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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of report (Date of earliest event reported): February 19, 2018

WAVE LIFE SCIENCES LTD.
(Exact name of registrant as specified in its charter)

Singapore	**001-37627**	**Not Applicable**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

7 Straits View #12-00 Marina One East Tower
Singapore 018936
(Address of principal executive offices) **018936** **(Zip Code)**

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

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

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. ☒

Item 1.01 Entry Into a Material Definitive Agreement.

Collaboration and License Agreement

On February 19, 2018, Wave Life Sciences USA, Inc. and Wave Life Sciences UK Limited (collectively, "Wave"), each direct, wholly-owned subsidiaries of Wave Life Sciences Ltd. (the "Company") entered into a Collaboration and License Agreement (the "Collaboration Agreement") with Takeda Pharmaceutical Company Limited ("Takeda"). Pursuant to the terms of the Collaboration Agreement, Wave and Takeda have agreed to collaborate on the research, development and commercialization of oligonucleotide therapeutics for disorders of the central nervous system ("CNS"). The collaboration provides Takeda with the option to globally co-develop and commercialize programs targeting Huntington's disease (HD), amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD) and spinocerebellar ataxia type 3 (SCA3), (collectively, "Category 1 Programs"), which Wave will have the right to co-commercialize in the U.S. In addition, Takeda will have the right to exclusively license multiple preclinical programs for CNS disorders, including Alzheimer's disease and Parkinson's disease (collectively, "Category 2 Programs").

With respect to Category 1 Programs, Wave will be responsible for researching and developing products and companion diagnostics for Category 1 Programs through completion of the first proof of mechanism study for such products. Takeda will have an exclusive option for each target and all associated products and companion diagnostics for such target, which it may exercise at any time through completion of the proof of mechanism study. If Takeda exercises this option, Wave will receive an opt-in payment and will lead manufacturing and joint clinical co-development activities; Takeda will lead joint co-commercial activities in the United States and all commercial activities outside of the United States. Global costs and potential profits will be shared 50:50 and Wave will be eligible to receive development and commercial milestone payments. In addition to its 50% profit share, Wave is 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, Wave has 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 Collaboration Agreement). During that term, the parties may collaborate on preclinical programs for up to six targets at any one time. Wave will be responsible for researching and preclinically developing products and companion diagnostics directed to the agreed upon targets through completion of IND-enabling studies in the first major market country. Thereafter, Takeda will have an exclusive worldwide license to develop and commercialize products and companion diagnostics directed to such targets, subject to Wave's retained rights to lead manufacturing activities for products directed to such targets. Takeda will fund Wave's research and preclinical activities in the amount of $60 million during the research term and will reimburse Wave for any collaboration-budgeted research and preclinical expenses incurred by Wave that exceed that amount. Wave is also eligible to receive tiered high single-digit to mid-teen royalties on Takeda's global commercial sales of products from each Category 2 Program.

In addition to the research support funding of $60 million over four years and the profit and loss sharing and royalty payments described above, Takeda will make an upfront payment of $110 million and an upfront equity investment of $60 million when the Collaboration Agreement takes effect (described under "*Equity Investment*" in this Item 1.01 below). Assuming Takeda advances six programs that achieve development, regulatory and commercial milestones, Wave would be eligible to receive more than $2 billion in cash milestone payments, of which more than $1 billion would be in precommercial milestone payments.

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

The term of the Collaboration Agreement runs from the date on which the closing has occurred under the Share Purchase Agreement for the Equity Investment described below, which is conditioned upon the expiration or early termination of the applicable pre-merger waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 (the "HSR Act"), and, unless terminated earlier, will continue until the date on which: (i) with respect to each Category 1 Program target for which Takeda does not exercise its option, expiration or termination of the development program with respect to such target; (ii) with respect to each Category 1 Program target for which Takeda exercises its option, the date on which neither party is researching, developing or manufacturing any products or companion diagnostics directed to such target; or (iii) with respect to each Category 2 Program target, the date on which royalties are no longer payable with respect to products directed to such target.

