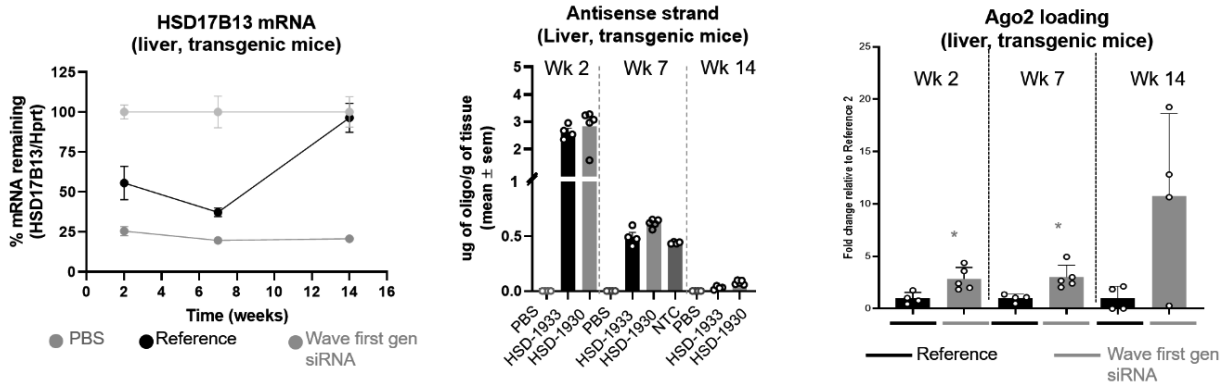
Silencing – RNAi and RNase H-mediated degradation

Using PRISM, we can produce stereopure PN-modified oligonucleotides that promote potent and specific RNA transcript silencing activity in preclinical experiments.

RNAi: We have applied our stereopure PS and PN modifications to the siRNA modality using double-stranded siRNAs and demonstrated potent and durable silencing *in vivo* in transgenic mice, leveraging GalNAc to enhance delivery to liver hepatocytes.

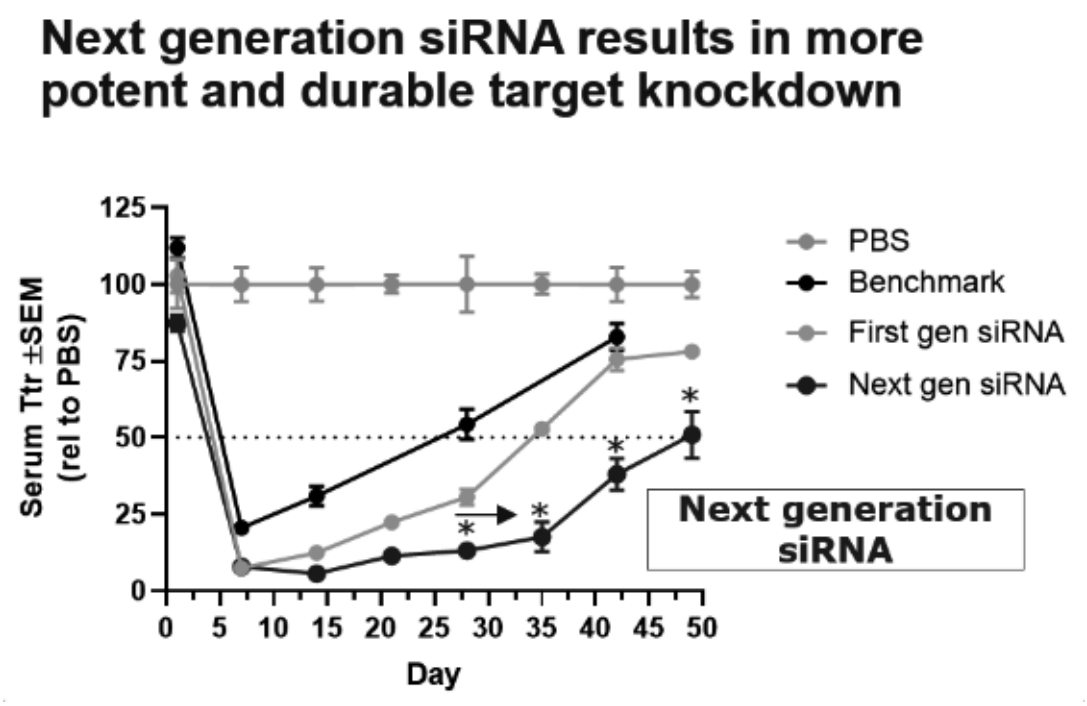
In April 2023, we announced the publication of preclinical data for our novel siRNA formats in the journal of *Nucleic Acids Research*. The preclinical data demonstrated unprecedented Argonaute2 ("Ago2") loading following administration of single subcutaneous GalNAc-siRNA doses, leading to improved potency and durability *in vivo* in mice versus comparator siRNA formats.

The data, shown below, illustrate a GalNAc-siRNA, with controlled stereochemistry and PN backbone chemistry, that led to remarkably durable transcript silencing in mice three months after a single dose, compared with mice treated with a siRNA based on state-of-the-art designs, where expression levels had recovered to control levels (left). The data below (middle and right) also highlight that siRNAs developed with PRISM show improved activity profiles because they support more Ago2 loading than controls.



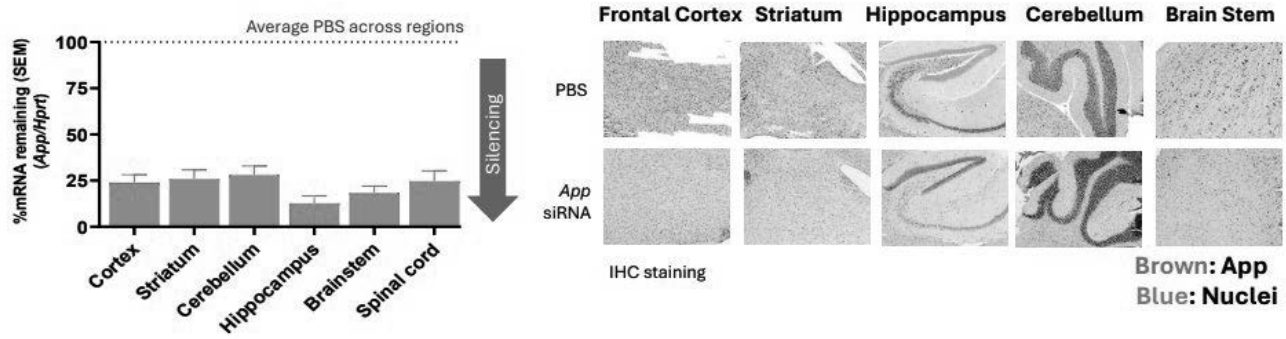
*Left, Middle, and right: Mice expressing human HSD17B13 transgene treated with siRNA (3 mg/kg) or PBS, liver mRNA, guide strand concentration, Ago2 loading quantified. Stats: Two-way ANOVA with post-hoc test * P<0.05, ****P<0.0001. Liu et al., 2023 Nuc Acids Res doi: 10.1093/nar/gkad*

We continue to improve upon our GalNAc-siRNA designs, and our next generation siRNA format has best-in-class potential. As shown in the figure below, our next generation GalNAc-siRNA (shown in dark blue) further improves on the potency and duration of silencing in mice over our first generation GalNAc-siRNA format (shown in light blue) and the benchmark, which is based on a clinically proven format. Translation from preclinical experiments to the clinic is well understood for RNAi, and we expect our next generation siRNA format may support six month or annual subcutaneous dosing.



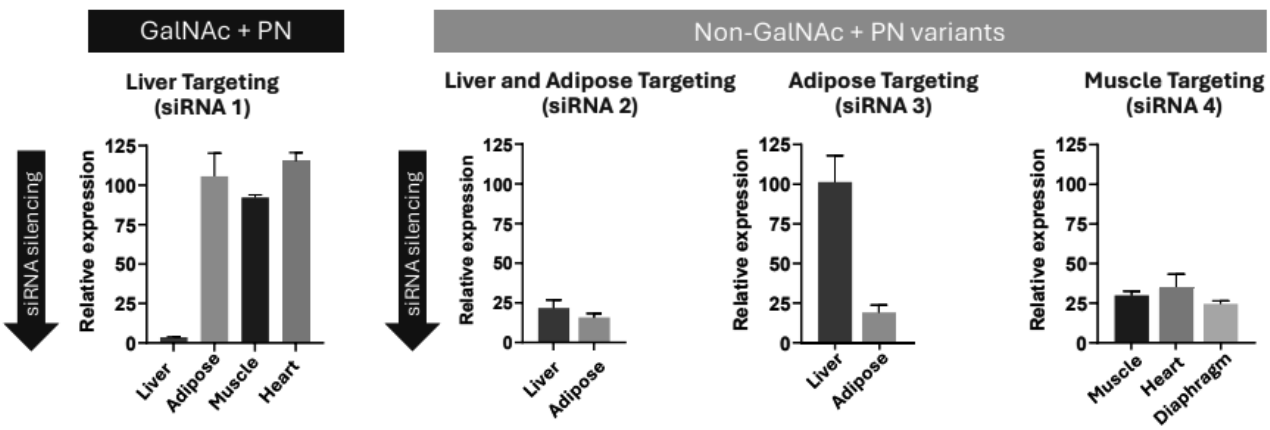
*Foster, DJ. et.al. Mol Ther. 2018, 26(3), 708. B6 mice administered PBS or 0.5 mg/kg of siRNA (subcutaneous). Benchmark: Stats: Mixed Two-way ANOVA followed by post hoc test comparing siRNA vs. Next gen siRNA per day derived from linear mixed effects model * P < 0.0001*

Additionally, in an *in vivo* non-GalNAc siRNA study, we demonstrated that we can achieve potent and sustained silencing with a single dose, with greater than 75% reduction in amyloid-beta precursor protein ("APP") transcripts across all the brain regions through the end of the 16 week study.



PBS (dotted line) or 100 µg of App siRNA administered ICV (n=5-6). PCR assays for RNA PD, relative fold changes of App to Hprt mRNA normalized to % of PBS; Stats: derived from Three-way ANOVA (treatment, tissue, time point) followed by Bonferroni-adjusted post hoc test comparing condition to PBS (data not shown), Next gen siRNA significantly lower than PBS at week 16 for all tissues at P < 0.0001 level; Immunohistochemical analysis of FFPE Mouse Brain tissue labeling App protein (Color Brown) with CS#19389 followed by a ready to use Polymer-HRP 2nd Detection antibody. Nuclei were counterstained with Hematoxylin (Color Blue). Single 100 ug ICV injection

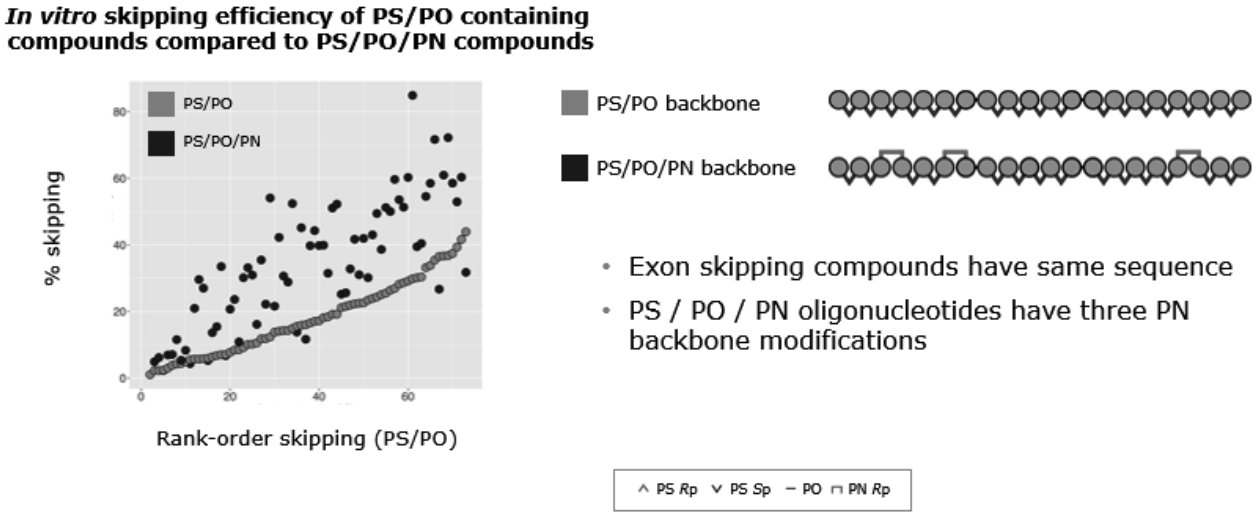
We further demonstrated how our PN chemistry allows us to access new tissues through eight-week mouse experiments using siRNAs to silence gene expression. On the far left, we highlight the well-described impact of using GalNAc to access hepatocytes in the liver. This graph also highlights the limits of a conjugate, as it is cell and tissue specific, so it does not enable silencing in other tissues of interest, like white adipose, muscle or cardiac tissue. To the right, we demonstrate our ability to alternate designs with PN variants to enable access to new and various combinations of tissues, including liver, adipose and muscle, in the absence of any targeting ligand. Depending on the target and indication, we can deploy the design that best fits the biology. Using PRISM, we can change the physicochemical properties of our oligos to deliver to numerous extrahepatic tissues and achieve potent and durable silencing with a single dose.



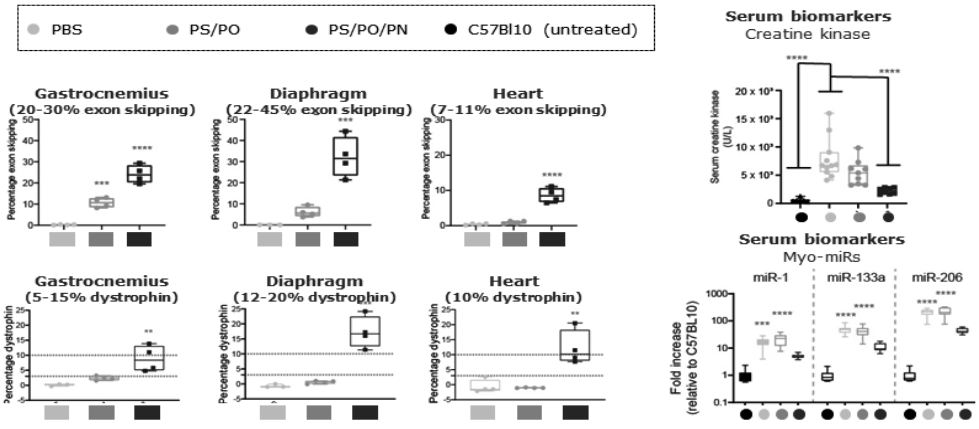
Splicing

With PRISM, we have optimized stereopure oligonucleotides that promote efficient splicing *in vitro*, *ex vivo*, and *in vivo* to restore protein production. In our splicing programs, as with our other modalities, the base modifications and sequence, chemistry and backbone stereochemistry of oligonucleotides impact their activity.

In our *Nucleic Acids Research* paper (Kandasamy et al., 2022; doi: 10.1093/nar/gkac018), we highlight the impact of PN chemistry on exon skipping. In one application from the paper, we plotted the *in vitro* skipping efficiency of compounds containing PS / PO backbone chemistry modifications, depicted in the graph below by the teal dots, which are rank-ordered from left-to-right based on their exon-skipping potency in human myoblasts. The more potent molecules are shifted upwards as they are restoring expression. The navy dots represent the impact of a few stereopure PN modifications in compounds with otherwise identical sequences and 2'-ribose chemical modifications. There is an overall shift upwards in activity among the PS / PO / PN compounds, representing a substantial potency gain in most cases.

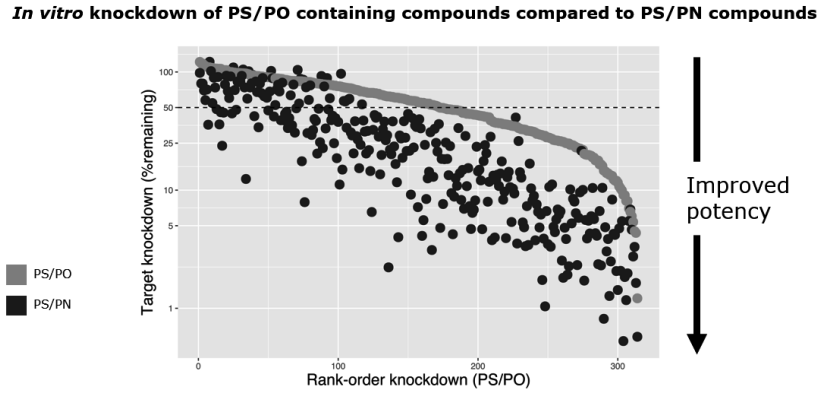


Moving *in vivo*, we demonstrated successful exon skipping in double knockout mice ("dKO"), which lack both utrophin and dystrophin and therefore develop a severe muscular dystrophy phenotype comparable to that observed in patients with DMD. In these mice, exon skipping correlated with dystrophin protein expression, and PN-modified oligonucleotides led to more exon skipping and dystrophin production in all muscles examined after six weeks of treatment (shown below, left). Exon skipping and dystrophin expression improvements correlated with improved serum biomarker profiles in the same mice (shown below, right). These results demonstrate the impact of the judicious placement of PN linkages – with no delivery vehicle or conjugate – which can significantly improve the pharmacological profiles for stereopure compounds.

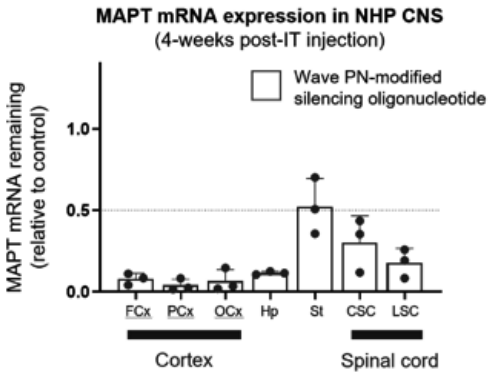


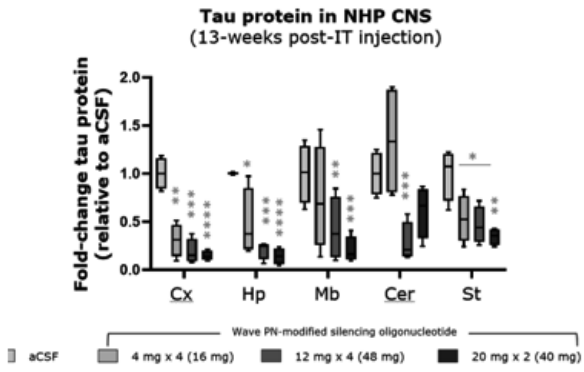
Data adapted from Figure 8, Kandasamy et al., 2022; doi: 10.1093/nar/gkac018 (Stats: One-way ANOVA: *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001)

RNase H-mediated degradation (antisense): In our *Nucleic Acids Research* paper (Kandasamy et al., 2022; doi: 10.1093/nar/gkac018), we illustrated the impact of PN backbone chemistry modifications for an RNase-H mediated silencing modality. In addition to the data reported in the paper, we have performed screens for identifying RNase H-targeting sequences in iCell neurons *in vitro* using free uptake. This screen was initially performed with stereopure molecules with PS and PO backbone chemistry modifications, and the oligonucleotides are rank-ordered from left to right according to their potency. Next, we performed a head-to-head comparison with molecules that contained the same sequence and the same 2'-ribose chemistry, but with the addition of PN chemistry at select locations in the backbone. The introduction of a few PN linkages significantly increases the potency of the vast majority of the stereopure PS / PO molecules, with ~80% of them yielding at least 75% knockdown. These results, shown below, suggest we are able to target sequence space that would otherwise be inaccessible.



Moving *in vivo*, we have demonstrated potent silencing activity of multiple targets in the CNS of non-human primates with stereopure, PN-modified oligonucleotides. In one study, non-human primates received a single 12 mg dose of PN-modified MAPT silencing oligonucleotide by intrathecal injection. This single dose led to substantial and widespread mRNA reduction in the CNS one month after administration, as well as potent mRNA silencing (as shown on the left). In a separate study (shown on the right), NHPs were treated with four monthly intrathecal doses of a stereopure PN-modified MAPT silencing oligonucleotide across three dose levels. This repeat dosing led to 80-90% knockdown though out the CNS.





Our Collaborations

Our business strategy is to develop and commercialize a broad pipeline of RNA medicines. 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 therapeutic programs and maximizing their potential for patients, investing in third-party technologies to further strengthen PRISM and leveraging external partnerships to extend the reach of PRISM into therapeutic areas where our platform demonstrates a competitive advantage.

GSK

On December 13, 2022, Wave Life Sciences USA, Inc. ("Wave USA") and Wave Life Sciences UK Limited ("Wave UK"), two of our direct, wholly-owned subsidiaries entered into a Collaboration and License Agreement (the "GSK Collaboration Agreement") with GSK, which became effective on January 27, 2023. Pursuant to the GSK Collaboration Agreement, we and GSK have agreed to collaborate on the research, development, and commercialization of oligonucleotide therapeutics, including a global exclusive license to WVE-006. The discovery collaboration has an initial four-year research term and combines our proprietary discovery and drug development platform, PRISM™, with GSK's novel genetic insights and its global development and commercial capabilities.

Under the terms of the GSK Collaboration Agreement, we received an upfront payment of $170.0 million, which included a cash payment of $120.0 million and a $50.0 million equity investment. In addition, assuming WVE-006 and GSK's eight collaboration programs achieve initiation, development, launch, and commercialization milestones, we would be eligible to receive up to $3.3 billion in cash milestone payments, which are described in the following paragraphs.

GSK received an exclusive global license to WVE-006, our first-in-class A-to-I(G) RNA editing candidate for alpha-1 antitrypsin deficiency, with development and commercialization responsibilities transferring to GSK after we complete the first-in-patient study. We will be responsible for preclinical, regulatory, manufacturing, and clinical activities for WVE-006 through the initial Phase 1/2 study (RestorAATion), at our sole cost. Thereafter, GSK will be responsible for advancing WVE-006 through pivotal studies, registration, and global commercialization at GSK's sole cost. For the WVE-006 program, we would be eligible to receive up to $225.0 million in development and launch milestone payments and up to $300.0 million in commercialization milestone payments, as well as double-digit tiered royalties up to the high teens as a percentage of net sales.

The collaboration has three components: (1) a discovery collaboration which enables us to advance up to three programs leveraging targets informed by GSK's novel genetic insights; (2) a discovery collaboration which enables GSK to advance up to eight programs leveraging PRISM and our oligonucleotide expertise and discovery capabilities; and (3) an exclusive global license for GSK to WVE-006, our AATD program, that uses our proprietary AIMer technology. Wave will maintain development responsibilities for WVE-006 through completion of RestorAATion-2, at which point development and commercial responsibilities will transition to GSK.

The collaboration will enable us to continue building a pipeline of transformational oligonucleotide-based therapeutics and unlock new areas of disease biology, as well as realize the full value of WVE-006 as a potential best-in-class treatment for AATD that has potential to simultaneously address both liver and lung manifestations of the disease.

The GSK Collaboration Agreement includes options to extend the research term for up to three additional years, which would increase the number of programs available to both parties. We will lead all preclinical research for GSK and our collaboration programs up to IND-enabling studies. We will lead IND-enabling studies, clinical development and commercialization for our collaboration programs. GSK collaboration programs will transfer to GSK for IND-enabling studies, clinical development, and commercialization. Assuming GSK advances eight programs under the collaboration that achieve initiation, development, launch and commercial milestones, we would be eligible to receive up to $1.2 billion in initiation, development, and launch milestones and up to $1.6 billion in commercialization milestones, as well as tiered royalties into the low-teens as a percentage of net sales. Assuming we advance our collaboration programs through the achievement of pre-determined milestones, GSK would be eligible to receive royalty payments and commercial milestones from us.

Under the GSK Collaboration Agreement, each party grants to the other party certain licenses to the collaboration products resulting from the parties' respective collaboration programs as well as specific intellectual property licenses to enable the other party to perform its obligations and exercise its rights under the GSK Collaboration Agreement, including license grants to enable each party to conduct research, development, and commercialization activities pursuant to the terms of the GSK Collaboration Agreement. The parties' exclusivity obligations to each other are limited on a target-by-target basis with regard to targets in the collaboration.

The GSK Collaboration Agreement, unless terminated earlier, will continue until the date on which: (i) with respect to a validation target, the date on which such validation target is not advanced into a collaboration program; or (ii) with respect to a collaboration target, the royalty term has expired for all collaboration products directed to the applicable collaboration target. The GSK Collaboration Agreement contains customary termination provisions, including certain termination rights for convenience, breach, and others, including on a target/program basis or of the GSK Collaboration Agreement in its entirety.

With respect to the $50.0 million equity investment referred to above, simultaneously with our entry into the GSK Collaboration Agreement, we entered into a share purchase agreement with Glaxo Group Limited ("GGL"), an affiliate of GSK, pursuant to which we agreed to sell to GGL 10,683,761 of our ordinary shares at a purchase price of $4.68 per share, for an aggregate purchase price of

approximately $50.0 million (the "GSK Equity Investment"). The GSK Equity Investment closed on January 26, 2023. The shares purchased by GGL in the GSK Equity Investment are subject to lock-up and standstill restrictions and carry certain registration rights, customary for transactions of this kind.

Asuragen

In November 2019, we entered into an agreement with Asuragen (which was acquired by Bio-Techne Corporation in April 2021), a molecular diagnostics company, for the development and potential commercialization of companion diagnostics for our investigational allele-selective therapeutic programs targeting HD. This collaboration uses Asuragen's market-leading repetitive sequence diagnostic expertise to provide scalable SNP phasing to support development programs and future commercialization at a global level. Asuragen has leveraged its AmplideX® PCR technology to develop companion diagnostic tests designed to size and phase HTT CAG repeats with the SNPs targeted by WVE-003, our current HD program being investigated in the ongoing SELECT-HD clinical trial as well as those SNPs targeted by our previous investigational therapeutic programs. These tests are designed to aid clinicians in selecting HD patients by identifying the SNPs that are in phase with the CAG-expanded allele.

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 initiated the build out of manufacturing space and related capabilities. Through our internal manufacturing, we have the capacity to support multiple discovery-, preclinical-, and early clinical-stage programs and have the established expertise to efficiently conduct manufacturing runs for oligonucleotides across a spectrum of modalities. In addition to manufacturing space, the Lexington facility includes additional laboratory and office space. This facility supplements our existing Cambridge, Massachusetts laboratory and office space headquarters, enhances our ability to secure drug substance 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 the fourth quarter of 2017.

We believe that leveraging our internal manufacturing capabilities along with expertise from CMOs facilitates our growth and enhances our ability to secure drug substance for current and future research, clinical and early-stage commercial development activities. 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 product candidates can be manufactured at scale and with production and procurement efficiencies that will result in commercially competitive costs.

Intellectual Property

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

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. Our portfolio includes multiple issued patents, including in major market jurisdictions such as the United States, Europe and Japan. We also have applications pending in multiple jurisdictions around the world, including these major market jurisdictions.

Synthetic Methodologies

Our patent portfolio includes multiple families that protect synthetic methodologies and/or reagents for generating stereopure oligonucleotide compositions.

Certain such families have 20-year expiration dates that range from 2029 to at least 2043. Some of these families have issued patents in several jurisdictions, including in major market jurisdictions such as the United States, Europe, and/or Japan, have pending applications in multiple jurisdictions including in these major market jurisdictions, or are in the international stage.

We also co-own with the University of Tokyo 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. Several of our patent filings directed to stereopure compositions have entered national stage prosecution in multiple jurisdictions and some have issued in one or more jurisdictions; others are in the international stage. Certain filings offer 20-year protection terms that range from 2033 to at least 2044.

We also co-own with Shin Nippon Biomedical Laboratories, Ltd. various patent families, some of which include one or more issued patents, including in major market jurisdictions; these filings 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 Patents Act 1994 of Singapore (the "Singapore Patents Act") provides that a person residing in Singapore is required to obtain written authorization from the Singapore Registrar of Patents (the "Registrar") 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 Registrar 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 are required to make such filings in the future, without first obtaining written authorization from the Registrar. We have notified the Registrar of such filings and we have since implemented measures to address the requirements of Section 34 moving forward. To date, the Registrar has offered a compound of some of the offences considered against payment of a sum of S$50 to S$150 per considered case. 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$2,500, or to prosecute the offence subject to the other penalties noted above. Per requests in the Registrar's most recent decision, we have submitted approximately 140 patent applications in multiple patent families, most of which are related to previously reported applications, to the Intellectual Property Office of Singapore ("IPOS"). The IPOS may consider the filing of some or all of these applications to have breached Section 34 requirements per IPOS' current interpretation of Section 34, and we are waiting for IPOS' decision on these applications. We cannot assure you that the Registrar will offer to compound any such violations of Section 34, or that any offer to compound will be for an amount similar to previous compound offers.

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 oligonucleotides, 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 oligonucleotides, 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.

Obesity
There are two GLP-1 receptor agonists approved in the United States for the treatment of obesity: Saxenda (liraglutide, Novo Nordisk) and Wegovy (semaglutide, Novo Nordisk). Zepbound (tirzepatide, Eli Lilly), approved by the FDA in November 2023, is a GLP-1/GIP receptor agonist. Beyond these approved therapies, there are investigational oral GLP-1 receptor agonists and other GLP-1 receptor agonist combinations (e.g., GLP-1/GIP/glucagon receptor agonists, GLP-1/glucagon receptor agonists, GLP-1/amylin receptor agonists, GLP-1/GLP-2 receptor agonists, etc.) in various stages of clinical development. Other FDA-approved therapies for obesity include Xenical (H2-Pharma), Qsymia (Vivus), and Contrave (Currax Pharmaceuticals).

Arrowhead has a program targeting INHBE in Phase 1/2 development, and Alnylam has a preclinical INHBE program. In addition, multiple other companies are pursuing approaches for obesity that are complementary to GLP-1 receptor agonists and aim to reduce fat mass while preserving or increasing lean mass.

Alpha-1 Antitrypsin Deficiency ("AATD")
There are five treatments approved in the United States for AATD: Prolastin (Grifols), Prolastin-C (Grifols), Aralast NP (Takeda), Zemaira (CSL Behring), and Glassia (Takeda). All five contain plasma-derived human alpha1-proteinase inhibitor and are indicated for chronic augmentation and maintenance therapy in adults with emphysema due to congenital deficiency of alpha1-proteinase inhibitor (Alpha1-PI). The prescribing information for each states that the effect of augmentation therapy with any alpha1-proteinase inhibitor on pulmonary exacerbations and on the progression of emphysema in Alpha1-PI deficiency has not been demonstrated in randomized, controlled clinical trials.

Beyond WVE-006, we are aware of one other clinical stage RNA editing program in development for AATD lung and/or liver disease from Korro Bio (Phase 1/2). Beam Therapeutics has a Phase 1/2 study ongoing with a DNA base editing approach. There are also a number of companies with investigational drugs in clinical development for AATD lung disease: Kamada (Phase 3), Krystal Biotech (Phase 1), Mereo BioPharma (Phase 2 completed), and Sanofi (Phase 2), among others. Arrowhead Pharmaceuticals and Takeda have an investigational drug in Phase 3 clinical development for AATD liver disease, and Biomarin is initiating a Phase 1 study for this indication.

Duchenne Muscular Dystrophy ("DMD")
There are two exon skipping treatments approved in the United States for the treatment of DMD in patients who have a confirmed mutation of the DMD gene amenable to exon 53 skipping: Sarepta Therapeutics' Vyondys 53 (golodirsen) was approved in 2019, and NS Pharma's Viltepso (viltolarsen) was approved in 2020. Both therapies received accelerated approval based on dystrophin production, and in accordance with US accelerated approval regulations, the FDA is requiring Sarepta and NS Pharma to each conduct a clinical trial to verify and describe their drug's clinical benefit. If the trials fail to verify clinical benefit, the FDA could initiate proceedings to withdraw approval of the respective drug. To date, no clinical benefit of Vyondys 53 or Viltepso has been established.

Sarepta Therapeutics' Elevidys, a microdystrophin gene therapy, is available in the United States and some ex-EU markets. Its current indication in the US is for ambulatory and non-ambulatory DMD patients aged at least four years who have a confirmed mutation in the DMD gene. This includes patients who have a DMD mutation amenable to exon 53 skipping. The indication that includes ambulatory DMD patients was granted under a traditional approval, and the indication that includes non-ambulatory DMD patients was approved under accelerated approval based on expression of Elevidys micro-dystrophin. Continued approval for non-ambulatory DMD patients may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Other therapies available for DMD include Santhera Pharmaceuticals' Agamree (vamorolone), an alternative steroid which was approved in the US and EU in 2023 and Italfarmaco/ITF Therapeutics' Duvyzat (givinostat), a histone deacetylase inhibitor which was approved in the United States in 2024.