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

Equity Investment

In connection with the parties' entry into the Collaboration Agreement, the Company has agreed to sell to Takeda 1,096,892 ordinary shares, no par value (the "Ordinary Shares"), for aggregate cash consideration of approximately $60 million, or $54.70 per Ordinary Share (the "Equity Investment"), pursuant to the terms of a Share Purchase Agreement, dated February 19, 2018, by and between Takeda and the Company (the "Share Purchase Agreement"). This sale does not involve a public offering and is therefore exempt from registration under Section 4(a)(2) of the Securities Act of 1933, as amended (the "Securities Act"). Based on 27,900,698 Ordinary Shares outstanding as of February 14, 2018 (on a pro forma basis), following the Equity Investment, Takeda will beneficially own approximately 4% of the Company's outstanding Ordinary Shares. The Share Purchase Agreement contains customary representations, warranties, and covenants of each of the parties thereto. Subject to customary closing conditions, including the expiration or early termination of the applicable pre-merger waiting period under the HSR Act, the Equity Investment is expected to close during the first quarter of 2018.

As a condition to the closing of the Equity Investment, Takeda will enter into an investor agreement with the Company (the "Investor Agreement"). Under the Investor Agreement, from the date of the Investor Agreement until the earliest to occur of (i) the expiration or earlier termination of the Collaboration Agreement, and (ii) the fourth anniversary of the closing of the Equity Investment (the "Restricted Term"), Takeda and its affiliates will be bound by certain "standstill" provisions. The standstill provisions include, among other provisions, agreements that Takeda will not: acquire beneficial ownership of more than 9.99% of the outstanding Ordinary Shares; nominate any person to the Company's Board of Directors (the "Board") whose nomination has not been approved by a majority of the Board; support a tender offer that would result in a change of control of the Company, unless the Company recommends that shareholders accept such offer; solicit proxies or consents in opposition to the recommendation of a majority of the Board; or propose a merger, business combination or extraordinary transaction with respect to the Company. Further, during the Restricted Term, Takeda will, and will cause its affiliates to, vote or execute a written consent with respect to all voting securities of the Company as to which Takeda and its affiliates are entitled to vote in accordance with the recommendation of the Board, except with respect to any transaction that would result in a change of control, liquidation or dissolution of the Company.

If at any time during the Restricted Term, the Company issues Ordinary Shares or securities convertible into or exercisable for Ordinary Shares in connection with a strategic collaboration or other strategic licensing arrangement to a third party that will initially hold at least the percentage of the Company's outstanding Ordinary Shares represented by the Ordinary Shares purchased by Takeda at the closing of the Equity Investment, the Company will offer Takeda an opportunity to amend the standstill and voting provisions in the Investor Agreement to be consistent with the terms provided to such third party. The standstill provisions would terminate prior to the expiration of the Restricted Term upon the occurrence of certain events, including the announcement of a definitive agreement between the Company and a third party that would result in a change of control or the filing of a Schedule TO by a third party offering to acquire all or substantially all of the Company's outstanding Ordinary Shares.

Under the Investor Agreement, Takeda also agreed not to dispose of any Ordinary Shares beneficially owned by it immediately after the closing of the Equity Investment, until the expiration of the Restricted Term. Following the expiration of the Restricted Term, Takeda will be permitted to sell such Ordinary Shares subject, in certain cases, to limitations such as volume and manner of sale restrictions.

Under the Investor Agreement, following the Restricted Term, Takeda will have two demand rights to require the Company to conduct a registered underwritten public offering with respect to the Ordinary Shares beneficially owned by Takeda immediately after the closing of the Equity Investment. In addition, following the Restricted Term and subject to certain conditions, Takeda will be entitled to participate in registered underwritten public offerings by the Company.

The rights and restrictions under the Investor Agreement are subject to termination upon the occurrence of certain events.

The foregoing description of the material terms of the Collaboration Agreement, Share Purchase Agreement and Investor Agreement (together, the "Agreements") is qualified in its entirety by reference to the complete texts of the Agreements, which the Company intends to file, with confidential terms redacted, with the Securities and Exchange Commission as exhibits to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2018.