Several other companies have investigational drugs in clinical development targeting DMD more broadly, including patients amenable to exon 53 skipping. These include Capricor Therapeutics (Preregistration with FDA), Dystrogen Therapeutics (Phase 1), Edgewise Therapeutics (Phase 2), Regenxbio (Phase 1/2), and Solid Biosciences (Phase 1/2), among others. Based on available information, we do not believe there are other companies with investigational programs specifically for exon 53 skipping in clinical development. Several companies also have ongoing preclinical programs for DMD that may directly or indirectly target patients amenable to exon 53 skipping. These companies include Code Bio, Dyne Therapeutics, PepGen, Precision BioSciences, Ultragenyx Pharmaceutical, and Vertex Pharmaceuticals, among others.

Huntington's Disease ("HD")
There are no approved treatments available to slow the progression of HD. Austedo (Teva), tetrabenazine (generic), and, in 2023, Ingrezza (Neurocrine Biosciences) have been approved for the treatment of chorea associated with HD.

We believe, based on publicly available information, that Alnylam (Phase 1), Annexon Biosciences (Phase 2 completed), Ionis Pharmaceuticals and Roche (Phase 2), Mitochon Pharmaceuticals (Phase 1/2), Prilenia Therapeutics (Preregistration with EMA), PTC Therapeutics (Phase 2), Skyhawk Therapeutics (Phase 1), uniQure (Phase 1/2), and Vico Therapeutics (Phase 1/2), among others, have investigational drugs aimed at slowing the progression of HD in clinical development. To our knowledge, we have the most advanced clinical stage program targeting allele-selective mHTT lowering.

Several companies have ongoing discovery or preclinical programs for HD, including Atalanta Therapeutics, Ophidion, Roche, Sangamo Therapeutics and Takeda, Spark Therapeutics, and Voyager Therapeutics and Novartis, among others.

Molecules to treat symptoms associated with HD are also in development. For instance, SOM Biotech has completed a Phase 2 study of an investigational agent for chorea in HD.

Government Regulation

FDA Approval Process for Drug Products

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 pharmaceutical 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 drug products, partial or total suspension of production, withdrawal of drug products 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 testing in compliance with applicable FDA good laboratory practice regulations and other requirements ("GLP");
- submission to the FDA of an 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 practice ("GCP"), as well as other clinical research regulations, 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 ensure suitable purity, identity, strength, quality and stability in compliance with cGMP;
- satisfactory completion of an FDA pre-approval inspection of the facility or facilities at which the product is manufactured to assess compliance with cGMP;
- 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 regulatory 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.

Nonclinical tests may include *in vitro* and *in vivo* (animal model) studies to assess the toxicity and other safety characteristics of the product candidate, as well as important aspects of drug pharmacology and PD. The Consolidated Appropriations Act for 2023, signed into law on December 29, 2022, (P.L. 117-328) amended the FDCA and the Public Health Service Act to specify that nonclinical testing for drugs and biologics may, but is not required to, include *in vivo* animal testing. According to the amended language, a sponsor may fulfill nonclinical testing requirements by completing various *in vitro* assays (e.g., cell-based assays, organ chips, or microphysiological systems), *in silico* studies (i.e., computer modeling), other human or nonhuman biology-based tests (e.g., bioprinting), or *in vivo* animal tests.

The results of nonclinical 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. Some long-term nonclinical testing to further establish the safety profile of the product candidate, as well as manufacturing processes development and drug quality evaluation, continues after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions related to the proposed clinical trial and places the IND 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 IRB for 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 the clinical plan or in compliance with GCP. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Clinical trials involve the administration of the product candidate to human subjects under the supervision of qualified investigators in accordance with GCP, as well as other regulations, which include, among other things, the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Sponsors of clinical trials of certain FDA-regulated products generally must register and disclose certain clinical trial information to a public registry maintained by the National Institutes of Health ("NIH"). In particular, information related to the product, patient population, phase of investigation, study site locations and other aspects of the clinical trial are made public as part of the registration of the clinical trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs. Although sponsors are also obligated to disclose the results of their clinical trials after completion, such disclosure can be delayed in some cases for up to two years after the date of completion of the trial. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government. The NIH's Final Rule on ClinicalTrials.gov registration and reporting requirements became effective in 2017, and the government has brought enforcement actions against non-compliant clinical trial sponsors.

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, statistical 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.

Progress reports detailing progress and safety data gathered from clinical trials must be submitted at least annually to the FDA. Safety reports are submitted more frequently if certain SAEs occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted as part of NDA review.

In the Consolidated Appropriations Act for 2023, Congress amended the FDCA to require sponsors of a Phase 3 clinical trial, or other "pivotal study" of a new drug to support marketing authorization, to submit a diversity action plan for such clinical trial. The action plan must include the sponsor's diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. A sponsor must submit a diversity action plan to FDA by the time the sponsor submits the trial protocol to the agency for review. The FDA may grant a waiver for some or all of the requirements for a diversity action plan. It is unknown at this time how the diversity action plan may affect Phase 3 trial planning and timing, but if FDA objects to a sponsor's diversity action plan and requires the sponsor to amend the plan or take other actions, it may delay trial initiation.

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, along with information relating to the product's pharmacology, chemistry, manufacturing, and controls, and proposed labeling, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. Under federal law, the fee for the submission of an NDA with clinical data is substantial (for example, for fiscal year 2025 this application fee exceeds $4.3 million), and the sponsor of an approved NDA is also subject to an annual program fee, currently more than $400,000 per program. These fees are typically adjusted annually, but exemptions and waivers may be available under certain circumstances, including NDA fees for products with orphan designation.

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 review. Any resubmitted application, following a refusal to file action, is also subject to 60-day review before the FDA accepts it for filing.

Under the Prescription Drug User Fee Act ("PDUFA"), for original NDAs, the FDA has ten months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months from the filing date for an application with priority review. For all new molecular entity ("NME") NDAs, the ten and six-month time periods run from the filing date; for all other original applications, the ten and six-month time periods run from the submission date. Despite these review goals, it is not uncommon for FDA review of an NDA to extend beyond the goal date.

Once the submission has been accepted for filing, the FDA begins an in-depth review. As noted above, the FDA has agreed to specified performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date it is accepted for filing (i.e., within 12 months from submission), and most applications for "priority review" products are meant to be reviewed within six months from the date the application is accepted for filing (i.e., within eight months from submission). The review process may be extended by the FDA for three additional months to consider new information or in the case of a clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

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.

Additionally, the FDA may refer any NDA, including applications for novel drug candidates which present difficult questions of safety or efficacy, to an advisory committee. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a 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 when making final decisions on approval. The FDA likely will re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the NDA review process. The FDA also may require submission of a risk evaluation and mitigation strategy ("REMS") if it determines that a REMS is necessary to ensure that the benefits of the drug outweigh its risks and to assure the safe use of the drug or biological product. The REMS could include medication guides, physician communication plans, assessment plans and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. In addition, the REMS must include a timetable to assess the strategy, often at 18 months, three years, and seven years after the strategy's approval. The FDA determines the requirement for a REMS, as well as the specific REMS

provisions, on a case-by-case basis. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve an NDA without a REMS, if required.

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 an 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. The FDA may 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.

Under the Pediatric Research Equity Act ("PREA"), as amended, an NDA or supplement to an NDA must contain data that are adequate to assess the safety and efficacy of the product candidate for the claimed indications in all relevant pediatric populations and to support dosing and administration for each pediatric population for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. PREA requires a sponsor who is planning to submit a marketing application for a product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration to submit an initial Pediatric Study Plan ("PSP") within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 clinical trial. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including trial objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from pre-clinical studies, early phase clinical trials or other clinical development programs.

The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. The approval process is lengthy and often difficult, and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, it may issue an approval letter or a Complete Response Letter ("CRL"). An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL indicates that the review cycle for an application is complete and that the application will not be approved in its present form. A CRL outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a CRL is issued, the applicant may choose to either resubmit the NDA addressing all of the deficiencies identified in the letter or withdraw the application. The FDA has committed to reviewing such resubmissions in response to an issued CRL in either two or six months depending on the type of information included. 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.

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 authority 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 nonclinical studies and clinical trials.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited development or review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include fast track designation, breakthrough therapy designation and priority review designation.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need by providing a therapy where none exists or a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast

track designation provides opportunities for more frequent interactions with the FDA review team to expedite development and review of the product. The FDA may also review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor and the FDA agree on a schedule for the submission of the application sections and the sponsor pays any required user fees upon submission of the first section of the NDA. In addition, fast track designation may be withdrawn by the sponsor or rescinded by the FDA if the designation is no longer supported by data emerging from the clinical trial process. In addition, in 2012 Congress created a regulatory program for product candidates designated by FDA as "breakthrough therapies" upon a request made by the IND sponsors. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs or biologics designated as breakthrough therapies are also eligible for accelerated approval of their respective marketing applications. The FDA must take certain actions with respect to breakthrough therapies, such as holding timely meetings with and providing advice to the product sponsor, which are intended to expedite the development and review of an application for approval of a breakthrough therapy. Finally, the FDA may designate a product for priority review if it is a drug or biologic that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness over existing therapy. The FDA determines at the time that the marketing application is submitted, on a case-by-case basis, whether the proposed drug represents a significant improvement in treatment, prevention or diagnosis of disease when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months for an NME NDA from the date of filing.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Furthermore, fast track designation, breakthrough therapy designation and priority review do not change the standards for approval and may not ultimately expedite the development or approval process.

Accelerated Approval Pathway

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval from the FDA and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a drug or biologic when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality ("IMM") and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA will require that a sponsor of a drug receiving accelerated approval perform post-marketing clinical trials to verify and describe the predicted effect on IMM or other clinical endpoint, and the product may be subject to expedited withdrawal procedures. Drugs and biologics granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval when the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate long-term clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. For example, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large clinical trials to demonstrate a clinical or survival benefit.
The accelerated approval pathway is contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory study(ies) to verify and describe the drug's clinical benefit. As a result, a drug approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of clinical trial(s) to establish the effect on the clinical endpoint. Failure to conduct and complete the required confirmatory study(ies) to confirm the predicted clinical benefit of the product

would allow the FDA to withdraw approval of the drug. As part of the Consolidated Appropriations Act for 2023, Congress provided the FDA additional statutory authority to mitigate potential risks to patients from continued marketing of ineffective drugs previously granted accelerated approval. Under the act's amendments to the FDCA, FDA may require the sponsor of a product to have a confirmatory trial underway as a condition for granting accelerated approval of the NDA. The sponsor must also submit progress reports on a confirmatory trial every six months until the trial is complete, and such reports are published on FDA's website. The amendments also give FDA the option of using expedited procedures to withdraw product approval if the sponsor's confirmatory trial fails to verify the claimed clinical benefits of the product.

All promotional materials for product candidates being considered and approved under the accelerated approval program are subject to prior review by the FDA.

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 (including third-party manufacturers) are required to register their establishments with the FDA and some state agencies and are subject to periodic announced or unannounced inspections by the FDA and some state agencies for assessment of compliance with cGMP. 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 mandatory revisions to the approved labeling to add new safety information; imposition of post-market or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, 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;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- fines, warning letters or other enforcement-related 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 approvals;
- withdrawal of approval for any products approved through FDA's accelerated approval pathway if required confirmatory trials are not completed on time, or at all;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment, or exclusion from federal healthcare programs.

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 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.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act ("PDMA") which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and

regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription drug product samples and impose requirements to ensure accountability in distribution. Furthermore, the Drug Supply Chain Security Act ("DSCSA") was enacted with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a ten-year period that culminated in November 2023. After an additional one-year stabilization period to give entities subject to the DSCSA additional time to finalize interoperable tracking systems and to ensure supply chain continuity, the applicable requirements under the DSCSA became fully enforceable as of November 27, 2024. From time to time, new legislation and regulations may be implemented that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. It is impossible to predict whether further legislative or regulatory changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

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.
Under PREA, submission of a pediatric assessment is not required for pediatric investigation of a product that has been granted orphan drug designation. However, under the FDA Reauthorization Act of 2017 ("FDASIA"), the scope of the PREA was extended to require pediatric studies for products intended for the treatment of an adult cancer that are directed at a molecular target and that are determined to be substantially relevant to the growth or progression of a pediatric cancer. In addition, the FDA finalized guidance in 2018 indicating that it does not expect to grant any additional orphan drug designation to products for pediatric subpopulations of common diseases. Nevertheless, the FDA intends to still grant orphan drug designation to a drug or biologic that otherwise meets all other criteria for designation when it prevents, diagnoses or treats either (i) a rare disease that includes a rare pediatric subpopulation, (ii) a pediatric subpopulation that constitutes a valid orphan subset, or (iii) a rare disease that is in fact a different disease in the pediatric population as compared to the adult population.

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 (such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or in instances of drug supply issues), for seven years. Orphan exclusivity does not block the approval of a different drug or biologic for the same rare disease or condition, nor does it block the approval of the same drug or biologic for different conditions. 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.
A product with orphan drug designation may not receive orphan exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Recent court cases have challenged the FDA's approach to determining the scope of orphan drug exclusivity; however, at this time the agency continues to apply its long-standing interpretation of the governing regulations and has stated that it does not plan to change any orphan drug implementing regulations.

European Union Orphan Drug Designation

In the EU, orphan drug designation by the European Commission (the "EC") provides regulatory and financial incentives for companies to develop and market therapies that meet the following requirements: (1) the product is intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. To be considered for orphan drug designation in the EU, companies must provide data that demonstrate the plausibility for use of the investigational therapy in the treatment of the disease and establish that the drug has the potential to provide relevant advantages or a major contribution to patient care over existing therapies.

Among the incentives available to medicines designated as orphan drugs by the EC are ten-year market exclusivity in the EU after product approval, eligibility for conditional marketing authorization, protocol assistance from the European Medicines Agency at reduced fees during the product development phase and direct access to centralized marketing authorization in the EU. The exclusivity period may be reduced to six years if, at the end of the fifth year, the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. In addition, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities of the product. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the similar product is deemed safer, more effective or otherwise clinically superior to the original orphan medicinal product. Orphan drug designation must be requested before submitting an application for marketing authorization. Orphan drug designation does not, in itself, convey any advantage in, or shorten the duration of, the regulatory review and authorization process.

Pediatric Exclusivity and Pediatric Use

The Best Pharmaceuticals for Children Act ("BPCA") provides NDA holders a six-month period of non-patent marketing 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, 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. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application for the same drug product for the same indications. The issuance of a written request does not require the sponsor to undertake the described studies. Applications under the BPCA are treated as priority applications.

The Hatch-Waxman Act and Marketing Exclusivity

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute and also enacted Section 505(b)(2) of the FDCA. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application ("ANDA") to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing conducted for a drug product previously approved under an NDA, known as the reference listed drug ("RLD"). Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug.

In contrast, Section 505(b)(2) enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy data for an existing product, or published literature, in support of its application. Section 505(b)(2) NDAs may provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products; for example, an applicant may be seeking approval to market a previously approved drug for new indications or for a new patient population that would require new clinical data to demonstrate safety or effectiveness. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. A Section 505(b)(2) applicant may eliminate the need to conduct certain nonclinical or clinical studies, if it can establish that reliance on studies conducted for a previously approved product is scientifically appropriate. Unlike the ANDA pathway used by developers of bioequivalent versions of innovator drugs, which does not allow applicants to submit new clinical data other than bioavailability or bioequivalence data, the 505(b)(2) regulatory pathway does not preclude the possibility that a follow-on applicant would need to conduct additional clinical trials or nonclinical studies; for example, they may be seeking approval to market a previously approved drug for new indications or for a new patient population that would require new clinical data to demonstrate safety or effectiveness. The FDA may then approve the new product for all or some of the label indications for which the RLD has been approved, or for any new indication sought by the Section 505(b)(2) applicant, as applicable.

Upon NDA approval of a new chemical entity ("NCE"), which is a drug that contains no active moiety that has been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity. During the exclusivity period, the FDA cannot accept for review any ANDA or 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, a follow-on product application may be submitted one year before NCE exclusivity expires if a Paragraph IV certification, which states that the listed patent for the RLD is invalid or will not be infringed by the follow-on product, is filed on an NCE patent and any time after approval if the application is filed based on a new indication or a new formulation.

The Hatch-Waxman Act also provides three years of data exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing 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, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving follow-on applications for drugs containing the original active agent. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA or 505(b)(2) NDA may be filed before the expiration of the exclusivity period. Five-year and three-year exclusivity also will not delay the submission or approval of a traditional NDA filed under Section 505(b)(1) of the FDCA. However, an applicant submitting a traditional NDA would be required to either 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.

Patent Term Restoration

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 Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for any 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 ("USPTO"), 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.

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 appropriate *in vitro* diagnostic product ("IVD") for such use. IVDs are regulated by the FDA as medical devices, and since 2014 the agency has 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 therapeutic product.

The three types of marketing pathways for medical devices, including IVDs, are clearance of a premarket notification under Section 510(k) of the FDCA ("510(k)"), approval of a premarket approval application ("PMA") or authorization of a De Novo classification request ("*De Novo*"). If a company is required to perform clinical trials to support the safety and effectiveness of an IVD, and the IVD is viewed as a significant risk device, the sponsor will have to submit an investigational device exemption application ("IDE") to the FDA, which is similar in format and function to an IND. If the diagnostic test and the therapeutic drug are studied together to support their respective approvals, any clinical trials involving both product candidates 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 or classified through the De Novo process, and placed on the market will be subject to many of the same regulatory requirements that apply to approved drugs. However, the FDA may decide that it is appropriate to approve such a therapeutic product without an approved or cleared *in vitro* companion diagnostic device when the drug or therapeutic biologic is intended to treat a serious or life-threatening condition for which no satisfactory alternative treatment exists and the FDA determines that the benefits from the use of a product with an unapproved or uncleared *in vitro* companion diagnostic device are so pronounced as to outweigh the risks from the lack of an approved or cleared *in vitro* companion diagnostic device. The FDA encourages sponsors considering developing a therapeutic product that requires a companion diagnostic to request a meeting with both relevant device and therapeutic product review divisions to ensure that the product development plan will produce sufficient data to establish the safety and effectiveness of both the

therapeutic product and the companion diagnostic. Because the FDA's policies on companion diagnostics is set forth only in guidance, this policy is subject to change and is not legally binding.

European Union Regulation of Drug Products

In addition to regulations in the United States, we are and will be subject, either directly or through our distribution partners, to a variety of regulations in other jurisdictions governing, among other things, clinical trials, the privacy of personal data and commercial sales and distribution of our products, if approved.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in non-U.S. countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a process that requires the submission of a clinical trial application much like an IND prior to the commencement of human clinical trials. In Europe, for example, a clinical trial application ("CTA"), must be submitted to the competent national health authority and to independent ethics committees in each country in which a company plans to conduct clinical trials. Once the CTA is approved in accordance with a country's requirements, clinical trials may proceed in that country. Under the EU Clinical Trials Regulation, which was adopted in April 2014 and replaced the Clinical Trials Directive, a harmonized assessment and supervision process was implemented as of January 31, 2022 for clinical trials throughout the EU, via a Clinical Trials Information System ("CTIS"). The CTIS will contain the centralized EU portal and database for clinical trials conducted in the EU and will allow for a centralized review process. This harmonized submission process became mandatory for new CTA submissions to be filed beginning on February 1, 2023. However, the extent to which ongoing and new clinical trials will be governed by the Clinical Trials Regulation varies. Clinical trials for which an application was submitted prior to January 31, 2022 under the Clinical Trials Directive, or between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive, remained governed by the Directive until January 31, 2025. After January 31, 2025, all clinical trials, including those that are ongoing, are now subject to the provisions of the Clinical Trials Regulation. Under the new centralized process, if the EU member state leading the CTA review approves or rejects the application, the decision will apply to all involved member states.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country, even though there is already some degree of legal harmonization in the EU member states resulting from the national implementation of underlying EU legislation. In all cases, the clinical trials are conducted in accordance with GCP and other applicable regulatory requirements.

To obtain a marketing license for a new drug or medicinal product in the European Union, the sponsor must obtain approval of a marketing authorization application ("MAA"). The way in which a medicinal product can be approved in the European Union depends on the nature of the medicinal product.

The centralized procedure results in a single marketing authorization granted by the European Commission that is valid across the European Union, as well as in Iceland, Liechtenstein, and Norway. The centralized procedure is compulsory for human drugs that: (i) are derived from biotechnology processes, such as genetic engineering, (ii) contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative diseases, autoimmune and other immune dysfunctions and viral diseases, (iii) are officially designated "orphan drugs" (drugs used for rare human diseases) and (iv) are advanced-therapy medicines, such as gene-therapy, somatic cell-therapy or tissue-engineered medicines. The centralized procedure may at the request of the applicant also be used for human drugs which do not fall within the above mentioned categories if (a) the human drug contains a new active substance which was not previously authorized in the European Community; or (b) the applicant shows that the medicinal product constitutes a significant therapeutic, scientific or technical innovation or that the granting of authorization in the centralized procedure is in the interests of patients at the European Community level.

Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of a marketing authorization application by the EMA is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP), with adoption of the actual marketing authorization by the European Commission thereafter. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest from the point of view of therapeutic innovation, defined by three cumulative criteria: the seriousness of the disease to be treated; the absence of an appropriate alternative therapeutic approach, and anticipation of exceptional high therapeutic benefit. In this circumstance, EMA ensures that the evaluation for the opinion of the CHMP is completed within 150 days (excluding clock stops) and the opinion issued thereafter.

The mutual recognition procedure ("MRP") for the approval of human drugs is an alternative approach to facilitate individual national marketing authorizations within the European Union. Basically, the MRP may be applied for all human drugs for which the centralized procedure is not obligatory. The MRP is applicable to the majority of conventional medicinal products and is based on the principle of recognition of an already existing national marketing authorization by one or more member states. In the MRP, a marketing authorization for a drug already exists in one or more member states of the European Union and subsequently marketing authorization applications are made in other European Union member states by referring to the initial marketing authorization. The member state in which the marketing authorization was first granted will then act as the reference member state. The member states where the marketing authorization is subsequently applied for act as concerned member states. After a product assessment is

completed by the reference member state, copies of the report are sent to all member states, together with the approved summary of product characteristics, labeling and package leaflet. The concerned member states then have 90 days to recognize the decision of the reference member state and the summary of product characteristics, labeling and package leaflet. National marketing authorizations within individual member states shall be granted within 30 days after acknowledgement of the agreement.

Should any member state refuse to recognize the marketing authorization by the reference member state, on the grounds of potential serious risk to public health, the issue will be referred to a coordination group. Within a timeframe of 60 days, member states shall, within the coordination group, make all efforts to reach a consensus. If this fails, the procedure is submitted to an EMA scientific committee for arbitration. The opinion of this EMA committee is then forwarded to the Commission, for the start of the decision-making process. As in the centralized procedure, this process entails consulting various European Commission Directorates General and the Standing Committee on Human Medicinal Products or Veterinary Medicinal Products, as appropriate.

European Union Regulation of IVD Products

In May 2022, the In Vitro Diagnostic Device Regulation ("IVDR") (EU) 2017/746 became effective, replacing the previous IVD Directive (EU-Directive 98/79/EC). The IVDR was published in May 2017 and given a five-year transition period until its full implementation on May 26, 2022. Unlike the IVD Directive (EU-Directive 98/79/EC), the IVDR has binding legal force throughout every Member State. The major goals of the IVDR are to standardize diagnostic procedures within the EU, increase reliability of diagnostic analysis and enhance patient safety. Among other things, the IVDR introduces a new risk-based classification system for IVDs and requirements for IVD conformity assessments. Under the IVDR and subsequent amendments, IVDs already certified by a Notified Body under the IVD Directive may remain on the market until December 31, 2027, and IVDs certified without the involvement of a Notified Body may remain on the market for up to two additional years (until December 31, 2029) depending on the classification of the IVD. The manufacturers of such devices remaining on the market must comply with specific requirements in the IVDR, but ultimately, such products, as with all new IVDs, will have to undergo the IVDR's conformity assessment procedures. In addition, IVDs in the highest risk class will have to be tested by a Designated Reference Laboratory. The IVDR imposes additional requirements relating to post-market surveillance and submission of post-market performance follow-up reports.

The EC has designated thirteen Notified Bodies to perform conformity assessments under the IVDR. MedTech Europe has issued guidance relating to the IVDR in several areas, e.g., clinical benefit, technical documentation, state of art, accessories, and EUDAMED.

In April 2023, the European Commission issued a proposal that will revise and replace the existing general pharmaceutical legislation. If adopted and implemented as currently proposed, these revisions will significantly change several aspects of drug development and approval in the European Union.

Regulation of Pharmaceutical Products in the United Kingdom

As of January 1, 2021, European Union law no longer directly applies in the United Kingdom. The United Kingdom has adopted existing European Union medicines regulation as standalone United Kingdom legislation with some amendments to reflect procedural and other requirements with respect to marketing authorizations and other regulatory provisions.

The Medicines and Healthcare products Regulatory Agency, or MHRA, is responsible for regulating medicinal products in the United Kingdom (Great Britain and Northern Ireland). An MHRA authorization must be obtained for each medicine to be marketed in the regions that comprise the United Kingdom. On January 1, 2021, all existing European Union marketing authorizations were converted to United Kingdom marketing authorizations subject to a manufacturer opt-out. Since then, the United Kingdom has introduced separate, specific processes for regulatory submissions and medicinal product marketing authorization.

The Windsor Framework, which was negotiated between the United Kingdom and the European Commission and became effective as of January 1, 2025, requires changes to the regulatory system that was previously in effect under the Northern Ireland Protocol, including the regulation of drug products in the United Kingdom. Specifically, the MHRA will be responsible for approving all medicines intended to be marketed in the United Kingdom (including Northern Ireland), while the EMA will no longer be involved in approving medicines intended for sale in Northern Ireland.

It is expected that the establishment of a separate United Kingdom authorization system, albeit with transitional recognition procedures in the United Kingdom, will lead to additional regulatory costs.

Rest of World Government Regulation

The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with GCP and the other applicable regulatory requirements.
If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension of clinical trials, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions, and criminal prosecution.

Other Healthcare Laws

Although we currently do not have any products on the market, if our product candidates are approved in the United States, we will have to comply with various U.S. federal and state laws, rules and regulations pertaining to healthcare fraud and abuse, including anti-kickback laws and physician self-referral laws, rules and regulations. Violations of the fraud and abuse laws are punishable by criminal and civil sanctions, including, in some instances, exclusion from participation in federal and state healthcare programs, including Medicare and Medicaid. These laws include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment 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 federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") imposes criminal and civil liability for 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, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Physician Payments Sunshine Act require manufacturers of FDA-approved drugs, devices, biologics and medical supplies covered by Medicare, Medicaid or the Children's Health Insurance Program to report, on an annual basis, to the Centers for Medicare and Medicaid Services ("CMS") information related to payments and other transfers of value to physicians, teaching hospitals, and certain advanced non-physician healthcare practitioners and physician ownership and investment interests; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by nongovernmental third-party payors, including private insurers.

Some state laws require pharmaceutical or medical device companies to comply with the relevant industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures.
State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. We also are subject to, or may in the future become subject to, U.S. federal and state, and foreign laws and regulations imposing obligations on how we collect, use, disclose, store and process personal information. Our actual or perceived failure to comply with such obligations could result in liability or reputational harm and could harm our business.

Pharmaceutical Coverage, Pricing, and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of our products, when and if approved for marketing in the United States, 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. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. In addition, these third-party payors are increasingly reducing reimbursements for medical products, drugs and services. Furthermore, 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.
In Europe and other countries outside of the United States, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed to. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. In some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product and therapeutic candidates, restrict or regulate post-approval activities, and affect the ability to profitably sell product and therapeutic candidates that obtain marketing approval. The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product and therapeutic candidates. In addition, future legislative and regulatory proposals may materially impact the ability of the FDA and other regulatory agencies to operate as they have historically operated. We cannot be sure whether additional legislative changes will be enacted, or whether any of the FDA's regulations, guidance or interpretations will be changed, or what the impact of such changes on the agency and its scientific review staff, if any, may be. For example, the next FDA user fee reauthorization package is expected to enter stakeholder negotiations beginning in mid-2025, with any agreement sent to Congress in early 2027 for purposes of initiating the legislative process. Reauthorization of the prescription drug user fee program would need to be finalized by Congress by the end of September 2027 in order to avoid a disruption in FDA's review goals for NDAs and other activities supported by user fees assessed against industry. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we otherwise may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations. Moreover, among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access.

For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "ACA"), was enacted in March 2010 and has had a significant impact on the healthcare industry in the United States. The ACA expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to biopharmaceutical products, the ACA, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by such manufacturers under the rebate program and extended the program to individuals enrolled in Medicaid managed care organizations; established annual fees on manufacturers of certain branded prescription drugs; and created a new Medicare Part D coverage gap discount program. We expect that future changes or additions to the ACA, the Medicare and Medicaid programs, and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry in the United States.

Additionally, on December 20, 2019, the Further Consolidated Appropriations Act for 2020 was signed into law (P.L. 116-94) and includes a piece of bipartisan legislation called the Creating and Restoring Equal Access to Equivalent Samples Act of 2019 ("CREATES Act"). The CREATES Act aims to address the concern articulated by both the FDA and others in the industry that some brand manufacturers have improperly restricted the distribution of their products, including by invoking the existence of a REMS for certain products, to deny generic product developers access to samples of brand products. Because generic product developers need samples of an RLD to conduct certain comparative testing required by the FDA, some have attributed the inability to timely obtain samples as a cause of delay in the entry of generic products. To remedy this concern, the CREATES Act establishes a private cause of action that permits a generic product developer to sue the brand manufacturer to compel it to furnish the necessary samples on "commercially reasonable, market-based terms." Although lawsuits have been filed under the CREATES Act since its enactment, those lawsuits have settled privately; therefore to date no federal court has reviewed or opined on the statutory language and there continues to be uncertainty regarding the scope and application of the law.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B Drug Pricing Program. The maximum amount that a manufacturer may charge a 340B covered entity for a given product is the average manufacturer price, or AMP, reduced by the rebate amount paid by the manufacturer to Medicaid for each unit of that product. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although, under the current state of the law, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs.

In addition, as 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, the 2021 Consolidated Appropriations Act signed into law on December 27, 2020 incorporated extensive healthcare provisions and amendments to existing laws, including a requirement that all manufacturers of drug products covered under Medicare Part B report the product's average sales price to CMS beginning on January 1, 2022, subject to enforcement via civil money penalties. The U.S. Department of Health and Human Services ("DHHS") has also solicited feedback on various measures intended to lower drug prices and reduce the out-of-pocket costs of drugs and has implemented others under its existing authority.

In August 2022, President Biden signed into the law the Inflation Reduction Act of 2022 ("IRA"). The IRA has multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. For example, a manufacturer of a drug or biological product covered by Medicare Parts B or D must pay a rebate to the federal government if the drug product's price increases faster than the rate of inflation. This calculation is made on a product-by-product basis and the amount of the rebate owed to the federal government is directly dependent on the volume of a drug product that is paid for by Medicare Parts B or D. Additionally, starting in payment year 2026, CMS will negotiate drug prices annually for a select number of single source Part D drugs without generic or biosimilar competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. CMS has begun to implement these new authorities and entered into the first set of agreements with drug and biological product manufacturers for negotiated prices of 10 products, which will become applicable for payment year 2026. However, the IRA's impact on the pharmaceutical industry in the United States remains uncertain, in part because multiple large pharmaceutical companies and other stakeholders (e.g., the U.S. Chamber of Commerce) have initiated federal lawsuits against CMS arguing the program is unconstitutional for a variety of reasons, among other complaints. Those lawsuits are currently ongoing.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, in recent years, several states have formed prescription drug affordability boards ("PDABs"). Much like the IRA's drug price negotiation program, these PDABs have attempted to implement upper payment limits ("UPLs") on drugs sold in their respective states in both public and commercial health plans. In August 2023, Colorado's PDAB announced a list of five prescription drugs that would undergo an affordability review. The effects of these efforts remain uncertain pending the outcomes of several federal lawsuits challenging state authority to regulate prescription drug payment limits. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers ("PBMs") and other members of the healthcare and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area. The Federal Trade Commission ("FTC") in mid-2022 also launched sweeping investigations into the practices of the PBM industry that could lead to additional federal and state legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements. Significant efforts to change the PBM industry as it currently exists in the United States may affect the entire pharmaceutical supply chain and the business of other stakeholders, including pharmaceutical product developers like us.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, including any future drug products for which we secure marketing approval.

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 announced or for-cause unannounced inspections of facilities by the FDA and other authorities, including procedures and operations used in the testing and manufacture of our commercial products, if any, 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 or other

enforcement 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 authority, 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 negatively impact our business, operating results and financial condition.

Human Capital

As of December 31, 2024, we employed 288 employees, of which 287 were full-time employees. A significant number of our management and employees have had prior experience with pharmaceutical, biotechnology or medical product companies. None of our employees are represented by a labor union or covered under a collective bargaining agreement. Management considers relations with our employees to be good.

Social Factors and Supporting Our Workforce: Our approach to how we recruit, develop, retain and manage our talent is driven by our values statement: Making an impact through innovation, inclusion, and inspiration. Our values are at the core of who we are as an organization, and what drive us to reimagine possible for science, for medicine, and for human health. Critical to achieving our strategic imperatives is our ability to build and retain an exceptional team in which each member plays a unique and important role. We were recently recognized by the Boston Business Journal and won the distinction of being one of the 2024 “Best Places to Work”, which underscores our employees’ recognition of our collective focus, resilience, and commitment to our mission. We also value diversity, equity, inclusion, and social responsibility, with the goal of fostering a strong sense of belonging and contributing, while being empowered to make a real difference. This commitment is company-wide. Our Nominating and Corporate Governance Committee of our Board of Directors (“Board”) oversees our strategies and policies related to our people and diversity, equity and inclusion (“DEI”) initiatives, in addition to those for our environmental, social and governance (“ESG”) initiatives.

We recognize that maintaining an engaged and high-performing workforce who share a connection with the communities we serve is critical to our success. Camaraderie and cohesion are key to our collective corporate identity and are integral facets of our human capital strategy. Whether it is coming together throughout the year to connect at our town halls or participating in local walks for the patient communities for whom we work, we take a team and human connections-based approach to our work. We are inspired by the communities we serve, the opportunities to engage and learn from individuals and their families, and the possibilities of what we can achieve together.

We understand that in order to drive innovation, we must continuously improve our people strategies and find ways to foster engagement and growth within our organization. To this end, below are some of our initiatives:

Employee Engagement: Having an engaged and dedicated workforce is essential for us to achieve our goals. It is also more apparent than ever that we set our employees up for success and continue to cultivate their engagement with Wave. We conduct surveys as a means of engaging with employees and gaining their insights. We use the data and input as a tool for improving our human resources management going forward. Engagement is also directly correlated to the interactions our employees have with each other and their teams. We also have a cross functional team dedicated to organizing activities, such as themed social gatherings, charity and volunteer opportunities, and health and wellness events, which enrich our culture and bring employees together. We also work to ensure that we are deeply aligned with our corporate goals as a company, that functional goals are clear and transparent, and that employees understand how their work contributes to the company’s success.

Professional Development Programs and Opportunities: Employees are our most valuable resource, and we focus on providing them with opportunities so that they can continue to grow and excel in their functions and our company. Professional development of our employees drives engagement and allows us to leverage opportunities to grow and promote key talent from within our organization. We encourage individual development planning and leadership and management development programs for our employees, including our Building Coaching Leaders program that is a learning series designed to build strong coaching capabilities and strengthen a manager’s engagement with their teams, and our Management Essentials Program that is focused on building the leadership skillset of first-time managers and rising leaders. Through development planning, we strive for employees at all levels to focus on strengthening the skills required in their current role and potentially their next role. We conduct annual performance reviews for all employees, but,

as importantly, we are focused on building a culture of continuous coaching, feedback and open communication between managers and their direct reports throughout the entire year. We provide managers and employees with training on how to conduct effective forward-looking performance conversations and to set effective goals that are specific, measurable, attainable, relevant and timebound (SMART). We also provide company-wide leadership and development opportunities through the Wave Learning Series, which was developed to build awareness of all functional areas, special areas of interest or importance, timely subject matters and to expand knowledge of industry trends and other matters of interest and relevance within the biopharmaceutical industry. The Wave Learning Series is conducted through company-wide presentations by employees at various levels, providing opportunities for development and cross-functional exposure for our employees. We also offer all full-time employees the option to participate in our Education Assistance Program, where we reimburse employees for tuition and eligible expenses.

Environmental Health and Safety: Compliance with environmental, health and safety ("EH&S") laws and regulations forms the basis of the EH&S policy and programs we have in place, which include occupational health and safety measures that apply to all of our employees, contractors and visitors. These programs detail the proactive, risk-based approach that we take to prevent workplace injuries and protect the health and safety of our employees and the communities around us. In addition, we engage independent third parties to evaluate and audit our compliance with EH&S laws and regulations. We foster a culture that strives to embed safety into all aspects of our operations, which includes implementing design safeguards for our employees and patients. Our EH&S management system engages all levels of the organization to monitor and track the effectiveness of our programs, ensure EH&S compliance, respond to incidents and manage corrective actions to reinforce safeguards. Our training programs provide training to our employees that is commensurate with their level of risk exposure and are designed to ensure that employees have the knowledge and equipment available to mitigate risk. Our cross-functional Safety Committee meets monthly to discuss any concerns and ways to improve our EH&S programs. Employees are also required to report any incidents, no matter how small, and are encouraged to voice any health or safety concerns to management or a member of our EH&S team.

Health and Well-Being: We believe that the overall well-being of our employees and ensuring that their basic health and wellness needs are met is fundamental for us to achieve success as a company. We understand that a key part of our ongoing efforts to prioritize wellness initiatives includes providing our employees with access to mental health, behavioral health, and/or substance abuse services through our medical plans. We provide an Employee Assistance Program as a cost-free benefit, which is available to help employees and their household members to confidentially manage everyday life, arising work challenges, stress, and other personal issues, by providing consultation, referrals, and resources, along with ongoing webinars on various work-life, mental health, and wellness topics for employees. We prioritize providing mental health resources for our employees, while creating forums for dialogue. In addition, we understand that workplace flexibility is an important component to our employees' well-being. Prioritizing employee safety while achieving our goals has provided us with a greater appreciation for workplace flexibility, which keeps our employees engaged and motivated, while also creating a sense of trust throughout our organization.

Diversity, Equity and Inclusion ("DEI"): Our commitment to maintaining a top-performing company means investing in and creating ongoing opportunities for employee development in a diverse and inclusive workplace. We believe that a diverse and inclusive workforce positively impacts our performance, fosters innovation and inspires us to achieve greater results. We provide equal employment opportunities without regard to race, color, religion, gender, sexual orientation, national origin, age, disability, veteran status or genetics, among other personal characteristics. Our DEI Steering Group leads various initiatives to help us maintain a diverse, equitable, culturally competent and supportive environment for all of our employees and other stakeholders. In addition to this, our intentional focus on DEI helps ensure that we continue to cultivate the next generation of experienced, diverse leaders and managers necessary to execute on our mission and plans for ambitious growth. As of December 31, 2024, women made up approximately 52% of our global workforce and constitute approximately 52% of senior management (defined as vice president level and above). As of December 31, 2024, racially diverse employees (those self-identifying as Black or African American, Hispanic or Latino, Asian, or being of two or more races) make up approximately 37% of our global workforce and approximately 23% of senior management (defined as vice president level and above) (10% of our employees did not provide us with this information).

Some of our DEI initiatives include DEI-focused training, educational and awareness building events, social hours celebrating various cultural themes, and our summer internship program with Project Onramp, which is an organization working to bridge the opportunity gap for Massachusetts-based college students in under-served and minority communities. We recently established a partnership with Bioversity, a nonprofit launched by MassBio to create and implement industry-aligned workforce training initiatives. Additionally, we encourage the formation of Employee Resource Groups and currently have three – Women+ of Wave, Black Employee Network, and LGBTQIA+ – with more likely to be formed. We also have a supplier diversity program that identifies and classifies our suppliers, encouraging the use of a more diversified supply base. We believe that having a diverse group of suppliers will allow us to effectively meet the needs of our organization while expanding our pool of suppliers to create more competitive business opportunities, and ultimately creating positive social impact by generating economic opportunities for those in our community who may be disadvantaged.

Patient Advocacy and Community Engagement: Our community engagement activities are focused on seeking to better understand the lived experience of people impacted by rare and prevalent diseases and identifying opportunities to support these communities. We believe that listening to, learning from, and partnering with individuals impacted by the diseases we hope to address, including families and caregivers, connects us more deeply to our mission, and enhances our ability to discover and develop meaningful therapies. Through collaboration with patient communities and advocacy organizations, including participation in community-focused conferences and events, we aim to incorporate community voices and perspectives into every aspect of our work. Insights from the community inform the design and execution of our clinical trials, shape our corporate culture, and drive activities and initiatives that are intended to make a positive impact on people's lives.

Employee volunteering is another important component of our community engagement initiatives. We partner with advocacy and service organizations to provide opportunities for employees to contribute directly to our local communities, including through our Wave Service Day and holiday giving drives. By participating in a broad range of volunteer activities, our employees donate time and resources to support individuals and families in our community and beyond. We also recognize that external factors and current events, including systems and policies, impact our employees, as well as the communities with which we are connected.

Rewards and Recognition: We have a multi-tiered awards program, including peer-to-peer recognition, which our employees use to recognize and reward one another for their contributions and achievements, taking into consideration the combination of employees who best exemplify our values and the achievement of results. We believe that providing a rewards program not only increases engagement and performance, but meaningfully recognizes those employees who go above and beyond to positively impact our company and culture. In addition, we offer a team rewards and recognition program to provide another opportunity to recognize and reward collaborative teamwork.

Compensation, Equity and Benefits (Total Rewards): Compensation programs are one of the most powerful tools available to companies to attract, retain and motivate employees, as well as align their interests with those of shareholders. We have developed a broad-based compensation program that is designed to attract, retain and motivate our employees, while driving sustainable long-term value creation. We seek to deliver performance-driven, market competitive reward opportunities commensurate with company and individual performance. All of our employees receive competitive base salaries, cash bonus eligibility, new hire equity grants and annual long-term incentive grants eligibility, in addition to our comprehensive benefits package. We believe that providing employees with an ownership interest in Wave through grants of equity awards further strengthens the level of employee engagement. In addition, our Employee Share Purchase Plan, as amended ("ESPP"), provides our U.S. employees with an opportunity to purchase our ordinary shares at a 15% discount to the market price.

Offering a highly competitive, industry-leading benefits package is another integral piece of our total rewards package and differentiated employee value proposition. Notably, we provide our employees with access to choice and offer employees a very progressive health insurance package, with no premiums. We also offer a 401(k) plan with matching contributions for all eligible employees. We provide innovative solutions that are key to attracting, engaging and motivating employees, including (i) our excellent benefits and compensation programs and strategies; (ii) our employee well-being approach and strategy; (iii) our health plan; and (iv) internal communications and education around our total rewards strategy.

We will continue to evolve and strengthen our strategies relating to talent, while furthering our investment in our employees, culture, community partnerships and outreach, and other human capital measures.

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, D01 X9R7, Ireland. Our registered office for Wave UK is 1 Chamberlain Square CS, Birmingham B3 3AX, 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 or our other filings with the SEC. 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 – SEC Filings" section of our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the 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 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

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 $97.0 million, $57.5 million, and $161.8 million for the fiscal years ended December 31, 2024, 2023, and 2022, respectively. As of December 31, 2024, and 2023 we had an accumulated deficit of $1,121.9 million and $1,024.9 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 are a clinical-stage biotechnology company focused on unlocking the broad potential of ribonucleic acid ("RNA") medicines (also known as oligonucleotides), or those targeting RNA, to transform human health. Our RNA medicines platform, PRISM®, combines multiple modalities, chemistry innovation and deep insights into human genetics to deliver scientific breakthroughs that treat both rare and common disorders. Our toolkit of RNA-targeting modalities includes RNA editing, splicing, silencing using RNA interference ("siRNA") and antisense silencing, providing us with unique capabilities for designing and sustainably delivering candidates that optimally address disease biology. Our diversified pipeline includes clinical programs in obesity, alpha-1 antitrypsin deficiency ("AATD"), Duchenne muscular dystrophy ("DMD"), and Huntington's disease ("HD"), as well as several preclinical programs utilizing our versatile RNA medicines platform. 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 PRISM, our proprietary discovery and 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 12 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 costs, timing and outcome of regulatory review of our product candidates;
- our ability to obtain marketing approval for our product candidates;
- the impacts of any local or global health issues, the conflict involving Russia and Ukraine, the conflict in the Middle East, global economic uncertainty, volatility in inflation, volatility in interest rates or market disruptions on our business;
- the achievement of milestones and other development targets that trigger payments under our agreements with our key collaboration partners, or any other strategic collaborations into which we may enter;
- 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;
- market acceptance of our product candidates, to the extent any are approved for commercial sale, and 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 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. Through December 31, 2024, we have received an aggregate of approximately $1,578.4 million in net proceeds from these transactions, consisting of $977.8 million in net proceeds from public and other registered offerings of our ordinary shares, $511.3 million from our collaborations, exclusive of any potential future milestone and royalty payments, and $89.3 million in net proceeds from private placements of our debt and equity securities.

On November 12, 2024, we filed an automatic shelf registration statement on Form S-3ASR with the SEC for which we registered for sale an indeterminate amount of any combination of our ordinary shares, debt securities, warrants, rights and/or units from time to time and at prices and on terms that we may determine, which we refer to as the "2024 WKSI Shelf". Our 2024 WKSI Shelf includes a prospectus covering up to an aggregate of $250.0 million in ordinary shares that we are able to issue and sell from time to time, through Jefferies LLC ("Jefferies") acting as our sales agent, pursuant to the Open Market Sale Agreement, dated May 10, 2019, as amended by Amendment No. 1, dated as of March 2, 2020, Amendment No. 2, dated as of March 3, 2022, and Amendment No. 3, dated as of November 12, 2024 (collectively, the "Sales Agreement"), for our "at-the-market" equity program.

Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. We may seek access to the capital and credit markets for working capital, capital expenditure, and other business initiatives. The capital and credit markets have experienced extreme volatility and disruption, which may lead to uncertainty and liquidity issues for both borrowers and investors. In the event of adverse market conditions, or other factors, additional funds may not be available to us on acceptable terms or at all. For example, the global economy has been experiencing volatility in interest rates and inflation, which could negatively impact our business and our ability to raise additional funds. 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 receive 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 business may be impacted by macroeconomic conditions, including fears concerning the financial services industry, inflation, volatility in interest rates and volatile market conditions, and other uncertainties beyond our control.

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. Our ability to effectively run our business could be adversely affected by general conditions in the global economy and in the financial services industry. Various macroeconomic factors could adversely affect our business, including fears concerning the banking sector, volatility in inflation, and interest rates and overall changes in economic conditions and uncertainties. A severe or prolonged economic downturn could result in a variety of risks, including our ability to raise additional funding on a timely basis or on

acceptable terms. A weak or declining economy could also impact third parties upon whom we depend to run our business. Concerns over bank failures and bailouts and their potential broader effects and potential systemic risk on the banking sector generally and on the biotechnology industry and its participants may adversely affect our access to capital and our business and operations more generally. Although we assess our banking relationships as we believe necessary or appropriate, our access to funding sources in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect us, the financial institutions with which we have arrangements directly, or the financial services industry or economy in general.

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 operating history as a clinical-stage biotechnology company 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 focused on unlocking the broad potential of RNA medicines (also known as oligonucleotides), or those targeting RNA, to transform human health. Our RNA medicines platform, PRISM, combines multiple modalities, chemistry innovation and deep insights into human genetics to deliver scientific breakthroughs that treat both rare and common disorders. Our toolkit of RNA-targeting modalities includes RNA editing, splicing, silencing using siRNA and antisense silencing, providing us with unique capabilities for designing and sustainably delivering candidates that optimally address disease biology. Our diversified pipeline includes clinical programs in obesity, AATD, DMD, and HD, as well as several preclinical programs utilizing our versatile RNA medicines platform. We have not yet demonstrated our ability to successfully complete pivotal clinical trials, obtain marketing approvals, or conduct sales and marketing activities necessary for successful product commercialization. We have limited experience manufacturing our products at commercial scale or arranging for a third party to do so on our behalf. 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.

We, or third parties upon whom we depend, may face risks related to local and global health epidemics, which may delay our ability to complete our ongoing clinical trials, initiate additional clinical trials, delay regulatory activities and have other adverse effects on our business and operations.

As a clinical-stage company with multiple programs and multiple clinical trials currently underway, any local or global health issues could impact the execution of our clinical trials. For example, beginning in March 2020, multiple countries throughout the world and their economies, including the United States, were subject to intermittent shutdowns and were adversely affected by the COVID-19 global pandemic. We had clinical trial sites located in countries that had been affected by COVID-19 and variants thereof. Clinical site initiation and patient enrollment was delayed due to prioritization of hospital resources in favor of COVID-19 patients and difficulties in recruiting clinical site investigators and clinical site staff. Some patients were not able to travel or gain access to clinical trial sites due to local restrictions. Similarly, our ability to recruit and retain patients and principal investigators and site staff was negatively impacted, which delayed the timelines of our clinical trial operations.

We rely upon third parties for many aspects of our business, including the raw materials used to make our product candidates and the conduct of our clinical trials and preclinical studies. While we have built up inventory to assist us through this uncertain operating environment, our suppliers may be disrupted now or in the future due to a local or global health epidemic, which could affect our ability to procure items that are essential for our research and development activities and could cause increases to our costs, inflation, and significant disruptions to our business.

While we have adapted our processes to lessen the impact of a potential local or global health epidemic may have on our business, any potential delays or long-term impacts on our business, our clinical trials, healthcare systems or the global economy could be highly uncertain. These effects could materially adversely affect our business, financial condition, results of operations, and prospects.

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

The approach we are taking to discover and develop RNA medicines is novel and may never lead to marketable products.

We have concentrated our efforts and research and development activities on RNA medicines (also known as oligonucleotides) and enhancing PRISM, our proprietary discovery and drug development platform. PRISM enables us to target genetically defined diseases with stereopure oligonucleotides across multiple therapeutic modalities. Our future success depends on the successful development of our RNA medicines and the effectiveness of PRISM. The scientific discoveries that form the basis for our efforts to discover and develop new product candidates, including our discoveries about the relationships between oligonucleotide stereochemistry and pharmacology, are relatively new. Our PRISM platform combines multiple modalities, chemistry innovation and deep insights into human genetics to deliver scientific breakthroughs that treat both rare and prevalent disorders. The scientific evidence to support the feasibility of developing medicines based on our discoveries is limited, as we have not yet completed successful clinical development of an oligonucleotide therapeutic.

Because we are developing oligonucleotides, 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 FDA and comparable ex-U.S. regulatory agencies have relatively limited experience with RNA medicines (also known as oligonucleotides), which may increase the complexity, uncertainty and length of the regulatory review process for our product candidates. The FDA has approved approximately 20 oligonucleotides for commercial use. The FDA has issued multiple guidance documents on the development and testing of oligonucleotide products, as well as guidance relating to regulatory submissions for such products, including in December 2021 two draft guidance documents relating to IND submissions for individualized antisense oligonucleotide drugs for severely debilitating or life-threatening genetic diseases, one with clinical focus, the other with chemistry manufacturing and controls focus, in June 2024 a final guidance on clinical pharmacology considerations for the development of oligonucleotide therapeutics, and in November 2024 a draft guidance on nonclinical safety assessment of oligonucleotide products. Although guidance documents issued by FDA do not have the force of law and are therefore not binding on the industry, we may decide to revise the design of our ongoing or planned nonclinical studies or clinical trials, or design new nonclinical studies or clinical trials, of our product candidates to align with the agency's current thinking as set forth in the recently published guidance. The general lack of extensive experience specific to oligonucleotides may hinder or slow review by the FDA or other foreign homologues of any regulatory filings that we may submit. Moreover, the FDA or other foreign homologues may respond to these submissions by defining requirements we may not have anticipated. Addressing such requirements 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. 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 may be materially harmed.

We have a robust and diverse pipeline of first- or best-in-class RNA medicines using our RNA editing, splicing, silencing using siRNA and antisense silencing modalities. Our diversified pipeline includes clinical programs in AATD, DMD, HD, and obesity, as well as several preclinical programs utilizing our broad RNA therapeutics toolkit.

However, we currently have no products on the market. We have invested a significant portion of our efforts and financial resources in the identification and preclinical and clinical development of our oligonucleotides, the development of our RNA medicines platform, PRISM, including our RNA editing capability, and our novel chemistry modifications, and the continued growth of our manufacturing capabilities. 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, regulatory approvals, 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 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 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 current collaborations, and any additional collaborations we may establish;
- 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;
- continuing to maintain an acceptable safety and efficacy profile of the products following regulatory approval; and
- appropriately addressing the post-marketing requirements and/or commitments made upon regulatory 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 in a timely manner 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 adverse 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, personnel issues and ease of participation in our clinical trials;
- open study sites, and enroll, treat, and monitor patients due to local restrictions implemented in response to local or global health issues;
- develop companion diagnostic tests for use with certain of our product candidates or identify partners with such expertise;
- 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;
- apply the appropriate pharmacovigilance measures in case of adverse effects emerging 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 contract research organizations ("CROs") involved in the clinical trial;
- negotiate contracts and other related documents with clinical trial parties and IRBs, 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 substance supply chain, and we began cGMP manufacturing in this facility at the beginning of 2018. This facility supplements our existing Cambridge, Massachusetts laboratory and office space headquarters, enhances our ability to secure drug substance for current and future development activities and may provide commercial-scale manufacturing capabilities. However, while we have established and continue to enhance our internal cGMP manufacturing capabilities, we have limited experience manufacturing drug substance on a commercial scale, and we will incur significant costs to develop this expertise internally.

In addition to the oligonucleotides that we manufacture internally, we may utilize 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 our ability or the ability of our CMOs to meet our delivery time requirements or provide adequate amounts of material to meet our clinical trial demands on our projected timelines. 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 and quality standards, 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. For example, we source certain materials used in the manufacture of our products from China and other countries outside of the United States, and supply chain disruptions could impact our business. 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.

The process of manufacturing oligonucleotides is complex and we may encounter difficulties in production, particularly with respect to process development or scaling-up of our manufacturing capabilities.

The process of manufacturing oligonucleotides 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 in quality that may interfere with preclinical studies 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 optimizing 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/or conduct animal 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 provide the FDA and comparable regulatory authorities adequate evidence of 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 produced via earlier manufacturing processes and supplied in clinical studies. We may be required to collect additional preclinical and/or clinical data from any modified process prior to obtaining marketing approval for the product candidate produced with such modified process. If preclinical and/or clinical data are not ultimately comparable to those seen in the earlier trials, 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.

We are a clinical-stage biotechnology company focused on unlocking the broad potential of RNA medicines (also known as oligonucleotides), or those targeting RNA, to transform human health. Our RNA medicines platform, PRISM, combines multiple modalities, chemistry innovation and deep insights into human genetics to deliver scientific breakthroughs that treat both rare and common disorders. Our toolkit of RNA-targeting modalities includes RNA editing, splicing, silencing using siRNA and antisense silencing, providing us with unique capabilities for designing and sustainably delivering candidates that optimally address disease biology. Our diversified pipeline includes clinical programs in obesity, AATD, DMD, and HD, as well as several preclinical programs utilizing our versatile RNA medicines platform. Although we continue to build on our experience in manufacturing oligonucleotides, we have limited 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 commercial use. Our manufacturing capabilities

could be affected by cost-overruns, unexpected delays, equipment failures, labor shortages, operator error, natural disasters, unavailability 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 preclinical or clinical 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, is uncertain as to outcome, and the historical failure rate for drugs in preclinical and clinical development is high. For example, we depend on the availability of non-human primates to conduct certain preclinical studies. Over the past several years there has been a global shortage of non-human primates available for drug development that has matured into an acute global supply chain issue. The supply of these non-human primates has been constrained due to factors such as their limited worldwide availability, domestic regulatory restrictions and trade relations. If we are unable to obtain access to a sufficient supply of these non-human primates in a timely manner or at all, our timelines and our ability to complete preclinical testing and submit IND/CTA or equivalent foreign applications may be adversely affected.

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 events 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 or ethics committees, which review the clinical protocols and informed consent form 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 and relevant regulatory authorities, as required throughout the study, such as emergent safety reports and annual updates, may result in suspension of the 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 INDs/CTAs 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;
- divergent views between FDA and other homologue regulatory authorities as to the objectives and/or design of the clinical trials required in support of marketing registration;
- 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 eligible for clinical trials;
- delays in developing and receiving regulatory approval for companion diagnostic tests, to the extent such tests are needed, to identify patients for our clinical trials;
- high drop-out rates for patients in clinical trials and substantial missing data;
- an inability to open study sites, or enroll, treat, and monitor patients due to local restrictions implemented in response to local or global health epidemics;
- 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 outcome of 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 manufacturing, preclinical, or clinical testing generally or with respect to the class, of any of 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 subsequent 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. 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 reach late development stages or obtain regulatory approval for marketing. For example, our preclinical studies for WVE-004 for C9orf72-associated amyotrophic lateral sclerosis and frontotemporal dementia ("C9-ALS/FTD") yielded positive results. However, in May 2023, the topline results of the Phase 1b/2a study of WVE-004 for patients with C9-ALS/FTD showed no trends in clinical benefit and reductions in poly(GP) were not correlated with changes in functional outcome and resulted in our discontinuation of the WVE-004 program. 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 local or global health issues, 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 a clinical trial for WVE-003, which targets a SNP associated with the mutant allele of the *HTT* gene. Approximately 40% of the HD patient population carry this SNP. 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, and we have partnered with a third party for testing in future trials. If we, or any third parties that we engage to assist us are unable to successfully identify patients with the appropriate SNP that we are targeting, the percentage of patients with the SNP we are targeting is lower than expected, or we experience delays in testing, we may not realize the full commercial potential of any product candidates we develop.

Congress also recently amended the FDCA to require sponsors of a Phase 3 clinical trial, or other "pivotal study" of a new drug to support marketing authorization, to design and submit a diversity action plan for such clinical trial. The action plan must describe appropriate diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. Although none of our product candidates has reached Phase 3 of clinical development, we must submit a diversity action plan to the FDA by the time we submit a Phase 3 trial, or pivotal study, protocol to the agency for review, unless we are able to obtain a waiver for some or all of the requirements for a diversity action plan. It is unknown at this time how the diversity action plan may affect the planning and timing of any future Phase 3 trial for our product candidates. However, initiation of such trials may be delayed if the FDA objects to our proposed diversity action plans for any future Phase 3 trial for our product candidates, and we may experience difficulties recruiting a diverse population of patients in attempting to fulfill the requirements of any approved diversity action plan.

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. Our goal is to develop and commercialize disease-modifying medicines for genetically defined diseases with a high degree of unmet medical need, and to become a fully integrated RNA

medicines company. 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 product candidates are being designed without performant, fit-for-purpose, accessible, relatively inexpensive, and 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, often *in vitro* devices, and require separate regulatory authorization 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 – Government Regulation – In Vitro Diagnostic Tests for Biomarkers." Given our limited experience in developing and commercializing companion diagnostic tests, we may seek to collaborate with third parties to assist us in the design, manufacture, regulatory authorization and commercialization of the companion diagnostic tests for some of our product candidates. In November 2019, we entered into a collaboration with Asuragen for the development and commercialization of companion diagnostics for our allele-selective product candidate in HD. We, Asuragen and other potential collaborators may encounter difficulties in developing and obtaining approval for the companion diagnostic tests, including issues relating to sensitivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by us or our collaborators to develop or obtain regulatory authorization of the relevant companion diagnostic tests could delay or prevent approval of our product candidates. If we, Asuragen or any other third parties that we engage to assist us, are unable to successfully develop, validate, 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 a continuously evolving regulatory environment and 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.

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 chemistry, manufacturing and controls, 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.

If we are granted orphan drug designations in the United States for any of our product candidates, there can be no guarantee that we will maintain orphan status for these product candidates or receive approval for any product candidate with an orphan drug designation.

Subject to receiving approval from the FDA of an NDA or Biologics License Application, products granted orphan drug designation are provided with seven years of orphan marketing exclusivity in the United States, meaning the FDA generally will not approve applications for other product candidates for the same orphan indication that contain the same active ingredient.

We are not guaranteed to maintain or receive orphan designation for our current or future product candidates, and if our product candidates that were granted orphan designation were to lose their status as an orphan drug or the orphan 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 periods 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 sole basis of orphan drug status. In addition, orphan exclusivity does not block the approval of a different drug or biologic for the same rare disease or condition, nor does it block the approval of the same drug or biologic for different conditions. Even if we are the first to obtain approval of an orphan product candidate and are granted exclusivity in the United States, there are circumstances under which a later competitor product may be approved for the same indication during the 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.

Even if we obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory oversight. If we or our collaborators or contractors fail to comply with continuing U.S. and foreign requirements, our approvals, if obtained, 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 GCP for any clinical trials that we conduct post-approval. Failure to comply with these requirements could result in warning or untitled letters, 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. We or our CMOs may not be able to comply with applicable cGMP regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our CMOs, to comply with applicable regulations could result in regulatory actions, such as the issuance of FDA Form 483 notices of observations, warning letters or sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, refusal to permit import or export of our products, operating restrictions, consent decrees and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. 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.

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 oligonucleotides. 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 industry 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 industry 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 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 that our current or future product candidates are or may be designed to treat. 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;

- more extensive coverage and higher levels of reimbursement; 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;
- HIPAA, which, among other things, criminalizes a wide array of conduct involving public and private healthcare benefits, creates new civil enforcement mechanisms and increases civil and criminal penalties for healthcare fraud;
- HIPAA, as amended by the HITECH Act, and its implementing regulations, which strengthen and expand 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 CMS all transfers of value made to physicians, certain advanced non-physician healthcare practitioners, or teaching hospitals and requires 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 for DHHS, 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, could divert our management's attention from

the operation of our business, and could harm our reputation, 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.

Furthermore, if the FDA or a comparable foreign regulatory authority approves any of our drug candidates, activities such as the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and record keeping for the products will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP. The FDA or a comparable foreign regulatory authority may also impose requirements for costly post-marketing nonclinical studies or clinical trials (often called "Phase 4 trials") and post-marketing surveillance to monitor the safety or efficacy of the product. If we or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, production issues with the facility where the product is manufactured or processed, such as product contamination or significant non-compliance with applicable cGMP requirements, a regulator may impose restrictions on that product, the manufacturing facility or us. If we or our collaborators or third-party service providers, including our CMOs, fail to comply fully with applicable regulations, then we may be required to initiate a recall or withdrawal of our products.

If previously unknown problems with one of our products, if approved, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes are discovered, or 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;
- restrictions on the labeling, use or distribution 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 or other measures to reduce drug prices.

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 of our drug products, if approved, 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.

Further, there have been, and may continue to be, legislative and regulatory proposals at the U.S. federal and state levels and in foreign jurisdictions directed at broadening the availability and containing or lowering the cost of healthcare. The continuing efforts of the government, insurance companies, managed care organizations and other third-party payors to contain or reduce costs of healthcare may adversely affect our ability to set prices for our products that would allow us to achieve or sustain profitability. In addition, governments may impose price controls on any of our products that obtain marketing approval, which may adversely affect our future profitability.

The Inflation Reduction Act of 2022 ("IRA") was signed into law in August 2022 (see above "Government Regulation—Healthcare Reform"). In addition, Executive Order 14087, issued October 2022, called for CMS to prepare and submit a report to the White House on potential payment and delivery modes that would complement to IRA, lower drug costs, and promote access to innovative drugs. In February 2023, CMS published its report which described three potential models focusing on affordability, accessibility and feasibility of implementation for further testing by the CMS Innovation Center. The CMS Innovation Center continues to test the proposed models and has started to roll out plans for access model testing of certain product types (e.g., cell and gene therapies) by states and manufacturers. Additional state and federal healthcare reform measures are expected to be adopted in the future, any of

which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for certain biopharmaceutical products or additional pricing pressures.

In some foreign countries, particularly the member states of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can be a long and expensive process after the receipt of marketing approval for a drug candidate. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct additional clinical trials that compare the cost-effectiveness of our drug candidates to other available therapies in order to obtain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount in a particular country, or if pricing is set at unsatisfactory levels, we may be unable to successfully commercialize and achieve or sustain profitability for sales of any of our drug candidates that are approved for marketing in that country and our business could be adversely affected.