Item 3.02 Unregistered Sales of Equity Securities.

The information set forth under the heading "*Equity Investment*" in Item 1.01 is incorporated herein by reference.

Item 7.01 Regulation FD Disclosure.

On February 20, 2018, the Company issued a press release concerning the Collaboration Agreement and the Equity Investment, a copy of which is being furnished as Exhibit 99.1 to this Report on Form 8-K.

From time to time, the Company presents and/or distributes slides and presentations to the investment community at various industry and other conferences to provide updates and summaries of its business. On February 20, 2018, the Company updated its corporate presentation, which is available on the Investors & Media section of the Company's website at http://ir.wavelifesciences.com/. This presentation is also attached as Exhibit 99.2 to this Report on Form 8-K.

The information in this Item 7.01 and Exhibits 99.1 and 99.2 attached hereto is intended to be furnished and shall not 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 of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

The following exhibits relating to Item 7.01 shall be deemed to be furnished, and not filed:

Exhibit No.	Document
99.1	Press Release issued by Wave Life Sciences Ltd. dated February 20, 2018
99.2	Corporate presentation of Wave Life Sciences Ltd. dated February 20, 2018

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

WAVE LIFE SCIENCES LTD.

Date: February 20, 2018

/s/ Keith C. Regnante
Keith C. Regnante
Chief Financial Officer

Exhibit 99.1

Wave Life Sciences and Takeda Form Global Strategic Collaboration to Advance Therapies for Central Nervous System Disorders

Wave to receive at least $230 million, including $110 million in upfront cash, $60 million in equity investment and at least $60 million in research support

Takeda to receive option to co-develop and co-commercialize investigational therapies in HD, ALS, FTD and SCA3 under a global 50:50 profit-split

Takeda to receive right to license additional preclinical CNS programs; Wave eligible to receive more than $1 billion in potential precommercial milestones

CAMBRIDGE, Mass., February 20, 2018 – Wave Life Sciences Ltd. (NASDAQ: WVE), a biotechnology company focused on delivering transformational therapies for patients with serious, genetically-defined diseases, today announced the formation of a global strategic collaboration with Takeda Pharmaceutical Company Limited to discover, develop and commercialize nucleic acid therapies for disorders of the central nervous system (CNS). Under the collaboration, Wave will provide Takeda the option to co-develop and co-commercialize programs in Huntington's disease (HD), amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD) and spinocerebellar ataxia type 3 (SCA3). In addition, Takeda will have the right to license multiple preclinical programs targeting CNS disorders, including Alzheimer's disease and Parkinson's disease. Wave will continue to independently advance its activities in neuromuscular diseases, including its lead clinical program for the treatment of Duchene muscular dystrophy (DMD).

Under terms of the two-component agreement, Takeda will make an initial payment of $110 million to Wave and purchase $60 million of Wave's ordinary shares at $54.70 per share. Takeda will also fund at least $60 million of Wave research over a four-year period to advance multiple preclinical targets selected by and licensed to Takeda.

"We are thrilled to be joining with Takeda in this ambitious alliance to bring meaningful therapies to patients suffering from devastating neurological diseases," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "This partnership provides additional resources to advance our clinical programs through multiple data readouts while continuing to expand our pipeline in neurology and other therapeutic areas. We look forward to working with Takeda and leveraging our expertise in oligonucleotides and clinical capabilities to grow our company and continue to make scientific and medical advances on behalf of patients."

"At Takeda, we are focused on partnering with companies that share our research focus and commitment to deliver transformative medicines to patients," Daniel Curran, MD, Head, Center for External Innovation at Takeda. "Wave's expertise in optimizing oligonucleotides offers a complementary approach to programs that Takeda is currently pursuing for neurological disorders, maximizing our potential for success, and their pipeline and focus are closely aligned with our own."