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 U.S. federal and state laws and agency regulation, as well as foreign laws and regulations, could have a materially negative impact on our business. In the United States and in some other jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates or any potential future product candidates of ours, restrict or regulate post-approval activities, or affect our ability to profitably sell any product candidates for which we obtain marketing approval. Increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements. Congress also must reauthorize the FDA's user fee programs every five years and often makes changes to those programs in addition to policy or procedural changes that may be negotiated between the FDA and industry stakeholders as part of this periodic reauthorization process. Congress most recently reauthorized the user fee programs in September 2022 without any substantive policy changes. The next FDA user fee reauthorization package is expected to enter stakeholder negotiations beginning in mid-2025, with any agreement sent to Congress in early 2027 for purposes of initiating the legislative process. Reauthorization of the prescription drug user fee program would need to be finalized by Congress by the end of September 2027 in order to avoid a disruption in FDA's review goals for NDAs and other activities supported by user fees assessed against industry.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a focus of these efforts and has been significantly affected by major legislative initiatives. For example, in March 2010, Congress passed the ACA, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs coverage under Medicare Part D; and established a Center for Medicare Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

In addition to the IRA's drug price negotiation provisions summarized above, Executive Order 14087, issued in October 2022, called for the CMS Innovation Center to prepare and submit a report to the White House on potential payment and delivery modes that would complement to IRA, lower drug costs, and promote access to innovative drugs. In February 2023, CMS published its report which described three potential models focusing on affordability, accessibility and feasibility of implementation for further testing by the CMS Innovation Center. The CMS Innovation Center's is still testing the majority of the proposed models.

We expect that future changes or additions to the ACA, the Medicare and Medicaid programs, and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry in the United States.

Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices considering the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, CMS promulgated a regulation permitting Medicare Advantage plans to use step therapy for Part B drugs

beginning January 1, 2020. In addition, the 2021 Consolidated Appropriations Act incorporated extensive healthcare provisions and amendments to existing laws, including a requirement that all manufacturers of drug products covered under Medicare Part B report the product's average sales price to CMS beginning on January 1, 2022, subject to enforcement via civil money penalties.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. The effects of these efforts remain uncertain pending the outcomes of several federal lawsuits challenging state authority to regulate prescription drug payment limits. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate PBMs and other members of the healthcare and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area. In mid-2022, the FTC also launched sweeping investigations into the practices of the PBM industry that could lead to additional federal and state legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements. In addition, in the last few years, several states have formed prescription drug affordability boards ("PDABs") with the authority to implement upper payment limits ("UPLs") on drugs sold in their respective jurisdictions. There are several pending federal lawsuits challenging the authority of states to impose UPLs, however.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services.

Risks associated with our operations outside of the United States and developments in international trade by the U.S. and foreign governments 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, including Russia's invasion of Ukraine, the conflict in the Middle East, and the potential for a wider European or global conflict; fluctuations in the value of foreign currency versus the U.S. dollar; volatility in inflation and interest rates; 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; global instability from an outbreak of pandemic or contagious disease, difficulties in attracting and retaining qualified personnel; and cultural differences in the conduct of business. For example, given developments related to international trade over the past few years, unexpected changes in tariffs could adversely affect our cost of goods sold and/or the foreign sales of our product candidates. Changes impacting our ability to conduct business outside of the United States, or changes to the regulatory regime applicable to our operations in countries outside of the United States (such as with respect to the approval of our product candidates), may materially and adversely impact our business, prospects, operating results, and financial condition.

We or third parties upon whom we depend may be adversely affected by natural disasters and/or health epidemics, and our business, financial condition and results of operations could be adversely affected.

Natural disasters could severely disrupt our operations and have a material adverse effect on our business operations. If a natural disaster, health epidemic, or other event beyond our control occurred that prevented us from using all or a significant portion of our office, manufacturing and/or lab spaces, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult for us to continue our business for a substantial period of time. Any outbreak of contagious diseases, or other adverse public health developments, could have a material and adverse effect on our business operations. For example, during the COVID-19 global pandemic, clinical site initiation and patient enrollment in our clinical trials were delayed due to prioritization of hospital resources in favor of COVID-19 patients and difficulties in recruiting clinical site investigators and clinical site staff. Any local or global health issues could impact our business, our preclinical studies and clinical trials, healthcare systems or the global economy. In addition, certain of our research and development efforts are conducted globally. A health epidemic or other outbreak could materially and adversely affect our business, financial condition and results of operations.

The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

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. 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. Our procedures for storing, handling and disposing of these materials are reviewed against the relevant guidelines and laws of the jurisdictions in which our facilities are located on a regular basis. Although we believe that our safety procedures for handling and disposing of these materials sufficiently mitigate the risk of accidental contamination or injury from these materials, the risk cannot be completely 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 or hazardous materials. Additional federal, state and local laws and regulations affecting our operations may become applicable 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 development and commercialization of certain of our product candidates. Our potential future collaborators include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. In January 2023, we commenced a collaboration with GSK to research, develop, and commercialize oligonucleotide therapeutics, including WVE-006, our first-in-class A-to-I(G) RNA editing candidate for AATD. 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 other 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 may 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;
- collaborators may require us to enter into collaboration agreements that contain exclusivity provisions and/or termination penalties;
- 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.

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 GSK, GSK is responsible for later clinical development and commercialization of our program in AATD.

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 may form collaborations to fund all or part of the costs of drug development and commercialization, such as our collaboration with GSK. 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, preclinical and clinical 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 preclinical studies that supports our INDs/CTAs is conducted in accordance with GLP requirements and, likewise, that our clinical trials are conducted in accordance with GCP requirements, the study plan and protocol for each 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 IND/CTA submissions and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize such product candidates.

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, 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, including our inability to control whether sufficient resources are applied to our programs. If any of our CROs are acquired or consolidated, these concerns are likely to be exacerbated and our preclinical studies or clinical trials may be further impacted due to potential integration, streamlining, staffing and logistical changes. 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 preclinical and 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 study or trial. The FDA and other health authorities require clinical trials to be conducted in accordance with GCP, 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 and other health authorities 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 in the supply and manufacture of our product candidates for our research, preclinical and clinical activities, and may do the same for commercial supplies of our product candidates.

While we have built 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. In addition, we currently rely on third parties in the supply and manufacture of 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, 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 oligonucleotides, there may be increased competition for the supply of the raw materials that are necessary to make our oligonucleotides, 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 their 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 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. In complying with the manufacturing regulations of the FDA and other comparable foreign regulatory authorities, we and our third-party manufacturers must spend significant time, money, and effort in the areas of design and development, testing, production, record-keeping and quality control to assure that the products meet applicable specifications and other regulatory requirements. Although our agreements with third-party manufacturers require them to perform according to certain cGMP requirements such as those relating to quality control, quality assurance and qualified personnel, we cannot otherwise control the conduct of our third-party manufacturers to implement and maintain these standards. If any of our third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the regulatory requirements of the FDA, or other comparable foreign authorities, we would be prevented from obtaining regulatory approval for our drug candidates unless and until we engage a substitute supplier that can comply with such requirements, which we may not be able to do on commercially reasonable terms or at all. In addition, we and our third-party manufacturers responsible for the manufacture of commercial supplies of our products for which we retain regulatory approval, if any, are subject to inspection and approval by regulatory authorities before we may commence the manufacture and sale of any of such products, and thereafter are subject to ongoing inspection from time to time. Our third-party manufacturers may not be able to comply with applicable cGMP regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in regulatory actions, such as the issuance of FDA Form 483 notices of observations, warning letters or sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. Any such failure by us or any of our suppliers would significantly impact our ability to develop, obtain regulatory approval for or market our drug candidates, if approved.

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.

We currently have no sales, marketing or distribution capabilities. In addition, while our collaboration with GSK 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, and we cannot assure you that we will be able to identify or employ qualified personnel for any such position on acceptable terms, if at all. Many of the biotechnology and pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. 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. In order to do so, we may need to pay higher compensation or fees to our employees or consultants than we currently expect, and such higher compensation payments may have a negative effect on our operating results. We face increased 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 medicines and obtaining regulatory approval to market those medicines, we have limited experience as a company in drug development. We are a clinical-stage biotechnology company focused on unlocking the broad potential of RNA medicines (also known as oligonucleotides), or those targeting RNA, to transform human health. Our RNA medicines platform, PRISM, combines multiple modalities, chemistry innovation and deep insights into human genetics to deliver scientific breakthroughs that treat both rare and common disorders. Our toolkit of RNA-targeting modalities includes RNA editing, splicing, silencing using siRNA and antisense silencing, providing us with unique capabilities for designing and sustainably delivering candidates that optimally address disease biology. Our diversified pipeline includes clinical programs in

obesity, AATD, DMD, and HD, as well as several preclinical programs utilizing our versatile RNA medicines platform. 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 collaboration with GSK. 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 and other misconduct by our employees, consultants and collaborators. Such misconduct could include intentional failures to comply with FDA and other foreign agency regulations, provide accurate information to the FDA, comply with manufacturing standards required by the FDA or us, 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, cybersecurity threats, 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, including our managed service providers ("MSPs"), on which we rely collect and store sensitive data, including legally protected patient health information, personally identifiable information about our employees, intellectual property, vendor information, and proprietary business information. We, along with our MSPs, manage and maintain our applications and data utilizing cloud-based and 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-party partners, is vital to our operations and business strategy. We also have systems in place at our facilities to mitigate disruptions to our communications systems, including the prevention of a loss to our electrical systems. Although we are proactive in our approach and take measures to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure, or that of our CROs or other third party partners, 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. For example, as previously disclosed in May 2023 and August 2023, we became aware that our mHTT assay vendor experienced a cybersecurity incident in April 2023. None of our data or patient samples were impacted by the incident and we remain in close contact with the vendor as they address this issue. The financial impact of this incident was not material, and there were no changes to the previously released financial results or financial statements. In addition, cyberattacks, malicious internet-based activity and fraud are prevalent and continue to increase in frequency. Any such event, including a cyberattack, 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. Furthermore, any such event could subject us to liability, negatively impact our business operations, or result in information theft, data corruption, operational disruption, damage to our reputation, or financial loss.

As part of our robust data protection practices, we regularly conduct business continuity and disaster recovery testing of our key information systems and data. 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 (including but not limited to GDPR, HIPAA and HITECH), government enforcement actions and regulatory penalties. Unauthorized access, loss or dissemination could also adversely

affect our business, damage our reputation, and disrupt our operations, including our ability to conduct research and development activities, process and prepare company financial information, and manage various general and administrative aspects of our business. For example, the loss of intellectual property or clinical trial data from completed or ongoing or planned clinical trials, in addition to privacy concerns, could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, while we take measures to help ensure early detection, there can be no assurance that we, or our CROs and other third party partners, 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 personal, confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

Numerous federal, state and international laws address privacy, data protection and the collection, storing, sharing, use, disclosure and protection of personally identifiable information and other user data, including in the context of the development and deployment of artificial intelligence technologies. In the United States, many states have already implemented state laws addressing privacy or are set to enact data protection legislation. In addition, several states have enacted privacy laws to specifically regulate consumer health data that is not subject to HIPAA.

As the patchwork of U.S. privacy laws expands, state enforcement of data privacy and cybersecurity breaches has increased, along with the cost. In addition to state enforcement of privacy laws, the Federal Trade Commission has increased enforcement of cybersecurity and data privacy, and related fines in 2024.

Outside the United States, personally identifiable information and other user data is increasingly subject to legislation and regulations in numerous jurisdictions around the world, the intent of which is to protect the privacy of information that is collected, processed and transmitted in or from the governing jurisdiction. Foreign data protection, privacy, information security, user protection and other laws and regulations are often more restrictive than those in the United States. For example, the General Data Protection Regulation ("GDPR") adopted by the European legislative bodies applies to any company, regardless of location, that collects or processes personal data of EU residents in connection with offering goods or services in the European Union or monitoring the behavior of EU residents. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, data minimization obligations, record-keeping requirements, mandatory data breach notification requirements, and correlated obligations on services providers. The GDPR also strictly regulates cross-border transfer of personal data, including requirements for data transfer impact assessments. Non-compliance with the GDPR may result in monetary penalties of up to €20 million or 4% of annual worldwide revenue, whichever is higher. Additionally, post-Brexit the United Kingdom has also adopted its own version of the GDPR.

While we have taken steps to comply with all applicable privacy laws and regulations, including the GDPR, by taking measures including but not limited to enhancing our security procedures, updating our website, revising our clinical trial informed consents, adopting the standard contractual clauses for cross-border transfers of personal data, increasing our cyber insurance, and entering into data processing agreements with relevant CROs and third party partners, we cannot completely assure you that our efforts to remain in compliance will be fully successful. The GDPR and other changes in laws or regulations associated with the enhanced protection of personal data may increase our costs of compliance and result in greater legal risks.

Foreign currency exchange rates may adversely affect our results.

Due to our operations outside of the United 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, 2024, 2023 and 2022, 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 U.S. tax legislation and future changes to applicable U.S. or foreign tax laws and regulations may have a material adverse effect on our business, financial condition and results of operations.

We are subject to income and other taxes in the United States and foreign jurisdictions. Changes in laws and policy relating to taxes or trade, including increases in tax rates or modifications, technical corrections or clarifications to tax laws, such as the Tax Cuts and Jobs Act of 2017, which eliminates the option to deduct research and development expenditures currently and requires corporations to capitalize and amortize them over a period of years, may have an adverse effect on our business, financial condition and results of operations. This Annual Report on Form 10-K does not discuss any such tax legislation or changes to tax laws and legislation, or the

manner in which it might affect us or purchasers of our securities. We urge our investors to consult with their legal and tax advisors with respect to such legislation and the potential tax consequences of investing in our securities.

We are also subject to different tax regulations in each of the jurisdictions where we conduct our business or where our management is located. We expect the scope and extent of regulation in the jurisdictions in which we conduct our business, or where our management is located, as well as regulatory oversight and supervision, to generally continue to increase. Generally, future changes in applicable U.S. or foreign tax laws and regulations, or their interpretation and application could have an adverse effect on our business, financial condition and results of operations.

Inadequate funding for the FDA, the SEC and other government agencies, or a work slowdown or stoppage at those agencies as part of a broader federal government shutdown, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also extend the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown or slowdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Risks Related to Our Intellectual Property

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

In our industry, the majority of an innovative product's commercial value is usually realized during the period in which it has market exclusivity. Market exclusivity is comprised of both patent and other intellectual property protection, as well as regulatory exclusivity. In the United States and some other countries, when market exclusivity expires and generic versions of a product are approved and marketed, there usually are very substantial and rapid declines in the product's sales. Accordingly, 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. Certain research and development activities involved in pharmaceutical development are exempt from patent infringement in the United States and other jurisdictions, for example, in the United States by the provisions of 35 U.S.C. § 271(e)(1) (the "Safe Harbor"). However, in the United States and certain other jurisdictions, the Safe Harbor exemption terminates when the sponsor submits an application for marketing approval (e.g., a NDA) in the United States). Therefore, the risk that a third party might allege patent infringement may increase as our products approach commercialization. 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. Certain jurisdictions 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 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, periodic changes to the patent laws and rules of patent offices around the world, including the USPTO can have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the America Invents Act, enacted in 2011, involved significant changes in patent legislation. Furthermore, 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 2013 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 oligonucleotides which contain modifications that we believe are not found in nature. However, 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, and by analogous bodies around the world, 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. For example, in 2012, European countries and the European Parliament agreed to a legislative package that would create a unitary patent protection system in the EU; aspects of this system were implemented beginning in 2023 for at least some European countries. The impact of the proposed unitary patent protection system on patents in Europe is currently unclear.

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, or that, 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 current or future collaborators or any future strategic partners.

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 United States 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 oligonucleotides and/or our platform.

As the field of oligonucleotides 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 oligonucleotides 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 oligonucleotides.

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 multiple jurisdictions, including major market jurisdictions. 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. For example, some jurisdictions may have heightened requirements for patentability compared to others, and may specifically require a detailed description of medical uses of a claimed drug. In some jurisdictions, 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. 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 oligonucleotide 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. There are numerous companies that have pending patent applications and issued patents directed to certain aspects of oligonucleotides. 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 oligonucleotides 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 our 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 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 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 2001 of Singapore (the "SFA"), which prohibit certain forms of market conduct and require certain information disclosures, and impose criminal and civil penalties on corporations, directors and officers in respect of any breach of such provisions. We are 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.

We are also subject to Section 34 of the Singapore Patents Act, which provides that a person residing in Singapore is required to obtain written authorization from the Singapore Registrar of Patents (the "Registrar") before filing an application for a patent for an invention outside of Singapore, unless certain conditions have been satisfied. 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 are required to make such filings in the future, without first obtaining written authorization from the Registrar. We have notified the Registrar of such filings and we have since implemented measures to address the requirements of Section 34 moving forward. To date, the Registrar has offered a compound of some of the offences considered against payment of a sum of S$50 to S$150 per considered case. 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$2,500, or to prosecute the offence subject to the other penalties noted above. Per requests in the Registrar's most recent decision, we have submitted approximately 140 patent applications in multiple patent families, most of which are related to previously reported applications, to the Intellectual Property Office of Singapore ("IPOS"). The IPOS may consider the filing of some or all of these applications to have breached Section 34 requirements per IPOS' current interpretation of Section 34, and we are waiting for IPOS' decision on these applications. We cannot assure you that the Registrar will offer to compound any such violations of Section 34, or that any offer to compound will be for an amount similar to previous compound offers.

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 1967 of Singapore (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 or our affiliated 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 its own or together with parties acting in concert with it, 30% or more of our voting shares, or if such person holds, either on its own or together with parties acting in concert with it, between 30% and 50% (both inclusive) of our voting shares, and if such person (or parties acting in concert with it) 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 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 most recent 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 us in a general meeting, such authority will continue in force until the earlier of (i) the conclusion of our next annual general meeting of shareholders, or (ii) the expiration of the period within which our next 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, which must be made annually after the close of each taxable year, 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 our gross income, the average value of our assets, including goodwill and the nature of our active business, we do not expect to be treated as a PFIC for U.S. federal income tax purposes for the taxable year ended December 31, 2024. Because the value of our assets for purposes of determining PFIC status will depend in part on the market price of our ordinary shares, which may fluctuate significantly, there can be no assurance that we will not be considered a PFIC for our current taxable year ending December 31, 2025 or 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. 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 United States 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. Under Singapore tax law, from January 1, 2024, subject to certain exceptions, gains from the sale or disposal by an entity without adequate economic substance and belonging to a relevant group of entities, of any movable or immovable property situated outside Singapore and that are received in Singapore from outside Singapore, are treated as income chargeable to tax.

We are also subject to income, withholding or other taxes in certain jurisdictions by reason of our activities and operations, and it is also possible that tax authorities in any such jurisdictions could assert that we are subject to greater taxation than we currently anticipate.

Any such Singaporean and non-Singaporean tax liability could materially adversely affect our results of operations.

Tax 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 conduct, and expect to continue 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.

Our financial results reflect the effect of certain tax credits and the operation of certain tax regimes within the United Kingdom. Legislation in the United Kingdom will limit the amount we may be able to claim as a payable tax credit in the future which could impact our financial condition, results of operations and cash flows.

As a company that carries out extensive research and development activities, we benefit from the U.K. research and development tax credit regime for small and medium-sized companies, whereby our subsidiary in the United Kingdom is able to surrender the trading losses that arise from its research and development activities for a payable tax credit of generally up to 18.6% of such expenditures. Expenditures of staff supplied by unconnected third parties incurred are eligible for a cash rebate of generally up to 12.1%.

Due to a change in the U.K. legislation affecting the U.K. research and development tax credit regime for small- and medium-sized companies, our ability to receive a payable tax credit for the surrender of our trading losses from research and development activities may be limited to the amount equal to three times our "pay as you earn" and U.K. national insurance tax liabilities, absent our qualification under an exception from such limitation.

Further, we may not be able to continue to claim a U.K. tax credit for research and development tax credits under the small and medium-sized companies regime in the future if our revenue or turnover exceeds €100 million for two consecutive years. In such an event, we will no longer qualify as a small or medium-sized enterprise.

Recently enacted U.K. legislation merges the small and medium-sized companies regime and the research and development expenditure credit regime generally for large companies. This legislation applies a 20% rate to qualifying research and development expenditures. The legislation also includes changes to other rules and types of qualifying expenditure, such as the treatment of subcontracted and overseas costs. We are currently evaluating the impact of the legislation on our future tax credit claims.

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.

Our ordinary shares are currently listed for trading on the Nasdaq Global Market. There is no assurance that the trading market for our shares will be or remain active. 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 continue 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 us.

We issued pre-funded warrants as part of our June 2022 and September 2024 financings, which may cause additional dilution to our shareholders.

In June 2022, we closed an underwritten offering in which we issued and sold 25,464,483 ordinary shares and, to RA Capital Management, L.P. in lieu of additional ordinary shares, pre-funded warrants (the "2022 Pre-Funded Warrants") to purchase up to 7,093,656 ordinary shares at an exercise price of $0.0001 per share. In September 2024, we closed an underwritten public offering (the "September 2024 Offering") in which we issued and sold 23,125,001 ordinary shares, and to certain investors in lieu of additional ordinary shares, the pre-funded warrants (the "2024 Pre-Funded Warrants", and together with the 2022 Pre-Funded Warrants, the "Pre-Funded Warrants") to purchase up to 1,875,023 ordinary shares at an exercise price of $0.0001 per share. The Pre-Funded Warrants contain a so-called "blocker" provision which provides that they are only exercisable upon receipt of shareholder approval or if such exercise would not cause the aggregate number of ordinary shares or the combined voting power of total securities, in each case, beneficially owned by the holder (together with its affiliates) to exceed, depending on the terms of the applicable Pre-Funded Warrants and in certain cases at the election of the holder, either 4.99%, 9.99% or 19.99% of the number of ordinary shares or total securities, respectively, outstanding immediately after giving effect to the exercise. To the extent the Pre-Funded Warrants above are exercised, additional ordinary shares will be issued and such issuance would dilute existing shareholders and increase the number of shares eligible for resale in the public market.

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, 2024, 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.

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 Exchange Act, the Sarbanes-Oxley Act of 2002 (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 result in substantial legal and financial compliance costs and will make some activities more time-consuming and costly. Our management and other personnel devote a substantial amount of time to these compliance requirements.

If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors' views of us.

We are required to comply with Section 404 of the Sarbanes-Oxley Act. Section 404 of the Sarbanes-Oxley Act requires public companies to maintain effective internal control over financial reporting. In particular, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our

internal control over financial reporting. Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that is evaluated frequently. If we fail to maintain the effectiveness of our internal controls or fail to comply in a timely manner with the requirements of the Sarbanes-Oxley Act, or if we identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, this could have a material adverse effect on our business. We could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on the price of our ordinary shares and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities, which would require additional financial and management resources. In addition, if our efforts to comply with new or changed laws, regulations, and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Our ability to successfully implement our business plan and comply with Section 404 of the Sarbanes-Oxley Act requires us to be able to prepare timely and accurate financial statements. We expect that we will need to continue to improve existing, and implement new operational and financial systems, procedures and controls to manage our business effectively. Any delay in the implementation of, or disruption in the transition to, new or enhanced systems, procedures or controls, may cause our operations to suffer and we may be unable to conclude that our internal control over financial reporting is effective and to obtain an unqualified report on internal controls from our independent registered public accounting firm as required under Section 404 of the Sarbanes-Oxley Act. This, in turn, could have an adverse impact on trading prices for our ordinary shares, and could adversely affect our ability to access the capital markets.

Although we determined that our internal controls over financing reporting were effective as of December 31, 2024, we may in the future identify internal control deficiencies that could rise to the level of a material weakness or uncover other errors in financial reporting. During the course of our evaluation of these material weaknesses, we may identify areas requiring improvement and may be required to design additional enhanced processes and controls to address issues identified through this review. There can be no assurance that such remediation efforts will be successful, that our internal control over financial reporting will be effective as a result of these efforts or that any such future deficiencies identified may not be material weaknesses that would be required to be reported in future periods. In addition, we cannot assure you that our independent registered public accounting firm will be able to attest that such internal controls are effective.

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 ("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 or otherwise 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 that 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 Pre-Funded Warrants or vesting of outstanding restricted share units, or the perception that such sales could occur, could adversely affect the price of our ordinary shares. Certain of our shareholders have required us, or have the right to require us, to register the sales of their shares under the Securities Act under agreements between us and such shareholders. For example, in August 2019, we filed a registration statement on Form S-3, which was declared effective on August 14, 2019, to register the resale from time to time by certain of our executive officers, directors and their affiliates of up to approximately 7.1 million ordinary shares.

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 1C. Cybersecurity

We recognize the importance of maintaining the trust and confidence of the patients we serve, our business partners, employees and our shareholders and are committed to protecting the confidentiality, integrity and reliance of our business operations and systems. Effective data protection practices, including responsible stewardship of our intellectual property and the secure processing, storage, maintenance and transmission of critical information by us and other third parties with whom we do business is vital to our operations.

Our cybersecurity practices, policies, and standards are based on recognized frameworks established by the National Institute of Standards and Technology ("NIST") (NIST SP 800-53), the Center for Internet Security ("CIS"), along with adopting best practices from Control Objectives for Information and Related Technologies ("COBIT") and other applicable industry standards. In general, we seek to address cybersecurity risks through a comprehensive, cross-functional approach that is focused on preserving the confidentiality, security and availability of the information that we collect and store by identifying, preventing and mitigating cybersecurity threats and effectively responding to cybersecurity incidents if they occur.

Cybersecurity Risk Management and Strategy

We may face risks related to cybersecurity, such as unauthorized access, cybersecurity attacks and other security incidents, which could adversely affect our business and operations. To identify and assess material risks from cybersecurity threats, we maintain a robust cybersecurity program to ensure our systems are effective and prepared for information security risks and have integrated these processes into our overall risk management systems and processes. We also identify our cybersecurity threat risks by comparing our processes to standards set by NIST, CIS, and COBIT, as well as by engaging experts to attempt to infiltrate our information systems. We consider risks from cybersecurity threats alongside other company risks as part of our overall risk assessment process. We employ a range of tools, services and capabilities, including regular network and endpoint monitoring, audits, vulnerability assessments, penetration testing, threat modeling, disaster recovery and business continuity planning activities, red team testing, mandatory training for our employees, and tabletop exercises to inform our risk identification and assessment.

Our processes also address cybersecurity threat risks associated with our use of third-party service providers, including our vendors, CROs, suppliers and/or manufacturers who may have access to patient and employee data or our systems. We perform diligence on third parties that have access to our systems, data or facilities that house such systems or data, and continually monitor cybersecurity threat risks identified through such diligence. Additionally, we generally require those third parties that could introduce significant cybersecurity risk to us to agree by contract to manage their cybersecurity risks in specified ways, and to agree to be subject to cybersecurity audits, which we conduct continuously through third-party risk management tools.

Our incident response plan coordinates the activities we take to prepare for, detect, respond to and recover from cybersecurity incidents, which include processes to triage, assess severity for, escalate, contain, investigate and remediate the incident, as well as to comply with potentially applicable legal obligations and mitigate damage to our business and reputation.

As part of the above processes, we regularly engage with consultants and other third parties, including a bi-annual review of our cybersecurity program by an independent Qualified Security Assessor.

In the last three fiscal years, we have not experienced any material cybersecurity incidents and the expenses we have incurred from cybersecurity incidents were immaterial. We describe whether and how risks from identified cybersecurity threats, including as a result of any previous cybersecurity incidents, have materially affected or are reasonably likely to materially affect us, including our business strategy, results of operations, or financial condition, under the heading "*Security breaches, cybersecurity threats, 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 Item 1A. Risk Factors, which disclosures are incorporated by reference herein.

Cybersecurity Governance

Our Board is actively involved in oversight of our risk management activities, and cybersecurity represents an important element of our overall approach to risk management. Our Board delegates to the Audit Committee oversight of certain aspects of our risk management process, including risks related to information technology, data privacy and cybersecurity.

At least quarterly, our Audit Committee receives an update from management of our cybersecurity threat risk management and strategy processes, including recent cybersecurity incidents and related responses, cybersecurity testing, activities of third parties, and other similar matters. Our cybersecurity risk management and strategy processes are led by our Data Security Officer, Data Privacy Officer, Chief Financial Officer and General Counsel. Such individuals have collectively over 50 years of prior work experience in various roles involving managing information security, developing cybersecurity strategy, implementing effective information and cybersecurity programs, as well as several relevant degrees and certifications.

Our Audit Committee is encouraged to regularly engage in conversations with management on cybersecurity-related news and events and discuss any updates to our cybersecurity risk management and strategy programs. Management is informed about and monitors the prevention, mitigation, detection, and remediation of cybersecurity incidents through their management of, and participation in, the cybersecurity risk management and strategy processes described above, including the operation of our incident response plan. We have processes in place to ensure that our Audit Committee shall receive prompt and timely information regarding any cybersecurity incident that meets establishing reporting thresholds, as well as ongoing updates regarding any such incident until it has been addressed.

Item 2. Properties

We maintain our U.S. corporate offices and research and development facilities in Cambridge, Massachusetts, where we lease office and laboratory space of approximately 44,000 square feet.

We lease approximately 90,000 square feet of office and laboratory space in Lexington, Massachusetts, which we use for our research, development and cGMP manufacturing.

We also occupy laboratory and office 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".

Shareholders

As of February 24, 2025, we had 153,486,021 ordinary shares outstanding and approximately nine shareholders of record of our ordinary shares.

Dividends

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.

Unregistered Sales of Securities

Not applicable.

Issuer Purchases of Equity Securities

None.

Item 6. [Reserved]

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.

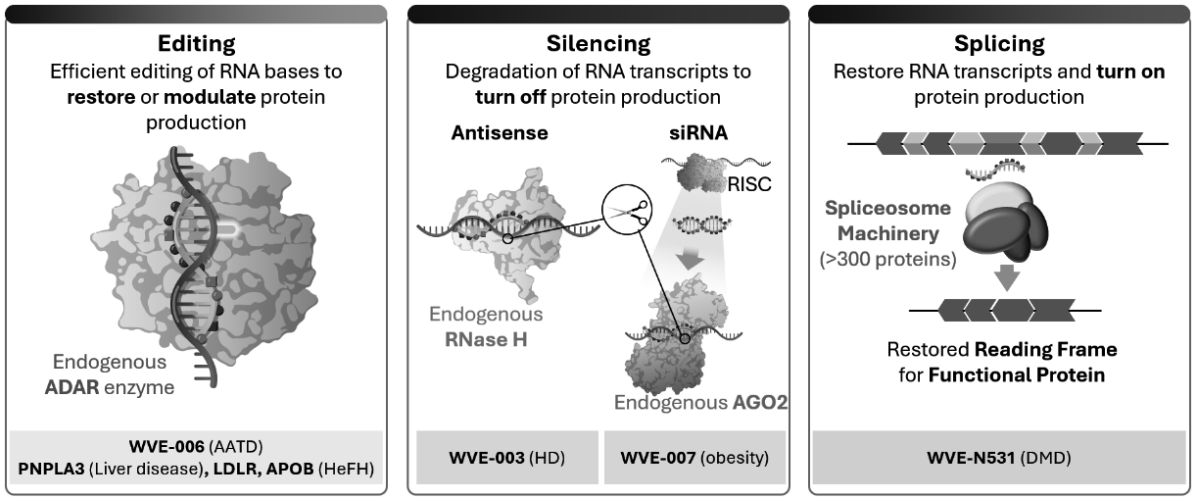
Overview

We are a clinical-stage biotechnology company focused on unlocking the broad potential of ribonucleic acid ("RNA") medicines (also known as oligonucleotides), or those targeting RNA, to transform human health. Our RNA medicines platform, PRISM®, combines multiple modalities, chemistry innovation and deep insights into human genetics to deliver scientific breakthroughs that treat both rare and common disorders. Our toolkit of RNA-targeting modalities includes RNA editing, splicing, silencing using RNA interference ("siRNA") and antisense silencing, providing us with unique capabilities for designing and sustainably delivering candidates that optimally address disease biology. Our diversified pipeline includes clinical programs in obesity, alpha-1 antitrypsin deficiency ("AATD"), Duchenne muscular dystrophy ("DMD"), and Huntington's disease ("HD"), as well as several preclinical programs utilizing our versatile RNA medicines platform.

We were founded on the recognition that there was a significant, untapped opportunity to use chemistry innovation to tune the pharmacological properties of oligonucleotides. We have more than a decade of experience challenging convention related to oligonucleotide design and pioneering novel chemistry modifications to optimize the pharmacological properties of our molecules. We have seen in clinical trials that these chemistry modifications enhance potency, distribution, and durability of effect of our molecules. Our novel chemistry also allows us to avoid using complex delivery vehicles, such as lipid nanoparticles and viruses, and instead use clinically proven conjugates (*e.g., N*-acetylgalactosamine or ("GalNAc")) or free uptake for delivery to a variety of cell and tissue types. We maintain strong and broad intellectual property, including for our novel chemistry modifications.

Our best-in-class chemistry capabilities have also unlocked new areas of biology, such as harnessing adenosine deaminases acting on RNA ("ADAR") enzymes for messenger RNA ("mRNA") correction and upregulation, selectively silencing a mutant allele, and more. By opening up new areas of biology, we have also opened up new opportunities to slow, stop or reverse disease and have expanded the possibilities offered through our platform.

The inspiration for our multimodal platform is based on the recognition that the biological machinery *(i.e.,* enzymes) needed to address human disease already exists within our cells and can be harnessed for therapeutic purposes with the right tools. We believe that we have built the most versatile toolkit of RNA-targeting modalities in the industry, with multiple means of repairing, restoring, or reducing proteins and designing best-fit solutions based on the unique biology of a given disease target. We are actively advancing programs using four distinct modalities, including novel A-to-I RNA editing oligonucleotides ("AIMers").



These modalities include:

- **RNA editing,** which uses AIMers that are designed to target single bases on an RNA transcript and recruit endogenous ADAR enzymes that naturally possess the ability to change an adenine (A) to an inosine (I), which cells read as guanine (G). This approach enables both the correction of G-to-A point mutations and the modulation of RNA to either upregulate protein expression, modify protein-protein interactions, or alter RNA folding and processing. AIMers are short in length, fully chemically modified, and use our novel chemistry, which make them distinct from other ADAR-mediated editing approaches.

- **Antisense (silencing)**, which uses our oligonucleotide designed to bind to a specific sequence in a target RNA strand that encodes a disease-associated protein or pathogenic RNA. The resulting double-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) (silencing)**, which uses our double-stranded RNAs called siRNAs to engage the RNAi machinery known as the RNA-induced silencing complex ("RISC") and 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 / exon skipping**, which is the processing of a nascent pre-mRNA transcript into mRNA by removing introns and joining exons together. Exon skipping uses our oligonucleotide designed to bind to a particular sequence within a target pre-mRNA and direct the cellular machinery to alter the final composition of exons in mature mRNA by deleting, or splicing out, certain specific regions of that RNA.

We intentionally focus on targeting the transcriptome using oligonucleotides rather than other nucleic acid modalities such as gene therapy and DNA editing. This focus enables us to:

- Leverage diversity of expression across cell types by modulating the many regulatory pathways that impact gene expression, including transcription, endogenous RNAi pathways, splicing, and translation;

- Address diseases that have historically been difficult to treat with small molecules or biologics;

- Access a variety of tissue types or cell types throughout the body and modulate the frequency of dosing for broad distribution in tissues over time;

- Avoid the risk of permanent off-target genetic changes and other challenges associated with DNA editing or gene therapy approaches; and

- Leverage well-established industry manufacturing processes and regulatory, access, and reimbursement pathways.

We have a robust and diverse pipeline of potential first-or best-in-class programs addressing both rare and common diseases:

- GalNAc-conjugated oligonucleotides for hepatic and metabolic diseases including:

    - Obesity: WVE-007 is a GalNAc-conjugated siRNA targeting inhibin βE ("INHBE");

    - Alpha-1 antitrypsin deficiency ("AATD"): WVE-006 is a GalNAc-conjugated SERPINA1 AIMer;

    - Liver disease: GalNAc-conjugated AIMer targeting PNPLA3 I148M for correction; and

    - Heterozygous Familial Hypercholesterolemia ("HeFH"): GalNAc-conjugated AIMer targeting low-density lipoprotein receptor ("LDLR") for upregulation and GalNAc-conjugated AIMer targeting apolipoprotein B ("APOB") for correction.

- Unconjugated oligonucleotides for muscle, CNS and other disease areas including:

    - Duchenne muscular dystrophy ("DMD"): WVE-N531 is an exon 53 splicing oligonucleotide; and

- Huntington's disease ("HD"): WVE-003 is an allele-selective oligonucleotide designed to lower mutant huntingtin ("mHTT") protein and preserve healthy, wild-type huntingtin ("wtHTT") protein.

Our RNA editing capability affords us the dexterity to address both rare and common diseases, as well as those diseases impacting large patient populations. AIMers are designed to target single bases on an RNA transcript and recruit proteins that exist in the body, called ADAR enzymes, which naturally possess the ability to change an adenine (A) to an inosine (I), which cells read as guanine (G). This approach enables both the correction of G-to-A point mutations and the modulation of RNA to either upregulate protein expression, modify protein-protein interactions, or alter RNA folding and processing. AIMers enable simplified delivery and avoid the risk of permanent changes to the genome and irreversible off-target effects with DNA-targeting approaches. AIMers are short in length, fully chemically modified, and use our novel chemistry, which make them distinct from other ADAR-mediated editing approaches.

GSK Collaboration

In December 2022, we announced a strategic collaboration with GlaxoSmithKline Intellectual Property (No. 3) ("GSK") to advance transformative oligonucleotide therapeutics, including WVE-006. The collaboration combines GSK's novel genetic insights, as well as its global development and commercial capabilities, with our PRISM platform and oligonucleotide expertise. The collaboration will enable us to continue building a pipeline of first-in-class oligonucleotide-based therapeutics and unlock new areas of disease biology, as well as realize the full value of WVE-006 as a potential best-in-class treatment for AATD that has the potential to simultaneously address both liver and lung manifestations of the disease.

Our GSK collaboration has three components:

(1) a discovery collaboration which enables us to advance up to three programs leveraging targets informed by GSK's novel genetic insights;

(2) a discovery collaboration which enables GSK to advance up to eight programs leveraging PRISM and our oligonucleotide expertise and discovery capabilities; and

(3) an exclusive global license for GSK to WVE-006, our AATD program, that uses our proprietary AIMer technology. We will maintain development responsibilities for WVE-006 through completion of RestorAATion-2, at which point development and commercial responsibilities will transition to GSK.

Takeda Collaboration (expired in October 2024)

In February 2018, we entered into a global strategic collaboration with Takeda Pharmaceutical Company Limited ("Takeda"), pursuant to which we agreed to collaborate with Takeda on the research, development and commercialization of oligonucleotide therapeutics for disorders of the CNS. On October 11, 2024, we were notified by Takeda that Takeda did not intend to exercise and therefore elected to terminate its option for the HD target under the collaboration. As HD was the last active collaboration target under the collaboration, the collaboration expired with immediate effect. As a result of the option termination, we are now free to advance WVE-003, our clinical-stage Huntington's disease program, as well as any other programs targeting HTT, independently or with other partners.

Financial Operations Overview

We have never been profitable, and since our inception, we have incurred significant operating losses. Our net loss was $97.0 million in 2024, $57.5 million in 2023, and $161.8 million in 2022. As of December 31, 2024 and 2023, we had an accumulated deficit of $1,121.9 million and $1,024.9 million, respectively. We expect to incur significant expenses and operating losses for the foreseeable future.

Revenue

We recognize collaboration revenue under the GSK Collaboration Agreement, which became effective in January 2023, and the Takeda Collaboration Agreement, which became effective in April 2018 and expired in the fourth quarter of 2024, (both of which are defined in Note 5 in the notes to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K). 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.

Operating Expenses

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

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 CROs that conduct research, preclinical and clinical activities on our behalf, as well as CMOs that manufacture drug product for use in our preclinical studies and clinical trials;
- expenses incurred related to our internal manufacturing of drug substance for use in our preclinical studies and clinical trials;
- expenses related to compliance with regulatory requirements;
- expenses related to third-party consultants;
- research and development supplies and services expenses; and
- facility-related expenses, including rent, maintenance and other general operating expenses.

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 has been the development of our RNA medicines platform, PRISM. We are using PRISM, which includes our novel chemistry modifications, to design, develop and commercialize a broad pipeline of first- or best-in class RNA medicines using our editing, splicing, RNAi, and antisense modalities.

Our research and development expenses consist primarily of expenses related to our CROs, CMOs, consultants, other external vendors and fees paid to global regulatory agencies to conduct our clinical trials, in addition to compensation-related expenses, internal manufacturing expenses, facility-related expenses and other general operating expenses. These expenses are incurred in connection with research and development efforts and our preclinical studies and clinical trials. We track certain external expenses on a program-by-program basis. However, we do not allocate compensation-related expenses, internal manufacturing expenses, equipment repairs and maintenance expense, facility-related expenses or other operating expenses to specific programs. These expenses, which are not allocated on a program-by-program basis, are included in the "Other research and development expenses[(1)], including INHBE, RNA

editing, PRISM, others" category along with other external expenses related to our discovery and development programs, as well as platform development and identification of potential drug discovery candidates.

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 to continue to incur significant research and development expenses 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, maintain our manufacturing capabilities and continue to discover and develop additional product candidates in multiple therapeutic areas.

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. 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.

Other Income, Net

Other income, net is comprised of refundable tax credits from tax authorities, dividend and interest income earned on cash and cash equivalents balances, gains and losses on foreign currency transactions, and real estate taxes. We recognize refundable tax credits when there is reasonable assurance that we will comply with the requirements of the refundable tax credit and that the refundable tax credit will be received.

Income Taxes

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

As of December 31, 2024 and 2023, we have recorded a full valuation allowance against our net operating loss carryforwards and federal and state tax credits in all jurisdictions due to uncertainty regarding future taxable income.

Results of Operations

In this section, we discuss the results of our operations for the year ended December 31, 2024 compared to the year ended December 31, 2023 and for the year ended December 31, 2023 compared to the year ended December 31, 2022.

Comparison of the Year Ended December 31, 2024 to the Year Ended December 31, 2023

The following table summarizes our results of operations for 2024 and 2023:

	For the Year Ended December 31,		
	2024	2023	Change
		(in thousands)	
Revenue	$ 108,302	$ 113,305	$ (5,003)
Operating expenses:			
Research and development	159,682	130,009	29,673
General and administrative	59,023	51,292	7,731
Total operating expenses	218,705	181,301	37,404
Loss from operations	(110,403)	(67,996)	(42,407)
Total other income, net	13,395	9,806	3,589
Loss before income taxes	(97,008)	(58,190)	(38,818)
Income tax benefit (provision)	—	677	(677)
Net loss	$ (97,008)	$ (57,513)	$ (39,495)

Revenue

Revenue for the years ended December 31, 2024 and 2023, was $108.3 million and $113.3 million, respectively, and was earned under the GSK Collaboration Agreement and the Takeda Collaboration Agreement.

The $5.0 million decrease in revenue year over year was driven by the revenue recognized under the GSK Collaboration Agreement, partially offset by the increase in revenue recognized under the Takeda Collaboration Agreement. The $108.3 million in revenue recognized during the year ended December 31, 2024 was comprised of $37.0 million in revenue recognized under the GSK Collaboration Agreement and $71.3 million of revenue recognized under the Takeda Collaboration Agreement. The $113.3 million in revenue recognized during the year ended December 31, 2023 was comprised of $66.3 million in revenue recognized under the GSK Collaboration Agreement and $47.0 million of revenue recognized under the Takeda Collaboration Agreement. The increase in the Takeda Collaboration revenue earned year over year was primarily due to the termination of the collaboration in October 2024, which led to the recognition of the remainder of the deferred revenue related to the research and development services, as well as the license related to the HD program. This was offset by the decrease in the GSK revenue earned year over year primarily related to the AATD program.

Research and Development Expenses

The following table summarizes our research and development expenses incurred for the years ended December 31, 2024 and 2023:

	For the Year Ended December 31,		
	2024	2023	Change
		(in thousands)	
AATD program	$ 11,666	$ 8,453	$ 3,213
DMD programs	15,536	7,808	7,728
HD programs	11,790	13,086	(1,296)
Other research and development expenses[(1)], including INHBE, RNA editing, PRISM, others	119,976	91,617	28,359
ALS and FTD programs *(discontinued)*	714	9,045	(8,331)
Total research and development expenses	$ 159,682	$ 130,009	$ 29,673

(1) Includes expenses related to other research and development programs, identification of potential drug discovery candidates, compensation-related expenses, internal manufacturing expenses, equipment repairs and maintenance expense, facility-related expenses, and other operating expenses, which are not allocated to specific programs.

Research and development expenses were $159.7 million for the year ended December 31, 2024, compared to $130.0 million for the year ended December 31, 2023. The increase of $29.7 million was due to the following:

- an increase of $3.2 million in external expenses related to our AATD program, WVE-006 (RNA editing);
- an increase of $7.7 million in external expenses related to our DMD programs, including WVE-N531 (splicing);
- a decrease of $1.3 million in external expenses related to our HD programs, including WVE-003 (silencing);
- an increase of $28.4 million in other research and development expenses, including INHBE, RNA editing, PRISM, and other internal and external research and development expenses that are not allocated on a program-by-program basis or are related to other discovery and development programs, and the identification of potential drug discovery candidates, mainly due to increases in compensation-related expenses and facilities-related expenses, partially offset by decreases in other external research and development expenses; and
- a decrease of $8.3 million in external expenses related to our discontinued ALS and FTD program, WVE-004.

General and Administrative Expenses

General and administrative expenses were $59.0 million for the year ended December 31, 2024, compared to $51.3 million for the year ended December 31, 2023. The increase of $7.7 million is primarily driven by increases in compensation related expenses and administrative expenses.

Other Income, Net

Other income, net for the years ended December 31, 2024 and 2023 was $13.4 million and $9.8 million, respectively. The increase of $3.6 million in other income, net was primarily driven by an increase in estimated refundable tax credits as well as an increase in dividend income during the year ended December 31, 2024.

Income Tax Benefit

During the years ended December 31, 2024 and 2023, we recorded no income tax benefit or provision and an income tax benefit of $0.7 million, respectively. The income tax benefit for the year ended December 31, 2023 was due to a change in estimate in connection with U.S. tax guidance relating to the capitalization of research and development expenditures.

Comparison of the Year Ended December 31, 2023 to the Year Ended December 31, 2022

The following table summarizes our results of operations for 2023 and 2022:

	For the Year Ended December 31,		
	2023	2022	Change
		(in thousands)	
Revenue	$ 113,305	$ 3,649	$ 109,656
Operating expenses:			
Research and development	130,009	115,856	14,153
General and administrative	51,292	50,513	779
Total operating expenses	181,301	166,369	14,932
Loss from operations	(67,996)	(162,720)	94,724
Total other income, net	9,806	1,578	8,228
Loss before income taxes	(58,190)	(161,142)	102,952
Income tax benefit (provision)	677	(681)	1,358
Net loss	$ (57,513)	$ (161,823)	$ 104,310

Revenue

Revenue for the year ended December 31, 2023 was $113.3 million and was earned under the GSK Collaboration Agreement and the Takeda Collaboration Agreement. Revenue for year ended December 31, 2022 was $3.6 million and was earned primarily under the Takeda Collaboration Agreement, as the GSK Collaboration Agreement became effective in January 2023.

The $109.7 million increase in revenue year over year was driven by the revenue recognized under the new GSK Collaboration Agreement, after it became effective in January 2023, as well as the increase in revenue recognized under the Takeda Collaboration Agreement. The $113.3 million in revenue recognized during the year ended December 31, 2023 was comprised of $66.3 million in revenue recognized under the GSK Collaboration Agreement and $47.0 million of revenue recognized under the Takeda Collaboration Agreement. The $3.6 million in revenue recognized during the year ended December 31, 2022 was primarily related to the research and development services under the Takeda Collaboration Agreement related to the HD, C9, and SCA3 programs. During the year ended December 31, 2023, the Company recognized revenue of $47.0 million under the Takeda Collaboration. The increase in revenue earned year over year related to the Takeda Collaboration is primarily due to the termination of the C9 and SCA3 programs in 2023 which led to the recognition of the remainder of the deferred revenue related to the research and development services, as well as the options related to the C9 and SCA3 programs.

Research and Development Expenses

The following table summarizes our research and development expenses incurred for the years ended December 31, 2023 and 2022:

	For the Year Ended December 31,		
	2023	2022	Change
		(in thousands)	
AATD program	$ 8,453	$ 3,763	$ 4,690
DMD programs	7,808	2,610	5,198
HD programs	13,086	7,952	5,134
Other research and development expenses[(1)], including INHBE, RNA editing, PRISM, others	91,617	89,992	1,625
ALS and FTD programs *(discontinued)*	9,045	11,539	(2,494)
Total research and development expenses	$ 130,009	$ 115,856	$ 14,153

(1) Includes expenses related to other research and development programs, identification of potential drug discovery candidates, compensation-related expenses, internal manufacturing expenses, equipment repairs and maintenance expense, facility-related expenses, and other operating expenses, which are not allocated to specific programs.

Research and development expenses were $130.0 million for the year ended December 31, 2023, compared to $115.9 million for the year ended December 31, 2022. The increase of $14.1 million was due to the following:

- an increase of $4.7 million in external expenses related to our AATD program, WVE-006 (RNA editing);
- an increase of $5.2 million in external expenses related to our DMD programs, including WVE-N531 (splicing);
- an increase of $5.1 million in external expenses related to our HD programs, including WVE-003 (silencing);
- an increase of $1.6 million in other research and development expenses, including INHBE, RNA editing, PRISM, and other internal and external research and development expenses that are not allocated on a program-by-program basis. or are related to other discovery and development programs, and the identification of potential drug discovery candidates, mainly due to increases in compensation-related expenses and facilities-related expenses, partially offset by decreases in other external research and development expenses; and
- a decrease of $2.5 million in external expenses related to our discontinued ALS and FTD program, WVE-004.

General and Administrative Expenses

General and administrative expenses were $51.3 million for the year ended December 31, 2023, compared to $50.5 million for the year ended December 31, 2022. The increase of $0.8 million was primarily driven by increases in other general and administrative operating expenses, partially offset by a decrease in compensation-related expenses.

Other Income, Net

Other income, net for the years ended December 31, 2023 and 2022 was $9.8 million and $1.6 million, respectively. The increase of $8.2 million in other income, net was primarily driven by an increase in dividend income as well as an increase in estimated refundable tax credits during the year ended December 31, 2023.

Income Tax Benefit (Provision)

During the years ended December 31, 2023 and 2022, we recorded an income tax benefit of $0.7 million and an income tax provision of $0.7 million, respectively. The income tax benefit for the year ended December 31, 2023 was due to a change in estimate in connection with recent U.S. tax guidance relating to the capitalization of research and development expenditures. The income tax provision for the year ended December 31, 2022 was primarily due to the requirement under the Tax Cuts and Jobs Act of 2017 for taxpayers to capitalize and amortize research and development expenditures over five or fifteen years pursuant to Section 174 of the Internal Revenue Code of 1986, as amended.

Liquidity and Capital Resources

Since our inception, we have not generated any product revenue and have incurred recurring net operating losses. To date, we have primarily funded our operations through public and other registered offerings of our ordinary shares and other securities, collaborations with third parties and private placements of debt and equity securities. Through December 31, 2024, we have received an aggregate of approximately $1,578.4 million in net proceeds from these transactions, consisting of $977.8 million in net proceeds from public and other registered offerings of our ordinary shares and other securities, $511.3 million from our collaborations and $89.3 million in net proceeds from private placements of our debt and equity securities.

In January 2024, the representatives of the underwriters in connection with the previously disclosed underwritten public offering (the "December 2023 Offering") exercised their option to purchase an additional 3,000,000 ordinary shares at a price of $5.00 per ordinary share as a part of the December 2023 Offering. We received an additional $14.0 million in net proceeds from the December 2023 Offering in January 2024.

On September 27, 2024, we closed the September 2024 Offering in which we issued and sold 23,125,001 of our ordinary shares and the 2024 Pre-Funded Warrants to purchase up to 1,875,023 of our ordinary shares. The gross proceeds to us from the September 2024 Offering were $200.0 million before deducting underwriting discounts and commissions and other offering expenses. On October 1, 2024, the representatives of the underwriters exercised their option in full to purchase an additional 3,750,000 ordinary shares, for additional net proceeds to us of approximately $28.2 million.

As of December 31, 2024, we had cash and cash equivalents of $302.1 million, restricted cash of $3.8 million and an accumulated deficit of $1,121.9 million.

We expect 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 expectation 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 expect we have sufficient funds for our current or future operating plans.

Our operating lease commitments as of December 31, 2024 total $29.1 million, of which $9.6 million is related to payments in 2025 and approximately $19.5 million is related to payments beyond 2025.

On November 12, 2024, we filed a shelf registration statement on Form S-3ASR with the SEC for which we registered for sale an indeterminate amount of any combination of our ordinary shares, debt securities, warrants, rights and/or units from time to time and at prices and on terms that we may determine, which we refer to as the "2024 WKSI Shelf". Our 2024 WKSI Shelf includes a prospectus covering up to an aggregate of $250.0 million in ordinary shares that we are able to issue and sell from time to time, through Jefferies LLC ("Jefferies") acting as our sales agent, pursuant to the Open Market Sale Agreement, dated May 10, 2019, as amended by Amendment No. 1, dated as of March 2, 2020, Amendment No. 2, dated as of March 3, 2022, and Amendment No. 3, dated November 12, 2024, (collectively, the "Sales Agreement"), for our "at-the-market" equity program. For the three months ended December 31, 2024, we received $5.2 million in net proceeds from sales under our "at-the-market" equity program.

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,		
	2024	2023	2022
	(in thousands)		
Net cash used in operating activities	$ (151,026)	$ (19,431)	$ (127,781)
Net cash used in investing activities	(938)	(1,115)	(1,255)
Net cash provided by financing activities	253,890	132,534	67,188
Effect of foreign exchange rates on cash	(138)	(95)	(210)
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 101,788	$ 111,893	$ (62,058)

Operating Activities

During 2024, operating activities used $151.0 million of cash, primarily due to our net loss of $97.0 million, partially offset by non-cash charges of $21.8 million and changes in our operating assets and liabilities of $75.8 million. The non-cash charges for 2024 related to share-based compensation expense of $13.1 million, amortization of right-of-use assets of $4.8 million, and depreciation expense of $3.9 million. The largest change in operating assets and liabilities was a $93.6 million decrease in deferred revenue, mainly driven by our Takeda Collaboration Agreement, which was partially offset by the second largest change in operating assets and liabilities, the $19.7 million decrease in accounts receivable primarily due to the collection of receivables related to the GSK Collaboration Agreement.

During 2023, operating activities used $19.4 million of cash, primarily due to our net loss of $57.5 million, partially offset by non-cash charges of $19.0 million and changes in our operating assets and liabilities of $19.1 million. The non-cash charges for 2023 related to share-based compensation expense of $9.8 million, amortization of right-of-use assets of $4.2 million, and depreciation expense of $5.0 million. The largest change in operating assets and liabilities was a $54.3 million increase in deferred revenue, mainly driven by our GSK Collaboration Agreement, which became effective in January 2023, which was partially offset by the second largest change in operating assets and liabilities, the $21.1 million increase in accounts receivable primarily related to the achievement of a milestone under the GSK Collaboration Agreement.

During 2022, operating activities used $127.8 million of cash, primarily due to our net loss of $161.8 million, partially offset by non-cash charges of $27.3 million and changes in our operating assets and liabilities of $6.7 million. The non-cash charges for 2022 related mainly to share-based compensation expense of $17.2 million and depreciation expense of $6.6 million. The largest change in operating assets and liabilities was a $9.3 million increase in accounts payable.

Investing Activities

During 2024, investing activities used $0.9 million of cash, primarily consisting of purchases of property and equipment.

During 2023, investing activities used $1.1 million of cash, primarily consisting of purchases of property and equipment.

During 2022, investing activities used $1.3 million of cash, primarily consisting of purchases of property and equipment. Additionally, we purchased $75.0 million of short-term investments during 2022, all of which matured in 2022.

Financing Activities

During 2024, net cash provided by financing activities was $253.9 million, which was primarily due to the $215.8 million in net proceeds from the September 2024 Offering of ordinary shares and the 2024 Pre-Funded Warrants; as well as the $14.0 million in net proceeds from the January 2024 exercise of the underwriters' option to purchase an additional 3,000,000 shares under the December 2023 Offering. Additionally, we received $20.4 million in net proceeds from sales under our "at-the-market" equity program.

During 2023, net cash provided by financing activities was $132.5 million, primarily due to the $93.6 million in net proceeds from the December 2023 Offering, which comprised of sales of ordinary shares, as well as $34.6 million in net proceeds from the GSK Equity Investment. Additionally, there were $3.1 million in net proceeds from our "at-the-market" equity program.

During 2022, net cash provided by financing activities was $67.2 million, primarily due to the $65.5 million in net proceeds from the underwritten offering we completed in June 2022, which was comprised of sales of ordinary shares and the 2022 Pre-Funded Warrants. Additionally, there were $1.1 million in net proceeds from our "at-the-market" equity program.

Funding Requirements

We expect to continue to incur significant expenses in connection with our ongoing research and development activities and our internal cGMP manufacturing activities. Furthermore, we anticipate that our expenses will continue to vary if and as we:

- continue to conduct our clinical trials evaluating our product candidates in patients;
- 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 continuing to innovate our research and development platform, PRISM, and in optimizing our manufacturing processes and formulations;
- maintain 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;
- respond to the impacts of local and global health epidemics, the conflict involving Russia and Ukraine, the conflict in the Middle East, global economic uncertainty, volatility in inflation, volatility in interest rates or market disruptions on our business; 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 future 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, results and costs of conducting research and continued preclinical and clinical development for our therapeutic programs and future potential pipeline candidates;
- the number and characteristics of product candidates and programs that we pursue;
- the cost of manufacturing clinical supplies of our product candidates;
- whether and to what extent milestone events are achieved under our collaborations with Takeda and GSK or any potential future licensee or collaborator;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to obtain marketing approval for our product candidates;

- the impacts of local and global health epidemics, the conflict involving Russia and Ukraine, the conflict in the Middle East, global economic uncertainty, volatility in inflation, volatility in interest rates or market disruptions on our business;
- 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;
- market acceptance of our product candidates, to the extent any are approved for commercial sale, and 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 GSK under our collaborations with them. 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.

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 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 our revenue recognition policy, particularly (a) assessing the number of performance obligations; (b) determining the transaction price; (c) allocating the transaction price to the performance obligations in the contract; and (d) determining the pattern over which performance obligations are satisfied, including estimates to complete performance obligations, and the assumptions and estimates used in our analysis of contracts with CROs and CMOs to estimate the contract expense, involve a greater degree of judgment, and therefore we consider them to be our critical accounting policies. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions and conditions.

Revenue Recognition

The Company recognizes revenue in accordance with Accounting Standards Codification ("ASC") Topic 606, Revenue from Contracts with Customers ("ASC 606"). This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that 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-step analysis: (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. The Company only applies the five-step analysis to contracts when it is probable that the entity will collect the consideration to which it is entitled in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract, determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company has entered into collaboration agreements for research, development, and commercial services, under which the Company licenses certain rights to its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, upfront license fees; prepayment or reimbursement of certain costs; customer option exercise fees; development, regulatory and commercial milestone payments; and royalties on net sales of licensed products. Any variable consideration is constrained, and therefore, the cumulative revenue associated with this consideration is not recognized until it is deemed not to be at significant risk of reversal.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under each of its agreements for which the collaboration partner is also a customer, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must use significant judgment to determine: (a) the number of performance obligations based on the determination under step (ii) above; (b) the transaction price under step (iii) above; and (c) the timing of satisfaction of performance obligations as a measure of progress in step (v) above. The Company uses significant judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price as described further below. The transaction price is allocated to the optional goods and services the Company expects to provide. The Company uses estimates to determine the timing of satisfaction of performance obligations.

Amounts received prior to being recognized as revenue 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.

Licenses of intellectual property: In assessing whether a promise or performance obligation is distinct from the other promises, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the customer and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the customer can benefit from a promise for its intended purpose without the receipt of the remaining promise, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Research and development services: If an arrangement is determined to contain a promise or obligation for the Company to perform research and development services, the Company must determine whether these services are distinct from other promises in the arrangement. In assessing whether the services are distinct from the other promises, the Company considers the capabilities of the customer to perform these same services. In addition, the Company considers whether the customer can benefit from a promise for its intended purpose without the receipt of the remaining promise, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For research and development services that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The

Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Customer options: If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options for material rights, that is, the option to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the standalone selling price. Amounts allocated to any material right are not recognized as revenue until the option is exercised and the performance obligation is satisfied.

Milestone payments: At the inception of each arrangement that includes milestone payments, the Company evaluates whether a significant reversal of cumulative revenue provided in conjunction with achieving the milestones is probable, and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant reversal of cumulative revenue would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. For other milestones, the Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant reversal of cumulative revenue would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

Contract costs: The Company recognizes as an asset the incremental costs of obtaining a contract with a customer if the costs are expected to be recovered. As a practical expedient, the Company recognizes the incremental costs of obtaining a contract as an expense when incurred if the amortization period of the asset that it otherwise would have recognized is one year or less. To date, the Company has not incurred any incremental costs of obtaining a contract with a customer.

For additional discussion of accounting for collaboration revenues, see Note 5 of our consolidated financial statements.

Prepaid and Accrued Research and Development Expenses

As we prepare our consolidated financial statements, we are required to estimate our prepaid and accrued expenses. For certain contracts with our CROs and CMOs, if the billing terms do not align with the pattern in which the work is completed by the CRO or CMO as of the end of the period, we are required to perform an analysis to estimate the expense, for the period and to date for each contract.

Contracts that are subject to this analysis generally relate to the following services: research and development services, manufacturing services, toxicology studies and clinical trial services. Once we have completed our analysis, we will record the estimated expense in the period for each contract and, depending on the invoicing activity related to each contract, we either have a prepayment or accrual as of the end of the period. We base our estimates on communications with internal study managers, our knowledge of the ongoing and past work at the CROs and CMOs, and communications and reporting from our CROs and CMOs, where applicable.

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 comprised of funds held in checking accounts and money market accounts.

Foreign Currency Risk

Due to our operations outside of the United 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, our results of operations or our cash flows. For the years ended December 31, 2024, 2023, and 2022, changes in foreign currency exchange rates did not have a material impact on our historical financial position, our business, our financial condition, our results of operations or our cash flows.

Inflation Risk

We do not believe that inflation had a material effect on our business, financial condition, results of operations, or cash flows in the last two years. If global inflation trends continue, we expect appreciable increases in clinical trial, labor, and other operating costs.

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, including global economic uncertainty on the capital markets.

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, 2024. 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, 2024, 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, 2024 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, 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, 2024. 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, 2024, our internal control over financial reporting is effective based on those criteria.

The effectiveness of our internal control over financial reporting as of December 31, 2024 has been audited by KPMG LLP, an independent registered public accounting firm, as stated in their report.

Item 9B. Other Information

Singapore Goods and Services Tax ("GST") Rate

The issue or transfer of ownership of our ordinary shares would be exempt from GST, although the sale of our ordinary shares by a GST-registered investor may be considered to be a taxable supply subject to GST at 0% if certain conditions are met. Services consisting of arranging, brokering, underwriting or advising on the issue, allotment or transfer of ownership of our ordinary shares rendered by a GST-registered person to an investor belonging in Singapore for GST purposes in connection with the investor's purchase, sale or holding of our ordinary shares will be subject to GST at the prevailing standard rate of 9%. Similar services rendered by a GST-registered person contractually to an investor belonging outside Singapore and for the direct benefit of an investor belonging outside Singapore or a GST-registered person in Singapore should generally, subject to the satisfaction of certain conditions, be subject to GST at 0%.

Rule 10b5-1 Trading Plans

During the three months ended December 31, 2024, certain of our officers (as defined in Rule 16a-1(f) of the Exchange Act) entered into contracts, instructions or written plans (each, a "Rule 10b5-1 Trading Plan" and collectively, the "Rule 10b5-1 Trading Plans") for the purchase or sale of our securities that are intended to satisfy the conditions specified in Rule 10b5-1(c) under the Exchange Act for an affirmative defense against liability for trading in securities on the basis of material nonpublic information. We describe the material terms of these Rule 10b5-1 Trading Plans below.