The first component of the agreement grants Takeda with the option to co-develop and co-commercialize the following nucleic acid investigational therapies upon Wave demonstrating proof of mechanism in initial clinical studies:

- WVE-120101 and WVE-120102, which selectively target the mutant allele of the *huntingtin (HTT)* gene and are currently in Phase 1b/2a clinical trials for the treatment of HD
- WVE-3972-01, which targets the *C9ORF72* gene and is expected to be evaluated in clinical studies for the treatment of ALS and FTD beginning in Q4 2018
- Program targeting the *ATXN3* gene for the treatment of SCA3

Upon opt-in by Takeda on any individual program, Wave will receive an opt-in payment and will lead manufacturing and joint clinical co-development activities; Takeda will lead joint co-commercial activities in the United States and all commercial activities outside of the United States. Global costs and potential profits will be shared 50:50 and Wave will be eligible to receive development and commercial milestone payments.

The second component of the strategic collaboration provides Takeda with the right to license multiple preclinical programs for CNS indications, including Alzheimer's disease and Parkinson's disease. During a four-year term, the companies may collaborate on up to six preclinical targets at any one time. Takeda will fund at least $60 million of Wave's preclinical activities and reimburse Wave for agreed-upon additional expenses. Assuming Takeda advances six programs that achieve regulatory approval and commercial milestones, Wave will be eligible to receive more than $2 billion in cash milestone payments, of which more than $1 billion would be in precommercial milestone payments. Wave is also eligible to receive tiered high single-digit to mid-teen royalty payments on global commercial sales of each licensed program.

The collaboration agreement will become effective upon satisfaction of customary closing conditions, including the requirements of the Hart-Scott-Rodino Antitrust Improvements Act of 1976.

Outside of the collaboration with Takeda, Wave continues to independently advance its activities in neuromuscular diseases, including its lead DMD program, an investigational therapy targeting exon 51 (WVE-210201) currently in a Phase 1 clinical trial. Wave's next DMD program, targeting exon 53, is expected to initiate clinical development in Q1 2019. The company also continues to expand its preclinical research pipeline in other therapeutic areas, including metabolic liver diseases in collaboration with Pfizer and ophthalmology where Wave has wholly-owned discovery programs.

About WVE-120101 and WVE-120102

HD is an autosomal-dominant, progressive neurodegenerative disorder caused by an expanded cytosine-adenine-guanine (CAG) triplet repeat in the *HTT* gene that results in production of mutant HTT (mHTT) protein. Accumulation of mHTT protein causes progressive loss of neurons in the brain. Wild-type, or healthy, HTT (wtHTT) protein is critical for neuronal function, and research suggests that long-term suppression may have detrimental consequences. WVE-120101 and WVE-120102 are investigational stereopure antisense oligonucleotides designed to selectively target the m*HTT* mRNA transcript of SNP rs362307 (SNP1) and SNP rs362331 (SNP2), respectively. *In vitro* studies in patient-derived cell lines have shown that WVE-120101 and WVE-120102 selectively reduce levels of m*HTT* mRNA and protein, while leaving wt*HTT* mRNA and protein largely intact.

About WVE-3972-01

ALS and FTD can be caused by mutations in the *C9ORF72* gene, which provides instructions for making protein found in various tissues, including nerve cells in the cerebral cortex and motor neurons. WVE-3972-01 is an investigational stereopure antisense oligonucleotide designed to preferentially target the pathogenic allele of the *C9ORF72* gene. *In vivo* studies conducted in a transgenic animal model containing the mutated *C9ORF72* gene demonstrated that WVE-3972-01 produced significant and sustained preferential knockdown of disease-associated biomarkers such as repeat-containing transcripts, RNA foci and dipeptide repeat proteins without altering total C9ORF72 protein levels.