On November 24, 2024, Christian Henry, MBA, Chairman of our Board, adopted a Rule 10b5-1 Trading Plan providing for the sale of up to an aggregate of 105,670 of our ordinary shares pursuant to the terms of such Rule 10b5-1 Trading Plan. Mr. Henry's Rule 10b5-

1 Trading Plan is active until August 29, 2025, or earlier, if and when all transactions under the Rule 10b5-1 Trading Plan are completed.

On November 25, 2024, Kyle Moran, CFA, our Chief Financial Officer, adopted a Rule 10b5-1 Trading Plan providing for the sale of up to an aggregate of 196,000 of our ordinary shares pursuant to the terms of such Rule 10b5-1 Trading Plan. Mr. Moran's Rule 10b5-1 Trading Plan is active until June 30, 2025, or earlier, if and when all transactions under the Rule 10b5-1 Trading Plan are completed.

On November 25, 2024, Christopher Francis, Ph.D., our Senior Vice President, Corporate Development, Head of Emerging Areas, adopted a Rule 10b5-1 Trading Plan providing for the sale of up to an aggregate of 435,564 of our ordinary shares pursuant to the terms of such Rule 10b5-1 Trading Plan. Dr. Francis' Rule 10b5-1 Trading Plan is active until November 3, 2025, or earlier, if and when all transactions under the Rule 10b5-1 Trading Plan are completed.

On November 25, 2024, Chandra Vargeese, Ph.D., our Chief Technology Officer, Head of Platform Discovery Sciences, adopted a Rule 10b5-1 Trading Plan providing for the sale of up to an aggregate of 86,972 of our ordinary shares pursuant to the terms of such Rule 10b5-1 Trading Plan. Dr. Vargeese's Rule 10b5-1 Trading Plan is active until August 31, 2025, or earlier, if and when all transactions under the Rule 10b5-1 Trading Plan are completed.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

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 SEC on Schedule 14A in connection with our 2025 Annual General Meeting of Shareholders, (the "Proxy Statement"), if the Proxy Statement is filed not later than 120 days after the end of our fiscal year ended December 31, 2024, in the sections titled “Management and Corporate Governance,” 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 SEC (the "Form 10-K/A").

Item 11. Executive Compensation

The information required by this item is incorporated by reference to the information set forth in the section titled “Executive Officer and Director Compensation” in our Proxy Statement. The section entitled “Pay Versus Performance” in our Proxy Statement is not incorporated by reference herein. If the Proxy Statement is not filed within 120 days after the end of our fiscal year ended December 31, 2024, 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 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, 2024, 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 is incorporated by reference to the information set forth in the sections titled “Certain Relationships and Related Person Transactions” and “Management and Corporate Governance – Director Independence” in our Proxy Statement. If the Proxy Statement is not filed within 120 days after the end of our fiscal year ended December 31, 2024, the information required by this item will be contained in the Form 10-K/A.

Item 14. Principal Accountant Fees and Services

The information required by this item regarding principal accountant fees and services is incorporated by reference to the information set forth in the sections titled “Principal Accountant Fees and Services” and “Policy on Audit Committee Pre-Approval of Audit and Permissible Non-Audit Services of Independent Public Accounting Firm” in our Proxy Statement. If the Proxy Statement is not filed within 120 days after the end of our fiscal year ended December 31, 2024, the information required by this item will be contained in the Form 10-K/A.

Our independent registered public accounting firm is KPMG LLP, Boston, MA, Auditor Firm ID: 185.

PART IV

Item 15. Exhibits and 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 108 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	Description of Securities of the Registrant and Comparison of Shareholder Rights	X			
4.3.1	Form of Pre-Funded Warrant (2022)		Form 8-K (Exhibit 4.1)	06/14/2022	001-37627
4.3.2	Form of Pre-Funded Warrant (2024)		Form 8-K (Exhibit 4.1)	9/26/2024	001-37627
4.4	Share Purchase Agreement by and between the Registrant and C.P. Pharmaceuticals International C.V., dated as of May 5, 2016		Form 10-Q (Exhibit 10.2)	08/15/2016	001-37627
Lease Agreements					
10.1.1	Lease Agreement by and between Wave Life Sciences USA, Inc., the Registrant, and King 733 Concord LLC, dated as of April 6, 2015		Form S-1 (Exhibit 10.7)	10/09/2015	333-207379
10.1.2	First Amendment (to Lease) by and between Wave Life Sciences USA, Inc. and CPI/King 733 Concord Owner, LLC, dated as of December 9, 2020		Form 10-K (Exhibit 10.5.2)	03/04/2021	001-37627
10.1.3	Second Amendment (to Lease) by and between Wave Life Sciences USA, Inc. and CPI/King 733 Concord Owner, LLC, dated as of August 8, 2022		Form 10-Q (Exhibit 10.1)	08/11/2022	001-37627
10.2.1	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)	01/06/2017	001-37627

10.2.2	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				
10.3††	Collaboration and License Agreement by and between Wave Life Sciences USA, Inc., Wave Life Sciences UK Limited and GlaxoSmithKline Intellectual Property (No. 3), dated as of December 13, 2022	Form 10-K (Exhibit 10.3)	03/23/2023	001-37627
10.4	Share Purchase Agreement by and between Glaxo Group Limited and the Registrant, dated as of December 13, 2022	Form 10-K (Exhibit 10.4)	03/23/2023	001-37627
10.5	Investor Agreement by and between Glaxo Group Limited and the Registrant, dated as of January 26, 2023	Form 10-K (Exhibit 10.5)	03/23/2023	001-37627
Agreements with Executive Officers and Directors				
10.6+	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
10.7+	Employment Agreement, as amended and restated, between the Registrant and Paul B. Bolno, dated as of May 8, 2020	Form 10-Q (Exhibit 10.1)	08/10/2020	333-207379
10.8+	Employment Agreement, as amended and restated, between the Registrant and Chandra Vargeese, dated as of May 8, 2020	Form 10-Q (Exhibit 10.2)	08/10/2020	333-207379
10.9+	Employment Agreement between the Registrant and Christopher Francis, Ph.D., dated as of November 8, 2022	Form 10-K (Exhibit 10.12)	03/23/2023	001-37627
10.10+	Employment Agreement, as amended and restated, between the Registrant and Kyle Moran, dated as of January 1, 2021	Form 10-K (Exhibit 10.15)	03/04/2021	001-37627
10.11+	Non-Employee Director Compensation Policy, as amended, effective as of August 6, 2024	Form 10-Q (Exhibit 10.2+)	11/12/2024	001-37627
10.12+	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
Equity and Other Compensation Plans				
10.13+	Wave Life Sciences Ltd. 2014 Equity Incentive Plan, as amended (the "2014 Equity Plan")	Form 10-Q (Exhibit 10.1)	11/09/2017	001-37627
10.14+	Wave Life Sciences Ltd. 2021 Equity Plan, as amended, (the "2021 Equity Plan") effective August 6, 2024	Form 8-K (Exhibit 10.1)	08/12/2024	001-37627
10.15+	Wave Life Sciences Ltd. 2019 Employee Share Purchase Plan, as amended, effective as of August 1, 2023	Form 8-K (Exhibit 10.2)	08/07/2023	001-37627
10.16.1+	Form of Non-qualified Share Option Agreement under the 2014 Equity Plan, effective as of September 20, 2016	Form 10-Q (Exhibit 10.2)	11/09/2017	001-37627

10.16.2+	Form of Non-qualified Share Option Agreement under the 2014 Equity Plan, effective as of January 1, 2018	Form 10-K (Exhibit 10.23.3)	03/01/2019	001-37627
10.16.3+	Form of Non-qualified Share Option Agreement under the 2021 Equity Plan, effective as August 10, 2021	Form 10-K (Exhibit 10.3)	11/10/2021	001-37627
10.17.1+	Form of Incentive Share Option Agreement under the 2014 Equity Plan, effective as of December 2014	Form S-8 (Exhibit 10.1)	12/17/2015	333-208598
10.17.2+	Form of Incentive Share Option Agreement under the 2014 Equity Plan, effective as of September 20, 2016	Form 10-Q (Exhibit 10.3)	11/09/2017	001-37627
10.18.1+	Form of Restricted Share Unit Agreement under the 2014 Equity Plan, effective as of June 16, 2016	Form 10-Q (Exhibit 10.4)	11/09/2017	001-37627
10.18.2+	Form of Restricted Share Unit Agreement under the 2014 Equity Plan, effective as of January 1, 2018	Form 10-K (Exhibit 10.25.2)	03/01/2019	001-37627
10.18.3+	Form of Restricted Share Unit Agreement under the 2014 Equity Incentive Plan, effective as of January 1, 2019	Form 10-Q (Exhibit 10.1)	05/10/2019	001-37627
10.18.4+	Form of Restricted Share Unit Agreement under the 2021 Equity Plan, effective as of August 10, 2021	Form 10-Q (Exhibit 10.4)	11/10/2021	001-37627
10.18.5+	Form of Amended and Restated 2019 Performance-Based Restricted Share Unit Agreement under the 2014 Equity Incentive Plan, effective as of March 17, 2021	Form 10-Q (Exhibit 10.2)	05/13/2021	001-37627
10.18.6+	Form of 2021 Performance-Based Restricted Share Unit Agreement under the 2014 Equity Incentive Plan, effective as of March 17, 2021	Form 10-Q (Exhibit 10.3)	05/13/2021	001-37627
10.19.1+	Form of Non-qualified Share Option Agreement for UK Participants under the 2014 Equity Plan, effective as of June 21, 2017	Form 10-Q (Exhibit 10.5)	11/09/2017	001-37627
10.19.2+	Form of Non-qualified Share Option Agreement for UK Participants under the 2014 Equity Plan, effective as of January 1, 2018	Form 10-K (Exhibit 10.26.2)	03/01/2019	001-37627
10.19.3+	Form of Non-qualified Share Option Agreement for UK Participants under the 2021 Equity Plan, effective as of August 10, 2021	Form 10-Q (Exhibit 10.5)	11/10/2021	001-37627
10.19.4+	Form of Restricted Share Unit Agreement for UK Participants under the 2021 Equity Plan, effective as of August 10, 2021	Form 10-Q (Exhibit 10.6)	11/10/2021	001-37627
10.20.1+	Form of Inducement Non-qualified Share Option Agreement, effective May 2024	Form 10-Q (Exhibit 10.1)	08/08/2024	001-37627
10.20.2+	Form of Inducement Restricted Share Unit Agreement, effective May 2024	Form 10-Q (Exhibit 10.2)	08/08/2024	001-37627

10.21.1	Open Market Sale Agreement, dated as of May 10, 2019, by and between the Registrant and Jefferies LLC		Form S-3ASR (Exhibit 1.2)	05/10/2019	333-231382
10.21.2	Amendment No. 1 to Open Market Sale Agreement, dated as of March 2, 2020, by and between the Registrant and Jefferies LLC		POSASR (Exhibit 1.3)	03/02/2020	333-231382
10.21.3	Amendment No. 2, dated March 3, 2022, to the Open Market Sale Agreement, dated as of May 10, 2019, by and between Wave Life Sciences Ltd. and Jefferies LLC		Form 8-K (Exhibit 10.1)	03/03/2022	001-37627
10.21.4	Amendment No. 3, dated November 12, 2024, to the Open Market Sale Agreement, dated as of May 10, 2019, by and between Wave Life Sciences Ltd. and Jefferies LLC		Form 10-Q (Exhibit 10.1)	11/12/2024	001-37627
19.1	Insider Trading Policy	X			
21.1	List of Subsidiaries of the Registrant		Form 10-K (Exhibit 21.1)	03/12/2018	001-37627
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			
97.1	Clawback Policy, effective as of October 2, 2023		Form 10-K (Exhibit 97.1)	03/06/2024	001-37627
101.INS	XBRL Instance Document – The Instance Document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document	X			
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents	X			
104	The cover page for this Annual Report on Form 10-K for the year ended December 31, 2024 is contained in Exhibit 101 and has been formatted in Inline XBRL	X			

(*) The certification attached as Exhibit 32 that accompanies this Annual Report on Form 10-K is not deemed filed with the SEC 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 SEC.

(††) Certain confidential portions of this Exhibit were omitted by means of marking such portions with brackets ("[***]") because the identified confidential portions (i) are not material and (ii) is the type that the Registrant treats as private or confidential.

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 4, 2025

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 or her true and lawful attorney-in-fact and agent to act in his or her 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 and 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 4, 2025
/s/ Kyle Moran Kyle Moran	Chief Financial Officer (*principal financial officer and principal accounting officer*)	March 4, 2025
/s/ Christian Henry Christian Henry	Chairman of the Board of Directors	March 4, 2025
/s/ Gregory L. Verdine, Ph.D. Gregory L. Verdine, Ph.D.	Director	March 4, 2025
/s/ Peter Kolchinsky, Ph.D. Peter Kolchinsky, Ph.D.	Director	March 4, 2025
/s/ Aik-Na Tan Aik-Na Tan	Director	March 4, 2025
/s/ Adrian Rawcliffe Adrian Rawcliffe	Director	March 4, 2025
/s/ Ken Takanashi Ken Takanashi	Director	March 4, 2025
/s/ Mark H. N. Corrigan, M.D. Mark H. N. Corrigan, M.D.	Director	March 4, 2025
/s/ Heidi L. Wagner Heidi L. Wagner	Director	March 4, 2025

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

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

Opinions on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheets of Wave Life Sciences Ltd. and subsidiaries (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, Series A preferred shares and shareholders' equity (deficit), and cash flows for the each of the years in the three-year period ended December 31, 2024, and the related notes (collectively, the consolidated financial statements). We also have audited the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024 based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Controls over Financial Reporting. Our responsibility is to express an opinion on the Company's consolidated financial statements and an opinion on the Company's internal control over financial reporting 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 audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements 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. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed 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. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) 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. Also, 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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Evaluation of revenue recognition for certain research and development services

As discussed in Note 5 to the consolidated financial statements, the Company is party to a collaboration agreement with GlaxoSmithKline (GSK) which has two performance obligations, including the promise to provide research and development (R&D) services. The Company recognizes R&D services revenue over time using an input method. This method measures progress based on costs incurred in relation to the R&D activities and the costs expected to be incurred in the future to satisfy each performance obligation. Amounts received by the Company before performance are recorded as deferred revenue. For the year ended December 31, 2024, the Company recognized over-time revenue under the GSK collaboration agreement of $37.0 million. In addition, as of December 31, 2024, a portion of the Company's current and long-term deferred revenue relates to R&D services.

We identified the evaluation of revenue recognition for certain R&D services as a critical audit matter. Specifically, evaluating the estimate of total costs expected to be incurred in satisfying certain R&D performance obligations required especially challenging auditor judgment. This involved an assessment of the nature of work to be performed and the method for measuring progress.

The following are the primary procedures we performed to address this critical audit matter. For a selection of R&D performance obligations, we read the underlying contract with the customer, evaluated the determination of the method for measuring progress, and tested the Company's estimate of total contract costs to be incurred by (1) comparing the Company's initial estimates to actual costs incurred to assess the Company's ability to estimate accurately, (2) inspecting underlying documentation and third-party evidence and comparing them to management's assumptions and inputs, (3) inquiring of R&D personnel of the Company to evaluate factors related to the nature of the work to be performed and their impact on the total contract costs to be incurred, including progress to date and the estimate of remaining contract costs, and (4) assessing the Company's history of estimating costs to be incurred in satisfying R&D performance obligations under similar contracts.

/s/ KPMG LLP

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

Boston, Massachusetts
March 4, 2025

WAVE LIFE SCIENCES LTD.
CONSOLIDATED BALANCE SHEETS

(In thousands, except share amounts)

	December 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 302,078	$ 200,351
Accounts receivable	1,422	21,086
Prepaid expenses	9,544	9,912
Other current assets	7,350	4,024
Total current assets	320,394	235,373
Long-term assets:		
Property and equipment, net of accumulated depreciation of $46,329 and $42,709 as of December 31, 2024 and 2023, respectively	10,128	13,084
Operating lease right-of-use assets	17,870	22,637
Restricted cash	3,760	3,699
Other assets	55	156
Total long-term assets	31,813	39,576
Total assets	$ 352,207	$ 274,949
Liabilities, Series A preferred shares and shareholders' equity		
Current liabilities:		
Accounts payable	$ 16,262	$ 12,839
Accrued expenses and other current liabilities	21,081	16,828
Current portion of deferred revenue	65,972	150,059
Current portion of operating lease liability	7,638	6,714
Total current liabilities	110,953	186,440
Long-term liabilities:		
Deferred revenue, net of current portion	6,099	15,601
Operating lease liability, net of current portion	17,766	25,404
Total long-term liabilities	23,865	41,005
Total liabilities	$ 134,818	$ 227,445
Series A preferred shares, no par value; 3,901,348 shares issued and outstanding at December 31, 2024 and 2023	$ 7,874	$ 7,874
Shareholders' equity:		
Ordinary shares, no par value; 153,037,286 and 119,162,234 shares issued and outstanding at December 31, 2024 and 2023, respectively	$ 1,175,181	$ 935,367
Additional paid-in capital	156,454	129,237
Accumulated other comprehensive loss	(262)	(124)
Accumulated deficit	(1,121,858)	(1,024,850)
Total shareholders' equity	209,515	39,630
Total liabilities, Series A preferred shares and shareholders' equity	$ 352,207	$ 274,949

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

WAVE LIFE SCIENCES LTD.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share amounts)

	For the Year Ended December 31,		
	2024	2023	2022
Revenue	$ 108,302	$ 113,305	$ 3,649
Operating expenses:			
Research and development	159,682	130,009	115,856
General and administrative	59,023	51,292	50,513
Total operating expenses	218,705	181,301	166,369
Loss from operations	(110,403)	(67,996)	(162,720)
Other income, net:			
Dividend income and interest income, net	10,163	7,928	1,571
Other income, net	3,232	1,878	7
Total other income, net	13,395	9,806	1,578
Loss before income taxes	(97,008)	(58,190)	(161,142)
Income tax benefit (provision)	—	677	(681)
Net loss	$ (97,008)	$ (57,513)	$ (161,823)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (0.70)	$ (0.54)	$ (2.05)
Weighted-average ordinary shares used in computing net loss per share attributable to ordinary shareholders—basic and diluted	138,277,468	106,097,268	78,855,810
Other comprehensive loss:			
Net loss	$ (97,008)	$ (57,513)	$ (161,823)
Foreign currency translation	(138)	(95)	(210)
Comprehensive loss	(97,146)	(57,608)	(162,033)

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 (DEFICIT)
(In thousands, except share amounts)

	Series A Preferred Shares		Ordinary Shares		Additional Paid-In-Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balance at December 31, 2021	3,901,348	$ 7,874	59,841,116	$ 749,851	$ 87,980	$ 181	$ (805,514)	$ 32,498
Issuance of ordinary shares, net of offering costs	—	—	25,464,483	51,220	—	—	—	51,220
Issuance of ordinary shares pursuant to the at-the-market equity program, net	—	—	458,092	1,167	—	—	—	1,167
Issuance of pre-funded warrants, net of offering costs	—	—	—	—	14,268	—	—	14,268
Share-based compensation	—	—	—	—	17,194	—	—	17,194
Vesting of RSUs	—	—	904,891	—	—	—	—	—
Option exercises	—	—	90,000	223	—	—	—	223
Issuance of ordinary shares under the ESPP	—	—	166,061	372	—	—	—	372
Other comprehensive loss	—	—	—	—	—	(210)	—	(210)
Net loss	—	—	—	—	—	—	(161,823)	(161,823)
Balance at December 31, 2022	3,901,348	$ 7,874	86,924,643	$ 802,833	$ 119,442	$ (29)	$ (967,337)	$ (45,091)
Issuance of ordinary shares, net of offering costs	—	—	20,000,000	93,574	—	—	—	93,574
Issuance of ordinary shares, pursuant to the GSK Collaboration Agreement	—	—	10,683,761	34,623	—	—	—	34,623
Issuance of ordinary shares pursuant to the at-the-market equity program, net	—	—	751,688	3,080	—	—	—	3,080
Share-based compensation	—	—	—	—	9,795	—	—	9,795
Vesting of RSUs	—	—	415,658	—	—	—	—	—
Option exercises	—	—	160,571	509	—	—	—	509
Issuance of ordinary shares under the ESPP	—	—	225,913	748	—	—	—	748
Other comprehensive loss	—	—	—	—	—	(95)	—	(95)
Net loss	—	—	—	—	—	—	(57,513)	(57,513)
Balance at December 31, 2023	3,901,348	$ 7,874	119,162,234	$ 935,367	$ 129,237	$ (124)	$ (1,024,850)	$ 39,630
Issuance of ordinary shares, net of offering costs	—	—	29,875,001	215,796	—	—	—	215,796
Issuance of ordinary shares pursuant to the at-the-market equity program, net	—	—	2,952,591	20,380	—	—	—	20,380
Issuance of pre-funded warrants, net of offering costs	—	—	—	—	14,076	—	—	14,076
Share-based compensation	—	—	—	—	13,141	—	—	13,141
Vesting of RSUs	—	—	100,326	—	—	—	—	—
Option exercises	—	—	770,636	2,979	—	—	—	2,979
Issuance of ordinary shares under the ESPP	—	—	176,498	659	—	—	—	659
Other comprehensive loss	—	—	—	—	—	(138)	—	(138)
Net loss	—	—	—	—	—	—	(97,008)	(97,008)
Balance at December 31, 2024	3,901,348	$ 7,874	153,037,286	$ 1,175,181	$ 156,454	$ (262)	$ (1,121,858)	$ 209,515

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,		
	2024	2023	2022
Cash flows from operating activities			
Net loss	$ (97,008)	$ (57,513)	$ (161,823)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Amortization of right-of-use assets	4,767	4,206	3,540
Depreciation of property and equipment	3,896	5,000	6,574
Share-based compensation expense	13,141	9,795	17,194
Loss on disposal of property and equipment	—	—	12
Changes in operating assets and liabilities:			
Accounts receivable	19,664	(21,086)	—
Prepaid expenses	368	(1,980)	(1,348)
Other assets	(3,225)	(2,010)	3,394
Accounts payable	3,421	(3,761)	9,348
Accrued expenses and other current liabilities	4,253	(724)	2,691
Deferred revenue	(93,589)	54,328	(3,245)
Operating lease liabilities	(6,714)	(5,496)	(4,308)
Other non-current liabilities	—	(190)	190
Net cash used in operating activities	(151,026)	(19,431)	(127,781)
Cash flows from investing activities			
Purchases of property and equipment	(938)	(1,115)	(1,361)
Proceeds from the sale of property and equipment	—	—	106
Purchase of short-term investments	—	—	(75,044)
Proceeds from the maturity of short-term investments	—	—	75,044
Net cash used in investing activities	(938)	(1,115)	(1,255)
Cash flows from financing activities			
Proceeds from the issuance of ordinary shares as a part of the June 2022 Offering, net of offering costs	—	—	51,220
Proceeds from the issuance of ordinary shares as a part of the December 2023 Offering, net of offering costs	14,038	93,574	—
Proceeds from the issuance of ordinary shares as a part of the September 2024 Offering, net of offering costs	201,758	—	—
Proceeds from issuance pre-funded warrants as a part of the June 2022 Offering, net of offering costs	—	—	14,268
Proceeds from issuance pre-funded warrants as a part of the, September 2024 Offering, net of offering costs	14,076	—	—
Proceeds from issuance of ordinary shares pursuant to the GSK Collaboration Agreement	—	34,623	—
Proceeds from issuance of ordinary shares pursuant to the at-the-market equity program, net	20,380	3,080	1,105
Proceeds from the exercise of share options	2,979	509	223
Proceeds from the ESPP	659	748	372
Net cash provided by financing activities	253,890	132,534	67,188
Effect of foreign exchange rates on cash	(138)	(95)	(210)
Net increase (decrease) in cash, cash equivalents and restricted cash	101,788	111,893	(62,058)
Cash, cash equivalents and restricted cash, beginning of period	204,050	92,157	154,215
Cash, cash equivalents and restricted cash, end of period	$ 305,838	$ 204,050	$ 92,157
Supplemental disclosure of cash flow information:			
Offering costs in accounts payable at period end	$ —	$ 210	$ —
Increase in operating lease right-of-use assets and lease liabilities related to new lease	$ —	$ —	$ 12,006

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 clinical-stage biotechnology company focused on unlocking the broad potential of RNA medicines (also known as oligonucleotides), or those targeting RNA, to transform human health. Wave's RNA medicines platform, PRISM, combines multiple modalities, chemistry innovation and deep insights into human genetics to deliver scientific breakthroughs that treat both rare and common disorders. The Company's toolkit of RNA-targeting modalities includes RNA editing, splicing, silencing using siRNA and antisense silencing, providing us with unique capabilities for designing and sustainably delivering candidates that optimally address disease biology. The Company's diversified pipeline includes clinical programs in obesity, AATD, DMD, and HD, as well as several preclinical programs utilizing our versatile RNA medicines platform.

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 have been developing and evolving PRISM to design, develop and commercialize RNA medicines, advancing the Company's differentiated portfolio, building the Company's research, development and manufacturing capabilities, advancing programs into the clinic, furthering clinical development of such clinical-stage programs, building the Company's intellectual property, and assuring adequate capital to support these activities.

Liquidity

Since its inception, the Company has not generated any product revenue and has incurred recurring operating losses. To date, the Company has primarily funded its operations through private placements of debt and equity securities, public and other registered offerings of its equity securities and collaborations with third parties. Until the Company can generate significant revenue from product sales, if ever, the Company expects to continue to finance operations through a combination of public or private equity or debt financings or other sources, which may include upfront and milestone payments from collaborations with third parties. Adequate additional financing may not be available to the Company on acceptable terms, or at all. The inability to raise capital as and when needed would have a negative impact on the Company's financial condition and ability to pursue its business strategy.

As of December 31, 2024, the Company had cash and cash equivalents of $302.1 million. The Company expects that its existing cash and cash equivalents will be sufficient to fund its operations for at least the next twelve months. The Company has based this expectation on the best information available, however the Company may use its available capital resources sooner than it currently expects. If the Company's anticipated operating results are not achieved in future periods, planned expenditures may need to be further reduced in order to extend the time period over which the then-available resources would be able to fund the Company's operations. In addition, the Company may elect to raise additional funds before it needs them if the conditions for raising capital are favorable due to market conditions or strategic considerations, even if the Company expects it has sufficient funds for its current or future operating plans.

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, maintaining 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 efforts will be successful, 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.

Basis of Presentation

The Company has prepared the accompanying consolidated financial statements in conformity with generally accepted accounting principles in the United States ("U.S. GAAP") and in U.S. dollars.

2. SIGNIFICANT ACCOUNTING POLICIES

Cash and Cash Equivalents

The Company considers all highly liquid securities with maturities of three months or less from the date of purchase to be cash equivalents. The Company's cash and cash equivalents are comprised of funds held in checking and money market accounts.

Principles of Consolidation

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

Use of Estimates

The Company's consolidated financial statements are prepared in accordance with U.S. GAAP. The preparation of the Company's financial statements and related disclosures requires the Company to make estimates and assumptions that affect the reported amount of assets, liabilities, revenue, costs and expenses and related disclosures. Management considers many factors in selecting appropriate financial accounting policies and in developing the estimates and assumptions that are used in the preparation of the financial statements. Management must apply significant judgment in this process. The Company believes that its revenue recognition policy, particularly (a) assessing the number of performance obligations; (b) determining the transaction price; (c) allocating the transaction price to the performance obligations in the contract; and (d) determining the pattern over which performance obligations are satisfied, including estimates to complete performance obligations, and the assumptions and estimates used in the Company's analysis of contracts with contract research organizations ("CROs") and contract manufacturing organizations ("CMOs") to estimate the contract expense, involve a greater degree of judgment, and therefore the Company considers them to be its critical accounting policies. The Company evaluates its estimates and assumptions on an ongoing basis. The Company's actual results may differ from these estimates under different assumptions and conditions.

Segment Data

The Company manages its operations as a single reportable and operating segment for the purposes of assessing performance and making operating decisions. The Company's focus is on developing its proprietary RNA medicines platform, PRISM, to develop and commercialize a broad pipeline of RNA medicines in a variety of therapeutic areas. This operating structure enables the Chief Executive Officer ("CEO") as chief operating decision maker ("CODM"), to allocate resources and assess business performance in order to achieve established long-term strategic goals. The determination of a single segment is consistent with the consolidated financial information regularly reviewed by the CODM for purposes of assessing performance, allocating resources and planning, monitoring budget versus actual results, and forecasting future periods. Within the single segment, there are significant expenses that are regularly considered by the CODM which are used in the review for performance and resource allocation. See Note 14 for additional disclosure of our segment information.

Going Concern

At each reporting period, the Company evaluates whether there are conditions or events that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the financial statements are issued. The Company is required to make certain additional disclosures if the Company concludes substantial doubt exists and it is not alleviated by the Company's plans or when the Company's plans alleviate substantial doubt about the Company's ability to continue as a going concern. The Company's evaluation entails analyzing prospective operating budgets and forecasts for expectations of the Company's cash needs and comparing those needs to the current cash and cash equivalent balance.

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 of Wave Japan are translated at average exchange rates for the period. Net unrealized gains and losses from foreign currency translation are reflected as other comprehensive income (loss) within the consolidated statements of Series A preferred shares and shareholders' equity (deficit) and the consolidated statements of operations and comprehensive loss. Gains and losses on foreign currency transactions are included in the consolidated statements of operations and comprehensive loss within other income, 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, cash equivalents and restricted cash are Level 1 assets which are comprised of funds held in checking and money market accounts. Cash, cash equivalents and restricted cash were recorded at fair value as of December 31, 2024 and 2023, totaling $305.8 million and $204.1 million, respectively. The carrying amounts of accounts payable and accrued expenses approximate their fair values due to their short-term maturities.

Concentration of Credit Risk

Cash, cash equivalents, restricted cash and short-term investments are financial instruments that potentially subject the Company to concentration of credit risk. The Company uses several financial institutions to maintain its cash, cash equivalents, restricted cash and short-term investments, 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, 2024 and 2023, the Company had $3.8 million and $3.7 million of restricted cash, respectively, of which $2.8 million and $2.7 million related to the Lexington facility, respectively, and $1.0 million related to the Cambridge facility.

Property and Equipment

Property and equipment, which consists primarily of equipment, furniture, software and leasehold improvements, are stated at cost less accumulated depreciation. 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 asset life or lease term

Depreciation 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 and comprehensive loss.

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.

Revenue Recognition

The Company recognizes revenue in accordance with Accounting Standards Codification ("ASC") Topic 606, Revenue from Contracts with Customers ("ASC 606"). This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that 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-step analysis: (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. The Company only applies the five-step analysis to contracts when it is probable that the entity will collect the consideration to which it is entitled in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract, determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company has entered into collaboration agreements for research, development, and commercial services, under which the Company licenses certain rights to its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, upfront license fees; reimbursement of certain costs; customer option exercise fees; development, regulatory and commercial milestone payments; and royalties on net sales of licensed products. Any variable consideration is allocated to a performance obligation, and the cumulative revenue associated with this consideration is not recognized until it is deemed not to be at significant risk of reversal.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under each of its agreements for which the collaboration partner is also a customer, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must use significant judgment to determine: (a) the number of performance obligations based on the determination under step (ii) above; (b) the transaction price under step (iii) above; and (c) the timing of satisfaction of performance obligations as a measure of progress in step (v) above. The Company uses significant judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price as described further below. The transaction price is allocated to the optional goods and services the Company expects to provide. The Company uses estimates to determine the timing of satisfaction of performance obligations.

Amounts received prior to being recognized as revenue 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.

Licenses of intellectual property: In assessing whether a promise or performance obligation is distinct from the other promises, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the customer and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the customer can benefit from a promise for its intended purpose without the receipt of the remaining promise, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Research and development services: If an arrangement is determined to contain a promise or obligation for the Company to perform research and development services, the Company must determine whether these services are distinct from other promises in the arrangement. In assessing whether the services are distinct from the other promises, the Company considers the capabilities of the customer to perform these same services. In addition, the Company considers whether the customer can benefit from a promise for its intended purpose without the receipt of the remaining promise, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For research and development services that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Customer options: If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options for material rights, that is, the option to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the standalone selling price. Amounts allocated to any material right are not recognized as revenue until the option is exercised and the performance obligation is satisfied.

Milestone payments: At the inception of each arrangement that includes milestone payments, the Company evaluates whether a significant reversal of cumulative revenue provided in conjunction with achieving the milestones is probable, and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant reversal of cumulative revenue would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. For other milestones, the Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant reversal of cumulative revenue would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

Contract costs: The Company recognizes as an asset the incremental costs of obtaining a contract with a customer if the costs are expected to be recovered. As a practical expedient, the Company recognizes the incremental costs of obtaining a contract as an expense when incurred if the amortization period of the asset that it otherwise would have recognized is one year or less. To date, the Company has not incurred any incremental costs of obtaining a contract with a customer.

Research and Development Expenses

Research and development expenses are expensed as incurred. External development costs are recognized based on an evaluation of the progress to completion of specific tasks. 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 the accompanying consolidated balance sheets as prepaid or accrued expenses.

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 and comprehensive loss.

Refundable Tax Credits

The Company is eligible for refundable tax credits with tax authorities for certain qualified operating expenses. The Company recognizes refundable tax credits when there is reasonable assurance that the Company will comply with the requirements of the refundable tax credit and that the refundable tax credit will be received. Refundable tax credits are recorded as income and classified in other income, net in the consolidated statements of operations and comprehensive loss.

Net Loss per Share

Basic net loss per share is computed using the weighted-average number of ordinary shares outstanding during the period. The outstanding Pre-Funded Warrants (as defined in Note 6) are included in the weighted-average number of ordinary shares outstanding used in the calculation of basic net loss per share as the exercise price is negligible and the warrants are fully vested and exercisable. 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 and the assumed vesting of RSUs (as defined in Note 7). The Company's Series A preferred shares do not entitle the holders of such shares to participate in dividends and do not contractually require the holders of such shares to participate in losses of the Company.

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 awards based on the grant date fair value of the underlying ordinary shares. 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. Equity instruments issued to non-employees as consideration for goods or services received by the Company have been accounted for based on the fair value of the equity instruments issued. 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 accounts for forfeitures as they occur.

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

The fair value of each share option grant was determined using the methods and assumptions discussed below. These inputs are generally subjective and require significant judgment and estimation by management.

- *Fair Value of Ordinary Shares* 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 was limited historical data for the Company's ordinary shares and limited company-specific historical volatility through the third quarter of 2021, the Company 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. Beginning in the fourth quarter of 2021, the Company had sufficient historical volatility data for its ordinary shares and as such no longer relies on an analysis of the volatility from a peer group to calculate expected volatility.

- *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 tax 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 and comprehensive loss.

The Company has certain service arrangements in place between its U.S., Japan, U.K. 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 as the related ongoing results of the comparable companies.

Leases

The Company accounts for leases in accordance with ASC Topic 842, *Leases* (“ASC 842”). At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Most leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew a lease are not included in the Company’s assessment unless there is reasonable certainty that the Company will renew the lease. The Company monitors its plans to renew its leases on a quarterly basis.

Certain lease agreements include rental payments that are adjusted periodically for inflation or other variables. In addition to rent, the leases may require the Company to pay additional amounts for taxes, insurance, maintenance, or other expenses, which are generally referred to as non-lease components. Such adjustments to rental payments and variable non-lease components are treated as variable lease payments and recognized in the period in which the obligation for these payments are incurred. Variable lease components and variable non-lease components are not measured as part of the right-of-use asset and lease liability. Only when lease components and their associated non-lease components are fixed are they accounted for as a single lease component and are recognized as part of a right-of-use asset and lease liability. Total contract consideration is allocated to the combined fixed lease and non-lease component. This policy election applies consistently to all asset classes under lease agreements.

Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment.

Recently Issued Accounting Pronouncements

In November 2023, the Financial Accounting Standards Board (the “FASB”) finalized Accounting Standards Update No. 2023-07, Segment Reporting (Topic 280): *Improvements to Reportable Segment Disclosures* (“ASU 2023-07”). ASU 2023-07 requires enhanced disclosures about reportable segments and the chief operating decision maker. The Company adopted ASU 2023-07 for the Company's fiscal year 2024 annual reporting period and applied it retrospectively. The adoption did not have a material impact on the Company's consolidated financial statements.

In December 2023, the FASB finalized Accounting Standards Update No. 2023-09, Income Taxes (Topic 740): *Improvements to Income Tax Disclosures* (“ASU 2023-09”). ASU 2023-09 requires a company's annual financial statements to include consistent categories and greater disaggregation of information in the rate reconciliation, and income taxes paid disaggregated by jurisdiction. ASU 2023-09 is effective for the Company’s annual reporting periods beginning after December 15, 2025. Adoption is either with a

prospective method or a fully retrospective method of transition. Early adoption is permitted. The Company is currently evaluating the effect that adoption of ASU 2023-09 will have on its consolidated financial statements.

In November 2024, the FASB issued ASU 2024-03, *Income Statement - Reporting Comprehensive Income - Expense Disaggregation Disclosures (Subtopic 220-40)* ("ASU 2024-03"). ASU 2024-03 modifies the rules on income statement disclosures to enhance the transparency of and include more detailed information about the types of expenses, including purchases of inventory, employee compensation, depreciation, amortization, and depletion, in commonly presented expense captions such as cost of sales, research and development, and selling, general and administrative expenses. The amendments are intended to address investors' requests for income statement expense disclosures that provide more information to help them better understand the components of an entity's expenses, make their own judgments about the entity's performance, and more accurately forecast expenses, and enable investors to better assess an entity's prospects for future cash flows. It will also provide contextual information for an entity's presentation and consideration of management's discussion and analysis of financial position and results of operations. The guidance is effective for all entities for annual periods beginning after December 15, 2026. All entities should apply the guidance prospectively but have the option to apply it retrospectively. Early adoption is permitted. The Company is continuing to assess the timing of adoption and the potential impacts of ASU 2024-03 on the consolidated financial statements and related disclosures.

3. PROPERTY AND EQUIPMENT, NET

Property and equipment, net, consists of the following:

	December 31,	
	2024	2023
	(in thousands)	
Furniture and equipment	$ 26,194	$ 26,072
Software	1,029	902
Leasehold improvements	28,885	28,525
Fixed assets in progress	349	294
Total	56,457	55,793
Less accumulated depreciation	(46,329)	(42,709)
Property and equipment, net	$ 10,128	$ 13,084

Substantially all of the Company's long-lived assets were located in the United States as of December 31, 2024 and 2023.

Depreciation expense was $3.9 million, $5.0 million, and $6.6 million for the years ended December 31, 2024, 2023, and 2022, respectively.

4. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

Accrued expenses and other current liabilities consist of the following:

	December 31,	
	2024	2023
	(in thousands)	
Accrued compensation	$ 15,358	$ 14,065
Accrued expenses related to CROs and CMOs	4,551	1,768
Accrued expenses and other current liabilities	1,172	995
Total accrued expenses and other current liabilities	$ 21,081	$ 16,828

5. COLLABORATION AGREEMENTS

GSK Collaboration and Equity Agreements

On December 13, 2022, Wave USA and Wave UK entered into a Collaboration and License Agreement (the "GSK Collaboration Agreement") with GlaxoSmithKline Intellectual Property (No. 3) ("GSK"). Pursuant to the GSK Collaboration Agreement, Wave and GSK have agreed to collaborate on the research, development, and commercialization of oligonucleotide therapeutics, including an exclusive global license to WVE-006. The discovery collaboration component has an initial four-year research term and combines Wave's proprietary discovery and drug development platform, PRISM, with GSK's unique genetic insights and its global

development and commercial capabilities. On January 27, 2023, the GSK Collaboration Agreement became effective, and GSK paid Wave an upfront payment of $120.0 million.

Simultaneously with the execution of the GSK Collaboration Agreement, Wave entered into a Share Purchase Agreement (the "SPA") on December 13, 2022, with Glaxo Group Limited ("GGL"), an affiliate of GSK, pursuant to which Wave agreed to sell 10,683,761 of its ordinary shares to GGL at a purchase price of $4.68 per share (the "GSK Equity Investment"). The GSK Equity Investment closed on January 26, 2023, following the completion of customary closing conditions. The ordinary shares purchased by GGL in the GSK Equity Investment are subject to lock-up and standstill restrictions and carry certain registration rights, customary for transactions of this kind. The Company did not incur any material costs in connection with the issuance of the ordinary shares under the SPA.

The GSK Collaboration Agreement has three components: (1) a discovery collaboration which enables the Company to advance up to three programs leveraging targets informed by GSK's novel genetic insights ("Wave's Collaboration Programs"); (2) a discovery collaboration which enables GSK to advance up to eight programs leveraging PRISM and the Company's oligonucleotide expertise and discovery capabilities (the "Discovery Research Collaboration"); and (3) an exclusive global license for GSK to WVE-006, the Company's alpha-1 antitrypsin deficiency ("AATD") program, that uses the Company's proprietary AIMer technology (the "AATD Collaboration"). The Company will be responsible for preclinical, regulatory, manufacturing, and clinical activities for WVE-006 through the initial Phase 1/2 study, at the Company's sole cost. Thereafter, GSK will be responsible for advancing WVE-006 through pivotal studies, registration, and global commercialization at GSK's sole cost.

Under the GSK Collaboration Agreement, each party grants to the other party certain licenses to the collaboration products to enable the other party to perform its obligations and exercise its rights under the GSK Collaboration Agreement, including license grants to enable each party to conduct research, development and commercialization activities pursuant to the terms of the GSK Collaboration Agreement. The parties' exclusivity obligations to each other are limited on a target-by-target basis with regard to targets in the collaboration. GSK may terminate the GSK Collaboration Agreement for convenience, in its entirety or on a target-by-target basis. Subject to certain exceptions, each party has the right to terminate the GSK Collaboration Agreement on a target-by-target basis if the other party, or a related party, challenges the patentability, enforceability or validity of any patents within the licensed technology that cover any product that is subject to the GSK Collaboration Agreement. In the event of any material breach of the GSK Collaboration Agreement by a party, subject to cure rights, the other party may terminate the GSK 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 GSK and its affiliates cease development, manufacturing and commercialization activities with respect to compounds or products subject to the GSK Collaboration Agreement and directed to a particular target, the Company may terminate the GSK Collaboration Agreement with respect to such target. Either party may terminate the GSK Collaboration Agreement for the other party's insolvency. In certain termination circumstances, the Company would receive a license from GSK to continue researching, developing and manufacturing certain products.

The GSK Collaboration Agreement, unless terminated earlier, will continue until the date on which: (i) with respect to a validation target, the date on which such validation target is not advanced into a collaboration program; or (ii) with respect to a collaboration target, the royalty term has expired for all collaboration products directed to the applicable collaboration target. The GSK Collaboration Agreement includes options to extend the research term for up to three additional years, which would increase the number of programs available to both parties. The Company will lead all preclinical research for GSK and the Company's collaboration programs up to investigational new drug ("IND")-enabling studies. The Company will lead IND-enabling studies, clinical development and commercialization for the Company's collaboration programs. GSK collaboration programs will transfer to GSK for IND-enabling studies, clinical development and commercialization.

The GSK Collaboration Agreement is managed by a joint steering committee in which both parties are represented equally. In addition, the AATD Collaboration is overseen by a joint development committee, a joint patent committee advises on intellectual property activities, and the Discovery Research Collaboration is overseen by a joint research committee. Both parties are represented equally for these committees and report to the joint steering committee.

The Company assessed this arrangement in accordance with ASC 606, Revenue from Contracts with Customers ("ASC 606") and concluded that the contract counterparty, GSK, is a customer for the AATD Collaboration prior to GSK exercising its option and, for the Discovery Research Collaboration programs during the target validation research term. The Company identified the following material promises under the arrangement: (1) the exclusive global license for WVE-006; (2) the research and development services for WVE-006 through the Phase 1/2 study; (3) the discovery research services under the Discovery Research Collaboration to perform target validation programs; (4) research and development license for the Discovery Research Collaboration; and (5) the research and development services for the GSK collaboration programs through completion of a candidate selection. The research and development services for WVE-006 were determined to not be distinct from the exclusive global license and should therefore be combined into a single performance obligation for the AATD Collaboration. The research and development services for the Discovery Research Collaboration were determined to not be distinct from the research and development license for the Discovery Research Collaboration and should therefore be combined into a single performance obligation. In addition, the Company determined the standalone selling price for the option to advance up to eight programs from the Discovery Research Collaboration and determined it did not provide a material right to GSK.

Based on these assessments, the Company identified two performance obligations in the GSK Collaboration Agreement: (1) AATD Collaboration consisting of the research and development services through completion of the Phase 1/2 study and research and development license for WVE-006 and (2) Discovery Research Collaboration which consists of research and development services for validating the targets and license for research and development license for targets.

At the outset of the arrangement, the transaction price included fixed consideration of the $120.0 million upfront, the $15.4 million in premium related to the GSK Equity Investment and the fixed consideration related to the additional target validation research funding. The Company allocated the estimated variable consideration relating to the target validation research to the Discovery Research Collaboration and the variable consideration relating to the development milestone to the AATD Collaboration and then allocated the fixed consideration to the performance obligations on a relative standalone selling price basis. The Company determined that the GSK Collaboration Agreement did not contain a significant financing component. The program initiation fees to advance up to eight programs from the Discovery Research Collaboration to preclinically develop the GSK collaboration programs and the additional potential milestone payments were excluded from the transaction price, as all milestone amounts were fully constrained at the inception of the GSK Collaboration Agreement. The Company will reevaluate the transaction price at the end of each reporting period, and as uncertain events are resolved or other changes in circumstances occur, the Company will adjust its estimate of the transaction price.

Under the GSK Collaboration Agreement, GSK can advance up to eight programs leveraging the Company's PRISM platform and multiple RNA-targeting modalities (RNA editing, splicing, siRNA, and antisense) with target validation work ongoing across multiple therapy areas. GSK selected its first two programs to advance to development candidates following achievement of target validation in the three months ended June 30, 2024. These programs utilize the Company's next generation GalNAc-siRNA format and are in hepatology. Under the GSK Collaboration Agreement, GSK was required to provide an aggregate initiation payment of $12.0 million to the Company for these two oligonucleotide programs, which was received during the three months ended June 30, 2024.

The following table summarizes the allocation of the total transaction price to the identified performance obligation under the GSK Collaboration Agreement, and the amount of the transaction price unsatisfied as of December 31, 2024 (in thousands):

	Transaction Price Allocated	Transaction Price Unsatisfied [1]
Performance Obligations:		
AATD Collaboration	$ 156,778	$ 59,392
Discovery Research Collaboration	18,098	13,737
GSK Collaboration Program	12,000	10,472
Total	$ 186,876	$ 83,601

(1) The Unsatisfied transaction price will be recognized over the remaining applicable research or program term.

The Company developed the estimated standalone selling price for the global license for WVE-006, under the AATD Collaboration, using a discounted cash flow model. For the performance obligation associated with the research and development services under the Discovery Research Collaboration and the research and development services for WVE-006 under the AATD Collaboration, the Company determined the standalone selling price using estimates of the costs to perform the research and development services, including expected internal and external costs for services and supplies, adjusted to reflect a profit margin. The total estimated cost of the research and development services reflected the nature of the services to be performed and the Company’s best estimate of the length of time required to perform the services.

Revenue associated with the AATD Collaboration performance obligation is being recognized as the research and development services are provided using an input measure, according to the costs incurred and the total costs expected to be incurred to satisfy the performance obligation. The revenue associated with the Discovery Research Collaboration performance obligation is being recognized as the research and development services are provided using an input measure, according to the costs incurred and the total costs expected to be incurred to satisfy the performance obligation. The amounts received that have not yet been recognized as revenue are recorded in deferred revenue on the Company’s consolidated balance sheet. Additional funding related to the Company’s research activities related to Discovery Research Collaboration will be recorded as accounts receivable when contractually enforceable and recorded as deferred revenue, or as revenue as the services are provided.

During the year ended December 31, 2023, the Company achieved a developmental milestone which pertained to the initiation of dosing in healthy volunteers in the RestorAATion clinical trial program, triggering a $20.0 million milestone payment to the Company from GSK. As of December 31, 2023, the $20.0 million related to the achievement of the milestone was included in the current portion of accounts receivable and payment was received from GSK in the first quarter of 2024.

Under the GSK Collaboration Agreement, during the years ended December 31, 2024 and December 31, 2023, the Company recognized revenue of $37.0 million and $66.3 million, respectively, using the input method described above.

The aggregate amount of the transaction price allocated to the Company's unsatisfied and partially unsatisfied performance obligations which are recorded in deferred revenue as of December 31, 2024 is approximately $72.1 million, of which approximately $66.0 million is included in current liabilities and $6.1 million is included in long-term liabilities. The aggregate amount of the transaction price allocated to the Company's unsatisfied and partially unsatisfied performance obligations which were recorded in deferred revenue as of December 31, 2023 was approximately $94.3 million, of which approximately $78.7 million was included in current liabilities and $15.6 million was included in long-term liabilities.

Takeda Collaboration and Equity Agreements

In February 2018, Wave USA and Wave UK entered into a global strategic collaboration (the "Takeda Collaboration") with Takeda Pharmaceutical Company Limited ("Takeda"), pursuant to which Wave USA, Wave UK and Takeda agreed to collaborate on the research, development and commercialization of oligonucleotide therapeutics for disorders of the Central Nervous System ("CNS"). The Takeda Collaboration provided the Company with at least $230.0 million in committed cash and Takeda with the option to co-develop and co-commercialize the Company's CNS development programs in (1) Huntington's disease ("HD"); (2) amyotrophic lateral sclerosis ("ALS") and frontotemporal dementia ("FTD"); and (3) the Company's discovery-stage program targeting ATXN3 for the treatment of spinocerebellar ataxia 3 ("SCA3") (collectively, "Category 1 Programs"). In addition, the Takeda Collaboration provided Takeda the right to exclusively license multiple preclinical programs for CNS disorders, including Alzheimer's disease and Parkinson's disease (collectively, "Category 2 Programs"). In April 2018, the Takeda Collaboration became effective and Takeda paid the Company $110.0 million as an upfront payment. Takeda also agreed to fund the Company's research and preclinical activities in the amount of $60.0 million during the four-year research term and to reimburse the Company for any collaboration-budgeted research and preclinical expenses incurred by Wave that exceed that amount.

Simultaneously with Wave USA and Wave UK's entry into the collaboration and license agreement with Takeda dated February 19, 2018, as amended (the "Takeda Collaboration Agreement"), the Company entered into a share purchase agreement with Takeda (the "Takeda Equity Agreement," and together with the Takeda Collaboration Agreement, the "Takeda Agreements") pursuant to which it agreed to sell to Takeda 1,096,892 of its ordinary shares at a purchase price of $54.70 per share. In April 2018, the Company closed the Takeda Equity Agreement and received aggregate cash proceeds of $60.0 million. The Company did not incur any material costs in connection with the issuance of the shares.

With respect to Category 1 Programs, the Company was 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 had an exclusive option for each target and all associated products and companion diagnostics for such target, which it could exercise at any time through completion of the proof of mechanism study. If Takeda had exercised this option, the Company would have received an opt-in payment and would have led manufacturing and joint clinical co-development activities and Takeda would have led joint co-commercial activities in the United States and all commercial activities outside of the United States. Global costs and potential profits would have been shared 50:50 and the Company would have been eligible to receive development and commercial milestone payments. In addition to its 50% profit share, the Company was 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, the Company 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) ("Category 2 Research Term"). During that term, the Takeda Collaboration provided that the parties may collaborate on preclinical programs for up to six targets at any one time. The Company was responsible for researching and preclinically developing products and companion diagnostics directed to the agreed upon targets through completion of Investigational IND enabling studies in the first major market country. Thereafter, Takeda would have an exclusive worldwide license to develop and commercialize products and companion diagnostics directed to such targets, subject to the Company's retained rights to lead manufacturing activities for products directed to such targets. Takeda agreed to fund the Company's research and preclinical activities in the amount of $60.0 million during the research term and reimburse the Company for any collaboration-budgeted research and preclinical expenses incurred by the Company that exceeded that amount. The Company was 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.

Under the Takeda Collaboration Agreement, each party granted 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 commenced on April 2, 2018 and, unless terminated earlier, would have continued until the date on which: (i) with respect to each Category 1 Program target for which Takeda does not exercise its option, the 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 had the right to terminate the Takeda Collaboration Agreement for convenience on 180 days' notice, in its entirety or on a target-by-target basis. Subject to certain exceptions, each party had 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 was 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 had the right to terminate the Takeda Collaboration Agreement in its entirety if the breach related to all targets or on a target-by-target basis if the breach related to a specific target. In the event that Takeda and its affiliates ceased development, manufacturing and commercialization activities with respect to compounds or products subject to the Takeda Collaboration Agreement and directed to a particular target, the Company had the right to terminate the Takeda Collaboration Agreement with respect to such target. Either party had the right to terminate the Takeda Collaboration Agreement for the other party's insolvency. In certain termination circumstances, the Company would have received a license from Takeda to continue researching, developing and manufacturing certain products, and companion diagnostics.

The Takeda Collaboration was managed by a joint steering committee in which both parties were represented equally. The joint steering committee was tasked with overseeing the scientific progression of each Category 1 Program and, prior to the Amendment (discussed below), the Category 2 Programs.

The Company assessed this arrangement in accordance with ASC 606 and concluded that the contract counterparty, Takeda, is a customer for Category 1 Programs prior to Takeda exercising its option, and for Category 2 Programs during the Category 2 Research Term. The Company identified the following material promises under the arrangement: (1) the non-exclusive, royalty-free research and development license for each Category 1 Program; (2) the research and development services for each Category 1 Program through completion of the first proof of mechanism study; (3) the exclusive option to license, co-develop and co-commercialize each Category 1 Program; (4) the right to exclusively license the Category 2 Programs; and (5) the research and preclinical development services of the Category 2 Programs through completion of IND-enabling studies. The research and development services for each Category 1 Program were determined to not be distinct from the research and development license and should therefore be combined into a single performance obligation for each Category 1 Program. The research and preclinical development services for the Category 2 Programs were determined to not be distinct from the exclusive licenses for the Category 2 Programs and therefore were combined into a single performance obligation.

Additionally, the Company determined that the exclusive option for each Category 1 Program was priced at a discount and, as such, provide material rights to Takeda, representing three separate performance obligations. Based on these assessments, the Company identified seven performance obligations in the Takeda Collaboration Agreement: (1) research and development services through completion of the first proof of mechanism and non-exclusive research and development license for HD; (2) research and development services through completion of the first proof of mechanism and non-exclusive research and development license for ALS and FTD; (3) research and development services through completion of the first proof of mechanism and non-exclusive research and development license for SCA3; (4) the material right provided for the exclusive option to license, co-develop and co-commercialize HD; (5) the material right provided for the exclusive option to license, co-develop and co-commercialize ALS and FTD; (6) the material right provided for the exclusive option to license, co-develop and co-commercialize SCA3; and (7) the research and preclinical development services and right to exclusively license the Category 2 Programs.

At the outset of the arrangement, the transaction price included the $110.0 million upfront consideration received and the $60.0 million of committed research and preclinical funding for the Category 2 Programs. The Company determined that the Takeda Collaboration Agreement did not contain a significant financing component. The option exercise fees to license, co-develop and co-commercialize each Category 1 Program that could have been received were excluded from the transaction price until each customer option was exercised. The potential milestone payments were excluded from the transaction price, as all milestone amounts were fully constrained at the inception of the Takeda Collaboration Agreement. The Company would have reevaluated the transaction price at the end of each reporting period and, as uncertain events were resolved or other changes in circumstances occurred, if necessary, would have adjusted its estimate of the transaction price.

The Company allocated the transaction price to the performance obligations on a relative standalone selling price basis. For the performance obligations associated with the research and development services through completion of the first proof of mechanism and non-exclusive research and development license for HD; the research and development services through completion of the first proof of mechanism and non-exclusive research and development license for ALS and FTD; the research and development services through completion of the first proof of mechanism and non-exclusive research and development license for SCA3; and the research and preclinical development services and right to exclusively license the Category 2 Programs, the Company determined the

standalone selling price using estimates of the costs to perform the research and development services, including expected internal and external costs for services and supplies, adjusted to reflect a profit margin. The total estimated cost of the research and development services reflected the nature of the services to be performed and the Company's best estimate of the length of time required to perform the services. For the performance obligations associated with the material right provided for the exclusive option to license, co-develop and co-commercialize HD; the material right provided for the exclusive option to license, co-develop and co-commercialize ALS and FTD; and the material right provided for the exclusive option to license, co-develop and co-commercialize SCA3, the Company estimated the standalone fair value of the option to license each Category 1 Program utilizing an adjusted market assessment approach, and determined that any standalone fair value in excess of the amounts to be paid by Takeda associated with each option represented a material right.

Revenue associated with the research and development services for each Category 1 Program performance obligation were recognized as the research and development services were provided using an input method, according to the costs incurred on each Category 1 Program and the total costs expected to be incurred to satisfy each Category 1 Program performance obligation. Prior to the Amendment described below, revenue associated with the research and preclinical development services for the Category 2 Programs performance obligation was recognized as the research and preclinical development services that were provided using an input method, according to the costs incurred on Category 2 Programs and the total costs expected to be incurred to satisfy the performance obligation. The amount allocated to the material right for each Category 1 Program option would have been recognized on the date that Takeda exercised each respective option, or immediately as each option expired unexercised. The amounts received that were not yet recognized as revenue were recorded in deferred revenue on the Company's consolidated balance sheet.

On October 15, 2021, Wave USA, Wave UK and Takeda entered into the Second Amendment to the Takeda Collaboration Agreement (the "Amendment"), which discontinued the Category 2 component of the Takeda Collaboration. The Category 1 Programs under the Collaboration Agreement remain in effect and are unchanged by the Amendment. Pursuant to the Amendment, Takeda agreed to pay the Company an additional $22.5 million as full payment for reimbursable Category 2 Programs collaboration-budgeted research and preclinical expenses. The Company received this payment from Takeda related to the Category 2 component and recognized the full amount as collaboration revenue in the year ended December 31, 2021. During the year ended December 31, 2021, in addition to the revenue recognized related to the Amendment, the Company recognized another $18.5 million of collaboration revenue related to services pertaining to the Category 1 Programs and Category 2 Programs.

In May 2023, the Company announced its decision to discontinue clinical development of WVE-004 for C9orf72-associated ALS and FTD ("C9 for ALS/FTD"), one of the Category 1 Programs. In July 2023, the joint steering committee that manages the Takeda Collaboration terminated C9 for ALS/FTD as a target under the collaboration (the "C9 Target") and consequently Takeda and the Company's rights and obligations under the Takeda Collaboration were terminated with respect to the C9 Target. As a result of the termination of the C9 for ALS/FTD Category 1 Program, the Company recognized $28.0 million in revenue during the three months ended September 30, 2023, which represented the remainder of the deferred revenue for the C9 for ALS/FTD Category 1 Program as of June 30, 2023.

In the third quarter of 2023, the Company achieved a developmental milestone related to the HD Category 1 Program, which pertained to the positive results from a non-clinical study of WVE-003 in non-human primates ("NHPs"). As a result of achieving the milestone, the Company recognized $7.0 million in revenue, which was not previously recorded in deferred revenue, as it was fully constrained at the inception of the Takeda Collaboration.

In December 2023, the joint steering committee that manages the Takeda Collaboration terminated the SCA3 Category 1 Program as a target under the collaboration and consequently Takeda and the Company's rights and obligations under the Takeda Collaboration were terminated with respect to the SCA3 Category 1 Program. As a result of the termination of the SCA3 Category 1 Program, the Company recognized $9.9 million in revenue during the three months ended December 31, 2023, which represented the remainder of the deferred revenue for the SCA3 Category 1 Program as of September 30, 2023.

In October 2024, the Company was notified by Takeda that Takeda did not intend to exercise and therefore elected to terminate its option ("Option Termination") for the HD target under the Takeda Collaboration Agreement. As HD was the last active collaboration target under the Takeda Collaboration Agreement, the Takeda Collaboration Agreement expired with immediate effect, and $70.2 million that was previously recorded as deferred revenue was recognized as revenue in the fourth quarter of 2024 related to this expiration.

In October 2024, the Company was notified by Takeda that Takeda did not intend to exercise and therefore elected to terminate its option ("Option Termination") for the HD target under the Takeda Collaboration Agreement. As HD was the last active collaboration target under the Takeda Collaboration Agreement, the Takeda Collaboration Agreement expired with immediate effect, and $70.2 million that was previously recorded as deferred revenue was recognized as revenue in the fourth quarter of 2024 related to this expiration.

During the years ended December 31, 2024, 2023, and 2022, the Company recognized revenue of approximately $71.3 million, $47.0 million, and $3.3 million, respectively, under the Takeda Collaboration Agreement in the Company's consolidated statements of operations and comprehensive loss. Through December 31, 2024, the Company has recognized revenue of $199.5 million under the Takeda Collaboration Agreement as collaboration revenue in the Company's consolidated statements of operations and comprehensive loss.

The aggregate amount of the transaction price allocated to the Company's unsatisfied and partially unsatisfied performance obligations which are recorded in deferred revenue as of December 31, 2024 and 2023, is $0.0 million and $71.3 million, respectively.

6. SHARE CAPITAL

The following represents the Company's financing transactions during the years ended December 31, 2024, 2023, and 2022:

- The Company entered into the Sales Agreement (as defined below) with Jefferies LLC ("Jefferies". During the years ended December 31, 2024, 2023, and 2022, the Company sold 2,952,591, 751,688, and 458,092 ordinary shares, respectively, under its "at-the-market" equity program for aggregate net proceeds of $20.4 million, $3.1 million, and $1.2 million, respectively, after deducting commissions and offering expenses.
- On June 16, 2022, the Company closed an underwritten offering (the "June 2022 Offering") in which the Company issued and sold 25,464,483 of the Company's ordinary shares at a price of $2.15 per share and pre-funded warrants (the "2022 Pre-Funded Warrants") to purchase up to 7,093,656 of the Company's ordinary shares at an offering price of $2.1499 per 2022 Pre-Funded Warrant, which represents the per share offering price for the ordinary shares less the $0.0001 per share exercise price for each 2022 Pre-Funded Warrant. These 2022 Pre-Funded Warrants were recorded as a component of shareholders' equity within additional paid-in capital. The gross proceeds to the Company from the June 2022 Offering were $70.0 million before deducting underwriting discounts and commissions and other offering expenses. The net proceeds to the Company from the June 2022 Offering were approximately $65.5 million, after deducting underwriting commissions and offering expenses. The 2022 Pre-Funded Warrants are exercisable at any time after their original issuance and on or prior to the five-year anniversary of the original issuance date. A holder of 2022 Pre-Funded Warrants may not exercise the warrant if the holder, together with its affiliates, would beneficially own more than 19.99% of the number of the Company's ordinary shares outstanding or more than 19.99% of the combined voting power of the Company's securities outstanding immediately after giving effect to such exercise, unless and until shareholder approval is obtained.
- On December 11, 2023, the Company closed an underwritten public offering (the "December 2023 Offering") in which the Company issued and sold 20,000,000 of the Company's ordinary shares at a price of $5.00 per share. The gross proceeds to the Company from the December 2023 Offering were $100.0 million before deducting underwriting discounts and commissions and other offering expenses. The net proceeds to the Company from the December 2023 Offering during the year ended December 31, 2023, were approximately $93.6 million, after deducting underwriting discounts and offering expenses. On January 4, 2024, the Company closed on the sale of an additional 3,000,000 ordinary shares at a price of $5.00 per share after the underwriters exercised their option to purchase the additional shares in full, which increased the aggregate number of ordinary shares sold in the December 2023 Offering to 23,000,000. The Company's aggregate gross proceeds from the December 2023 Offering were $115.0 million, before deducting underwriting discounts and commissions and offering expenses; $15.0 million of which relates to the exercise of the underwriters' option in January 2024. Subsequent to December 31, 2023, the Company received $14.0 million in net proceeds after deducting the underwriting discounts and commissions and offering expenses related to the December 2023 Offering.
- On September 27, 2024, the Company closed an underwritten public offering (the "September 2024 Offering") in which the Company issued and sold 23,125,001 of the Company's ordinary shares at a price of $8.00 per share and pre-funded warrants (the "2024 Pre-Funded Warrants") to purchase up to 1,875,023 of the Company's ordinary shares at an offering price of $7.9999 per 2024 Pre-Funded Warrant, which represents the per share offering price for the ordinary shares less the $0.0001 per share exercise price for each 2024 Pre-Funded Warrant. These 2024 Pre-Funded Warrants were recorded as a component of shareholders' equity within additional paid-in capital. The gross proceeds to the Company from the September 2024 Offering were $200.0 million before deducting underwriting discounts and commissions and other offering expenses. The net proceeds to the Company from the September 2024 Offering were approximately $187.5 million, after deducting underwriting commissions and offering expenses. The 2024 Pre-Funded Warrants are exercisable at any time after their original issuance and on or prior to the five-year anniversary of the original issuance date. A holder of the 2024 Pre-Funded Warrants may not exercise the warrant if the holder, together with its affiliates, would beneficially own more than 4.99% (or at the election of such holder, 9.99% or 19.99%) of the number of the Company's ordinary shares outstanding or more than 4.99% (or at the election of such holder, 9.99% or 19.99%) of the combined voting power of the Company's securities outstanding immediately after giving effect to such exercise, unless and until shareholder approval is obtained.

- On October 1, 2024, the representatives of the underwriters in connection with the September 2024 Offering exercised their option in full to purchase an additional 3,750,000 ordinary shares, which increased the aggregate number of ordinary shares sold in the September 2024 Offering to 26,875,001. The Company's aggregate gross proceeds from the September 2024 Offering were $230.0 million, before deducting underwriting discounts and commissions and offering expenses; $30.0 million of which relates to the exercise of the underwriters' option in October 2024.
- On November 12, 2024, the Company filed an automatic shelf registration statement on Form S-3ASR with the SEC for which the Company registered for sale an indeterminate amount of any combination of its ordinary shares, debt securities, warrants, rights and/or units from time to time and at prices and on terms that the Company may determine, which is referred to as the "2024 WKSI Shelf". The 2024 WKSI Shelf includes a prospectus covering up to an aggregate of $250.0 million in ordinary shares that the Company is able to issue and sell from time to time, through Jefferies acting as its sales agent, pursuant to the Open Market Sale Agreement, dated May 10, 2019, as amended by Amendment No. 1, dated as of March 2, 2020, Amendment No. 2, dated as of March 3, 2022, and Amendment No. 3, dated as of November 12, 2024, (as amended, the "Sales Agreement"), for its "at-the-market" equity program.

Features of the Series A Preferred Shares and Ordinary Shares

The Series A preferred shares and ordinary 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 and have no entitlement to dividends.

Voting

The holders of Series A preferred shares are not entitled to vote on any of the matters proposed to shareholders, other than as specified in the Company's Constitution. 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 ordinary 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 an aggregate of approximately $10 thousand for Series A preferred shares.

7. SHARE-BASED COMPENSATION

The Wave Life Sciences Ltd. 2021 Equity Incentive Plan was approved by the Company's shareholders and went into effect on August 10, 2021 and was amended effective as of August 9, 2022, August 1, 2023, and August 6, 2024 (as amended, the "2021 Plan"). The 2021 Plan serves as the successor to the Wave Life Sciences Ltd. 2014 Equity Incentive Plan, as amended (the "2014 Plan"), such that outstanding awards granted under the 2014 Plan continue to be governed by the terms of the 2014 Plan, but no awards may be made under the 2014 Plan after August 10, 2021. The aggregate number of ordinary shares authorized for issuance of awards under the 2021 Plan was originally 5,450,000 ordinary shares, and was subsequently increased to 11,450,000, 17,950,000, and 22,950,000 in August 2022, August 2023, and August 2024, respectively, plus the number of ordinary shares underlying any awards under the 2014 Plan that are forfeited, cancelled or otherwise terminated (other than by exercise or withheld by the Company to satisfy any tax withholding obligation) on or after August 10, 2021.

The 2021 Plan authorizes (and the 2014 Plan previously authorized) the board of directors or a committee of the board of directors to, among other things, grant non-qualified share options, restricted awards, which include restricted shares and restricted share units ("RSUs"), and performance awards to eligible employees and directors of the Company. The Company accounts for grants to its board of directors as grants to employees.

As of December 31, 2024, 7,052,136 ordinary shares remained available for future grant under the 2021 Plan. In accordance with Nasdaq Listing Rule 5635(c)(4), the board of directors or a committee of the board may also issue inducement grants outside of the 2021 Plan, as an inducement material to an individual's entering into employment with the Company.

Options and RSUs

Share option activity 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, 2024	14,107,710	$ 6.58		
Granted	7,480,600	4.36		
Exercised	(770,636)	3.87		
Forfeited or cancelled	(1,364,543)	7.32		
Outstanding as of December 31, 2024	19,453,131	$ 5.78	7.11	$ 144,819
Options exercisable as of December 31, 2024	9,155,502	$ 7.34	5.44	$ 62,214

(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 periods of one to 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.

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,		
	2024	2023	2022
Risk-free interest rate	3.56% – 4.64%	3.46% – 4.71%	1.35% – 4.23%
Expected term (in years)	3.0 – 6.1	3.0 – 6.1	3.0 – 6.1
Expected volatility	88% – 100%	87% – 93%	63% – 96%
Expected dividend yield	0%	0%	0%

In October 2022, the compensation committee of the Company's board of directors (the "Compensation Committee") granted Dr. Verdine, one of the Company's founders and a member of the Company's board of directors, a non-qualified share option for 163,467 ordinary shares ("Verdine Scientific Advisory Grant") as form of payment under Dr. Verdine's consulting agreement for scientific advisory services (as described in Note 13) for the service period of October 1, 2022 through December 31, 2024, the vesting of which is subject to Dr. Verdine's continued service under the consulting agreement.

The Verdine Scientific Advisory Grant was granted as a non-employee grant during the year ended December 31, 2022, and there were no equity grants made to non-employees during the years ended December 31, 2023 and 2024. The assumptions used in the Black-Scholes option pricing model to determine the fair value of the Verdine Scientific Advisory Grant were as follows:

	Year Ended December 31, 2022
Risk-free interest rate	4.29%
Expected term (in years)	2.5
Expected volatility	99%
Expected dividend yield	0%

RSU activity for the year ended December 31, 2024 is summarized as follows:

	RSUs	Average Grant Date Fair Value (in dollars per share)
Outstanding as of January 1, 2024	637,557	$ 7.08
Granted	379,100	7.04
Vested	(100,326)	4.90
Forfeited	(84,288)	5.01
RSUs Outstanding at December 31, 2024	832,043	$ 7.54

RSUs can be time-based or performance-based. Vesting of the performance-based RSUs is contingent on the occurrence of certain regulatory or commercial milestones. In March 2021, the Compensation Committee approved an amendment and restatement of the Company's outstanding 2019 performance-based RSUs to add an additional milestone to the existing milestones. In 2021, the Company also granted performance-based RSUs with the same terms to certain employees who did not receive the 2019 performance-based RSUs. The Company did not recognize expense in 2024 related to the performance-based RSUs as the remaining milestones were not considered probable of achievement. In April 2022, the Company determined that a performance-based RSU milestone was achieved and consequently 50% of the outstanding performance-based RSUs vested, which resulted in the issuance of 384,646 ordinary shares. During the year ended December 31, 2022, the Company recorded share-based compensation expense of approximately $3.8 million related to the performance-based RSUs, which represents all of the expense related to the achievement of this performance-based RSU milestone. During the years ended December 31, 2024, 2023, and 2022, the Company recognized share-based compensation expense of $0.8 million, $1.0 million, and $10.3 million, respectively, related to RSUs.

RSUs that are forfeited are available to be granted again. During the year ended December 31, 2024, 379,100 time-based RSUs were granted to employees. Of the RSUs outstanding at December 31, 2024, 540,779 are time-based RSUs and 291,264 are performance-based RSUs. Time-based RSUs generally vest over periods of one to four years.

During the years ended December 31, 2024, 2023, and 2022, the Company recognized share-based compensation expense related to options of $11.9 million, $8.5 million, and $6.7 million, respectively. The total intrinsic value of options exercised was $4.4 million, $0.3 million, and $0.4 million for the years ended December 31, 2024, 2023, and 2022, respectively. As of December 31, 2024, the unrecognized compensation cost related to outstanding options was $28.9 million. The unrecognized compensation cost related to outstanding options is expected to be recognized over a weighted-average period of approximately 2.67 years. For the years ended December 31, 2024 and 2023, the weighted-average grant date fair value per granted option was $3.38 and $3.45, respectively. The aggregate fair value of options that vested during the years ended December 31, 2024 and 2023 was $11.4 million and $8.4 million, respectively.

The unrecognized compensation costs related to outstanding time-based RSUs was $2.8 million as of December 31, 2024, and is expected to be recognized over a weighted-average period of approximately 2.25 years. The total fair value of RSUs vested during the years ended December 31, 2024, and 2023 was $0.7 million and $2.0 million, respectively.

Employee Share Purchase Plan

The Wave Life Sciences Ltd. Employee Share Purchase Plan, as amended ("ESPP"), allows full-time and certain part-time employees to purchase the Company's ordinary shares at a discount to fair market value. Eligible employees may enroll in a six-month offering period beginning every January 15th and July 15th. Shares are purchased at a price equal to 85% of the lower of the fair market value of the Company's ordinary shares on the first business day or the last business day of an offering period. During the years ended December 31, 2024, and 2023, 176,498 and 225,913 ordinary shares were issued under the ESPP, respectively. The aggregate number of ordinary shares authorized for issuance under the ESPP was originally 1,000,000 and was subsequently increased to 3,000,000 in August 2023. As of December 31, 2024, there were 2,314,002 ordinary shares available for issuance under the ESPP.

Share-Based Compensation Expense

Share-based compensation expense for the years ended December 31, 2024, 2023, and 2022 is classified as operating expenses in the consolidated statements of operations and comprehensive loss as follows:

	For the Year Ended December 31,		
	2024	2023	2022
		(in thousands)	
Research and development expenses	$ 6,332	$ 4,617	$ 7,467
General and administrative expenses	6,809	5,178	9,727
Total share-based compensation expense	$ 13,141	$ 9,795	$ 17,194

Of the total share-based compensation expense recorded for the years ended December 31, 2024, 2023, and 2022, $0.3 million, $0.2 million, and less than $0.1 million, respectively, were related to non-employee option grants, specifically the Verdine Scientific Advisory Grant, and all of the related expense is included in research and development expenses on the consolidated statements of operations and comprehensive loss.

8. LEASES

Lease Arrangements

The Company enters into lease arrangements for its facilities. A summary of the arrangements is as follows:

Operating Leases

Lexington

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 current good manufacturing practices ("cGMP") manufacturing, as well as for additional laboratory and office space. As there is not reasonable certainty that the renewal options will be exercised, the lease liabilities and the right-of-use assets pertaining to the Lexington Lease do not account for the two successive five-year renewal options. 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. As required under the terms of the lease agreement, the Company has placed restricted cash of approximately $2.8 million and $2.7 million in a separate bank account as of December 31, 2024 and 2023, respectively.

Cambridge

In April 2015, the Company entered into a lease agreement for an office and laboratory facility in Cambridge, Massachusetts (the "Cambridge Lease"), which commenced in October 2015 with a term of 7.5 years with a five-year renewal option to extend the lease. 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. As required under the terms of the lease agreement, the Company has placed restricted cash of $1.0 million in a separate bank account as of December 31, 2024 and 2023.

In December 2020, the Company exercised its option under the Cambridge Lease to lease the additional office and laboratory space at the existing facility. The combined space constitutes the entire building. The lease for the additional space commenced on October 1, 2021, with a term of five years and is considered a separate lease from the Cambridge Lease. On the commencement date, the Company utilized the operating lease classification and recorded a right-of-use asset and corresponding operating lease liability of $4.5 million and began recognizing straight-line rent expense under ASC 842. 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 June 2022, the Company exercised the five-year renewal option under the Cambridge Lease to extend the lease term through March 2028 (the "Cambridge Lease Extension"). Therefore, as required by ASC 842, the Company calculated an incremental borrowing rate of 10.53% and remeasured the right-of-use asset and the lease liabilities related to the Cambridge Lease Extension. As a result, an additional $12.0 million of operating right-of-use asset and corresponding operating lease liabilities were recorded relating to the Cambridge Lease Extension.

The following table contains a summary of the lease costs recognized under ASC 842 and other information pertaining to the Company's operating leases for the years ended December 31, 2024 and 2023:

	For the Year Ended December 31,		
	2024	2023	2022
	(in thousands)		
Lease cost			
Operating lease cost	$ 7,365	$ 7,365	$ 6,458
Variable lease cost	2,998	2,798	2,508
Total lease cost	$ 10,363	$ 10,163	$ 8,966
Other information			
Operating cash flows used for operating leases	$ 9,311	$ 8,655	$ 7,226
Increase in operating right-of-use assets	$ —	$ —	$ 12,006
Operating lease liabilities arising from obtaining right-of-use assets	$ —	$ —	$ 12,006
Weighted average remaining lease term	3 years	4 years	5 years
Weighted average discount rate	9.2%	9.2%	9.2%

Future minimum lease payments under the Company's non-cancelable operating leases as of December 31, 2024, are as follows:

	As of December 31, 2024
	(in thousands)
2025	9,591
2026	9,584
2027	8,987
2028	886
2029 and thereafter	-
Total lease payments	$ 29,048
Less: imputed interest	(3,644)
Total operating lease liabilities	$ 25,404

9. COMMITMENTS AND CONTINGENCIES

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.

10. NET LOSS PER ORDINARY SHARE

In connection with the September 2024 Offering, the Company sold 1,875,023 2024 Pre-Funded Warrants, which are included in the total vested and exercisable pre-funded warrants (the 2022 Pre-Funded Warrants and the 2024 Pre-Funded Warrants are referred to together as the "Pre-Funded Warrants"). As of December 31, 2024 and 2023, there were 8,968,679 and 7,093,656, respectively, vested and exercisable Pre-Funded Warrants outstanding to purchase ordinary shares for the exercise price of $0.0001 per share, provided that, unless and until the Company obtains shareholder approval for the issuance of the shares underlying the Pre-Funded Warrants, a holder will not be entitled to exercise any portion of any Pre-Funded Warrant, which, upon giving effect to such exercise, would cause (i) the aggregate number of our ordinary shares beneficially owned by the holder (together with its affiliates) to exceed, depending on the terms of the applicable Pre-Funded Warrants and in certain cases at the election of the holder, either 4.99%, 9.99% or 19.99% of the number of our ordinary shares outstanding immediately after giving effect to the exercise, or (ii) the combined voting power of our securities beneficially owned by the holder (together with its affiliates) to exceed, depending on the terms of the applicable Pre-Funded Warrants and in certain cases at the election of the holder, either 4.99%, 9.99% or 19.99% of the combined voting power of all of our securities then outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the applicable Pre-Funded Warrants. The Pre-Funded Warrants are included in the weighted-average shares outstanding used in the calculation of basic net loss per share as the exercise price is negligible and the warrants are fully vested and exercisable.

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

The Company's potentially dilutive shares, which include outstanding share options to purchase ordinary shares and RSUs, 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 table below sets forth the computation of the Company's basic and diluted net loss attributable to ordinary shareholders:

	Year Ended December 31,		
	2024	2023	2022
	(in thousands except share and per share data)		
Numerator:			
Net loss attributable to ordinary shareholders	$ (97,008)	$ (57,513)	$ (161,823)
Denominator:			
Weighted-average ordinary shares outstanding	138,277,468	106,097,268	78,855,810
Net loss per share, basic and diluted	$ (0.70)	$ (0.54)	$ (2.05)

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,		
	2024	2023	2022
Options to purchase ordinary shares	19,453,131	14,107,710	9,682,054
RSUs	832,043	637,557	934,342

11. INCOME TAXES

The components of loss before income taxes were as follows:

	Year Ended December 31,		
	2024	2023	2022
		(in thousands)	
Singapore	$ (4,202)	$ (7,441)	$ (8,714)
Rest of world	(92,806)	(50,749)	(152,428)
Loss before income taxes	$ (97,008)	$ (58,190)	$ (161,142)

During the years ended December 31, 2024, 2023, and 2022, the Company recorded no income tax benefit or provision, an income tax benefit of $0.7 million, and an income tax provision of $0.7 million, respectively. The income tax benefit for the year ended December 31, 2023 was due to a change in estimate in connection with U.S. tax guidance relating to the capitalization of research and development expenditures. The income tax provision for the year ended December 31, 2022 was primarily due to the requirement

under the Tax Cuts and Jobs Act of 2017 for taxpayers to capitalize and amortize research and development expenditures over five or fifteen years pursuant to Section 174 of the Internal Revenue Code of 1986, as amended (the "Code").

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

	Year Ended December 31,		
	2024	2023	2022
	(in thousands)		
Current benefit (provision) for income taxes:			
Singapore	$ —	$ —	$ —
Rest of world	—	677	(681)
Total current benefit (provision) for income taxes	$ —	$ 677	$ (681)
Deferred benefit for income taxes:			
Singapore	$ —	$ —	$ —
Rest of world	—	—	—
Total deferred benefit (provision) for income taxes	$ —	$ —	$ —
Total benefit (provision) for income taxes	$ —	$ 677	$ (681)

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

	Year Ended December 31,		
	2024	2023	2022
Singapore statutory income tax rate	17.0%	17.0%	17.0%
Federal and state tax credits	9.8	11.5	3.3
Permanent differences	(3.1)	—	0.1
Changes in reserves for uncertain tax positions	(6.0)	(2.8)	0.4
Foreign rate differential	7.2	7.4	8.8
Tax rate change	(2.2)	0.4	—
Return to provision	0.9	4.4	(0.9)
Other	(0.4)	0.1	(0.1)
Change in deferred tax asset valuation allowance	(26.0)	(36.1)	7.3
Deferred tax adjustments	2.8	(0.7)	(36.3)
Effective income tax rate	0.0%	1.2%	(0.4)%

The components of the Company's deferred tax assets and liabilities as of December 31, 2024 and 2023 are as follows:

	December 31,	
	2024	2023
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 177,639	$ 172,547
Federal and state tax credits	15,800	8,155
Share-based compensation	8,649	7,512
Accumulated amortization	578	694
Operating lease liabilities	6,626	8,775
Deferred revenue	8,836	10,716
Capitalized research and development	54,035	41,239
Accumulated depreciation	3,873	3,508
Other	942	237
Total deferred tax assets	276,978	253,383
Valuation allowance	(272,313)	(247,193)
Net deferred tax assets	4,665	6,190
Deferred tax liabilities:		
Operating lease right-of-use assets	(4,661)	(6,185)
Other	(4)	(5)
Total deferred tax liabilities	(4,665)	(6,190)
Net deferred tax assets (liabilities)	$ —	$ —

A roll-forward of the valuation allowance for the years ended December 31, 2024 and 2023 is as follows:

	Year Ended December 31,	
	2024	2023
	(in thousands)	
Balance at beginning of year	$ 247,193	$ 226,273
Increase in valuation allowance	25,169	20,969
Effect of foreign currency translation	(49)	(49)
Balance at end of year	$ 272,313	$ 247,193

As of December 31, 2024, the Company had federal net operating loss carryforwards in the United States of $313.7 million, of which $312.9 million may be available to offset future U.S. federal taxable income indefinitely, while $0.8 million of carryforwards may offset future U.S. federal taxable income through 2037. As of December 31, 2024, the Company had U.S. state net operating loss carryforwards of $64.9 million available to offset future U.S. state taxable income that will begin to expire in 2038. As of December 31, 2024 and 2023, the Company had U.S. federal research and development tax credit carryforwards of approximately $11.2 million and $6.1 million, respectively, available to offset future U.S. federal income taxes and will begin to expire in 2042. As of December 31, 2024 and 2023, the Company had U.S. state research and development tax credit carryforwards of approximately $4.8 million and $2.6 million, respectively, available to offset future U.S. state income taxes and will begin to expire in 2037. As of December 31, 2024, the Company had a U.S. orphan drug credit carryforward of $0.8 million available to offset future U.S. federal income taxes that will begin to expire in 2042.

As of December 31, 2024 and 2023, the Company had net operating loss carryforwards in Japan of $0.7 million and $1.4 million, respectively, which may be available to offset future Japan taxable income and begin to expire in 2025.

As of December 31, 2024 and 2023, the Company had net operating loss carryforwards in Singapore of $132.7 million and $122.0 million, respectively, which may be available to offset future Singapore taxable income and can be carried forward indefinitely.

As of December 31, 2024 and 2023, the Company had net operating loss carryforwards in the United Kingdom (“UK”) of $339.5 million and $335.7 million, respectively, which may be available to offset future UK taxable income 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, 2024, 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 all jurisdictions. Accordingly, a full valuation allowance has been established against the Company's deferred tax assets as of December 31, 2024.

The valuation allowance increased by $25.1 million in 2024. The increase in the valuation allowance for 2024 was primarily 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 income 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 gross unrecognized tax benefits, excluding interest and penalties, is as follows:

	2024	2023	2022
		(in thousands)	
Unrecognized tax benefit at the beginning of the year	$ 15,790	$ 13,945	$ 19,864
Tax positions related to prior years	2,091	114	(7,320)
Tax positions related to the current year	2,917	1,731	1,401
Unrecognized tax benefit at the end of the year	$ 20,798	$ 15,790	$ 13,945

As of December 31, 2024 and 2023, the total amount of gross unrecognized tax benefits, which excludes interest and penalties, was $20.8 million and $15.8 million, respectively. At December 31, 2024, none of the net unrecognized tax benefits would affect the Company’s effective tax rate due to the Company's full valuation allowance.

The Company anticipates that $2.6 million of the total unrecognized tax benefits at December 31, 2024 will decrease within the next twelve months due to certain tax return filings.

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 tax authorities in the United States, Japan, Singapore and the United Kingdom. Tax years from 2021 to the present are still open to examination in the United States, from 2019 to the present in Japan, from 2020 to the present in Singapore and from 2023 to the present in the United Kingdom. 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, 2024 and 2023, $37.8 million and $23.9 million, respectively, of cash and cash equivalents were held by the Company's subsidiaries outside of Singapore. The Company does not provide for Singapore income tax or withholding taxes on the outside basis differences, including foreign unremitted earnings of its subsidiaries as they are permanently reinvested. If the Company decides to change its indefinite reversal assertion in the future, the Company may be required to record deferred taxes. Because of the complexity of Singapore and the rest-of-the-world tax rules applicable to the method of recovery of the investment in its subsidiaries, including distribution of earnings from its subsidiaries to Singapore, the determination of the unrecognized deferred tax liability is not practicable.

Utilization of the net operating loss carryforwards and research and development tax credit carryforwards in the United States may be subject to a substantial annual limitation under Section 382 of the 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. The Company has completed Section 382 studies to assess whether there have been ownership changes since its formation through 2022. The results of the studies indicated that the Company experienced ownership changes as defined by Section 382 of the Code, and, as such, the Company has adjusted its net operating losses and research and development credit carryforwards to reflect the limitations as a result of such ownership changes. Should one or more ownership changes occur in the future, the Company's ability to utilize its net operating losses and research and development credit carryforwards may be further limited.

12. EMPLOYEE BENEFIT PLANS

The Company has a 401(k) retirement and savings plan (the "401(k) Plan") covering employees of Wave USA. The 401(k) Plan allows employees to make contributions up to the maximum allowable amount set by the Internal Revenue Service. Under the 401(k) Plan, the Company may make discretionary contributions as approved by the board of directors. The Company made contributions of $1.7 million and $1.4 million in the years ended December 31, 2024 and 2023, respectively.

13. RELATED PARTIES

The Company had the following related party transactions for the periods presented in the accompanying consolidated financial statements:

- In 2012, the Company entered into a consulting agreement for scientific advisory 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. In October 2022, the Compensation Committee granted Dr. Verdine a non-qualified share option for 163,467 ordinary shares in lieu of cash as payment under this consulting agreement for the service period of October 1, 2022 through December 31, 2024, the monthly vesting of which is subject to Dr. Verdine's continued service under the consulting agreement.
- In April 2023, the Company engaged Shin Nippon Biomedical Laboratories Ltd. ("SNBL"), one of the Company's shareholders, to provide approximately $2.8 million in certain NHPs contract research services to the Company. During the years ended December 31, 2024 and 2023, the Company made payments of $0.9 million and $1.4 million, respectively, to SNBL. Through December 31, 2024, the Company has paid $2.3 million to SNBL for the aforementioned NHP contract research services.

14. SEGMENT INFORMATION

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the CODM in deciding how to allocate resources to an individual segment and in assessing performance. The Company operates as a single reporting segment, focused on developing its proprietary RNA medicines platform, PRISM, to develop and commercialize a broad pipeline of RNA medicines in a variety of therapeutic areas. Consistent with our operational structure, our CEO, as the CODM, manages and allocates resources on a consolidated basis at the global corporate level. The results of our operations are reported on a consolidated basis for purposes of segment reporting. The CEO uses consolidated net loss that is reported on the consolidated statements of operations and comprehensive loss for the purposes of assessing performance, allocating resources and planning, monitoring budget versus actual results, and forecasting future periods.

The following table is representative of the significant expense categories regularly provided to the CODM when managing the Company's single reporting segment. A reconciliation to consolidated operating expenses as our single segment operating loss for the years ended December 31, 2024, 2023, and 2022 is included in the table below:

	For the Year Ended December 31,		
	2024	2023	2022
		(in thousands)	
Research and development expenses:			
AATD program	$ 11,666	$ 8,453	$ 3,763
DMD programs	15,536	7,808	2,610
HD programs	11,790	13,086	7,952
Other research and development expenses[(1)], including INHBE, RNA editing, PRISM, others	119,976	91,617	89,992
ALS and FTD programs *(discontinued)*	714	9,045	11,539
Total research and development expenses	159,682	130,009	115,856
General and administrative expenses	59,023	51,292	50,513
Total operating expenses	$ 218,705	$ 181,301	$ 166,369

(1) Includes expenses related to other research and development programs, identification of potential drug discovery candidates, compensation-related expenses, internal manufacturing expenses, equipment repairs and maintenance expense, facility-related expenses, and other operating expenses, which are not allocated to specific programs.

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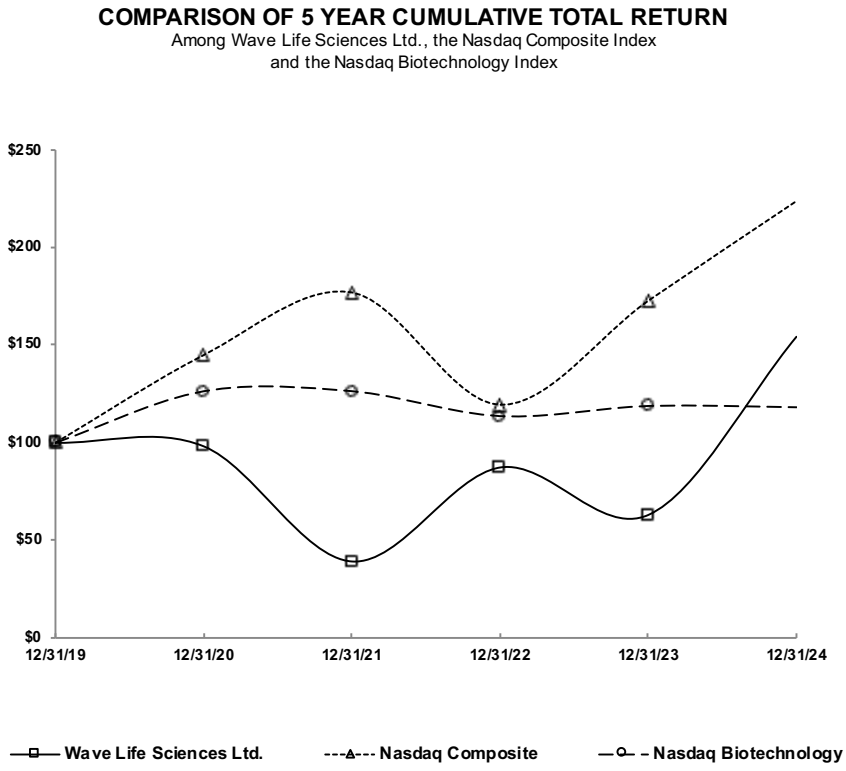
SHARE PERFORMANCE GRAPH

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 December 31, 2019 through December 31, 2024. The figures represented below assume an investment of $100.00 in our ordinary shares at the closing price of $8.015 on December 31, 2019 and in the Nasdaq Composite Index and the Nasdaq Biotechnology Index on December 31, 2019 and the reinvestment of dividends, if any, into ordinary shares. The share return shown in the share performance graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future share return.



This share performance graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (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 of 1933, as amended, or the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

MANAGEMENT TEAM
Paul Bolno, MD, MBA
President and Chief Executive Officer

Chris Francis, PhD
SVP, Corporate Development, Head of Emerging Areas

Erik Ingelsson, MD, PhD
Chief Scientific Officer

Daryn Lewis
SVP, Head of Human Resources

Kyle Moran, CFA
Chief Financial Officer

Linda Rockett, Esq.
SVP, General Counsel

Sridhar Vaddeboina, PhD, MBA
SVP, Chemistry, Manufacturing and Controls

Chandra Vargeese, PhD
Chief Technology Officer, Head of Platform Discovery Sciences

Chris Wright, MD, PhD
Chief Medical Officer

Ginnie (Hsiu-Chiung) Yang, PhD
SVP, Translational Medicine

BOARD OF DIRECTORS
Christian Henry, MBA
Chairman of the Board, Wave Life Sciences Ltd.
President and Chief Executive Officer, Pacific Biosciences

Paul B. Bolno, MD, MBA
President and Chief Executive Officer, Wave Life Sciences Ltd.

Mark H.N. Corrigan, MD
Strategic Advisor, Ceretype Neuromedicine.

Peter Kolchinsky, PhD
Founder & Managing Partner, RA Capital Management

Adrian Rawcliffe
Chief Executive Officer, Adaptimmune Therapeutics plc

Ken Takanashi, MBA, CPA
EVP, Representative Director, Shin Nippon Biomedical Laboratories Ltd.

Aik Na Tan
SVP (Administration) at Nanyang Technological University, Singapore

Gregory Verdine, PhD
Erving Professor of Chemistry, Harvard University

Heidi L. Wagner, JD
Global Head of Government Affairs, ElevateBio, LLC

ORDINARY SHARE LISTING
Nasdaq Global Market

TRADING SYMBOL
WVE

INDEPENDENT ACCOUNTING FIRM
KPMG LLP

INVESTOR RELATIONS
Kate Rausch
VP, Investor Relations and Corporate Affairs
James Salierno
Director, Investor Relations

InvestorRelations@wavelifesci.com

TRANSFER AGENT
Computershare
By Regular Mail
PO Box 43078, Providence, RI 02940-3078, USA
By Overnight Delivery
150 Royall Street, Suite 101, Canton, MA 02021, USA
Phone: 1-877-373-6374
(1-781-575-3100 for shareholders residing outside of the USA/Canada)

CORPORATE COUNSEL
Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

REPORTS
Copies of the Company's annual and quarterly reports as filed with the Securities and Exchange Commission are available at www.wavelifesciences.com

FORWARD-LOOKING STATEMENTS
Any statements in this annual report, including the letter to shareholders, about our future expectations, plans and prospects, including statements about our research and development activities, the success, progress, and timing or results of our clinical trials, development of our product candidates and expectations regarding our financial condition, including the period for which our existing cash resources will be sufficient to meet our operating requirements, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the factors discussed in the "Risk Factors" section of our Annual Report on Form 10-K included in this annual report.

In addition, forward-looking statements included in this annual report, including in our letter to shareholders, represent our views only as of the date such statements were made and should not be relied upon as representing our views as of any subsequent date. We specifically disclaim any obligation to update any forward-looking statements included in this annual report, including in our letter to shareholders.

LOCATIONS
Wave Life Sciences Ltd. (Registered Address)
7 Straits View #12-00, Marina One East Tower
Singapore 018936

Wave Life Sciences USA, Inc. (US Headquarters)
733 Concord Avenue
Cambridge, MA 02138, USA

Wave Life Sciences USA, Inc.
115 Hartwell Avenue
Lexington, MA 02421, USA

Wave Life Sciences Japan, Inc.
2438 Miyanoura-cho
Kagoshima-shi
Kagoshima pref. 891-1394, Japan

Wave Life Sciences UK Limited
1 Chamberlain Square CS
Birmingham, B3 3AX
United Kingdom

Wave Life Sciences Ireland Limited
1 Spencer Dock, North Wall Quay
Dublin 1, Ireland, D01 X9R7

ANNUAL MEETING
Our 2025 Annual General Meeting of Shareholders will be held on Tuesday, August 5, 2025, at 11:30 a.m., Eastern Time, at Wave Life Sciences Ltd., 733 Concord Avenue, Cambridge, MA 02138.

Wave Life Sciences is a clinical-stage biotechnology company focused on unlocking the broad potential of RNA medicines to transform human health.

Wave Life Sciences
United States Headquarters
733 Concord Avenue
Cambridge, MA 02138

wavelifesciences.com