About Wave Life Sciences

Wave Life Sciences is a biotechnology company focused on delivering transformational therapies for patients with serious, genetically-defined diseases. Our chemistry platform enables the creation of highly specific, well characterized oligonucleotides designed to deliver superior efficacy and safety across multiple therapeutic modalities. Our pipeline is initially focused on neurological disorders and extends across several other therapeutic areas. For more information, please visit www.wavelifesci.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding the collaboration and license agreement between Wave and Takeda, including anticipated payments, as well as the future discovery, development, manufacture and commercialization of potential therapies for CNS disorders under the agreement; Wave's and Takeda's ability to successfully develop and commercialize potential therapies for CNS disorders; and Wave's strategy and business plans. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks and uncertainties related to Wave's ability to successfully advance multiple potential preclinical programs simultaneously on its platform; the delay of any current or planned clinical trials or the other development activities for Wave's investigational therapies; Wave's ability to successfully demonstrate the safety and efficacy of its investigational therapies; the preclinical and clinical results of Wave's investigational therapies; actions of regulatory authorities that may affect the initiation, timing and progress of clinical trials; and Wave's ability to successfully commercialize any investigational therapies that receive regulatory approval. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Wave's Annual Report on Form 10-K for the year ended December 31, 2016, as filed with the Securities and Exchange Commission (SEC) on March 16, 2017, and other filings that Wave may make with the SEC from time to time. Any forward-looking statements contained in this press release represent Wave's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Wave explicitly disclaims any obligation to update any forward-looking statements.

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Exhibit 99.2

Wave Life Sciences

Corporate Presentation

February 20, 2018

Forward looking statements

This document contains forward-looking statements. All statements other than statements of historical facts contained in this document, including statements regarding possible or assumed future results of operations, preclinical and clinical studies, business strategies, research and development plans, collaborations and partnerships, regulatory activities and timing thereof, competitive position, potential growth opportunities, use of proceeds and the effects of competition are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause the actual results, performance or achievements of Wave Life Sciences Ltd. (the "Company") to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "aim," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this presentation are only predictions. The Company has based these forward-looking statements largely on its current expectations and projections about future events and financial trends that it believes may affect the Company's business, financial condition and results of operations. These forward-looking statements speak only as of the date of this presentation and are subject to a number of risks, uncertainties and assumptions, including those listed under Risk Factors in the Company's Form 10-K and other filings with the SEC, some of which cannot be predicted or quantified and some of which are beyond the Company's control. The events and circumstances reflected in the Company's forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, the Company operates in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that the Company may face. Except as required by applicable law, the Company does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Genetic medicines company

Developing targeted therapies for patients impacted by rare diseases

- Rationally designed stereopure nucleic acid therapeutics
- Utilizing multiple modalities including antisense, exon skipping and RNAi
- 6 neurology development programs by the end of 2018
- Expertise and core focus in neurology
  - 2 Phase 1b/2a trials initiated in Huntington's disease
  - DMD Exon 51 trial initiated
  - Clinical data readouts anticipated in 2019 for first 3 programs
- Robust R&D platform, ability to partner additional therapeutic areas
- Cash position $169MM as of September 30 2017

WAVE™
LIFE SCIENCES

Paving the way to potentially safer, more effective medicines

1
first to design and bring stereopure and allele-specific medicines to clinic

6
neurology development programs by end of 2018

3
clinical studies initiated in 2017

10K+
oligonucleotides created and analyzed to date

5
nucleic acid modalities being advanced with Wave stereopure chemistry

12+
discovery programs

5
therapeutic areas under active investigation

25M+
total potentially addressable patients amenable to Wave's partnered and proprietary programs

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Pipeline spanning multiple modalities, novel targets

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

WAVE LIFE SCIENCES

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

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

Neurology leadership

Current programs

- **Huntington's disease (HTT SNP1)**
- **Huntington's disease (HTT SNP2)**
- **Duchenne muscular dystrophy (exon 51)**
- **Duchenne muscular dystrophy (exon 53)**
- **Amyotrophic lateral sclerosis (C9orf72)**
- **Frontotemporal dementia (C9orf72)**

Discovery engine

Neuromuscular diseases
- DMD (additional exons)
- Spinal muscular atrophy (SMN2)
- Charcot-Marie-Tooth type 1A (PMP22)

Neurodegenerative movement disorders
- Spinocerebellar ataxia 3 (ATXN3)

Opportunities for expansion

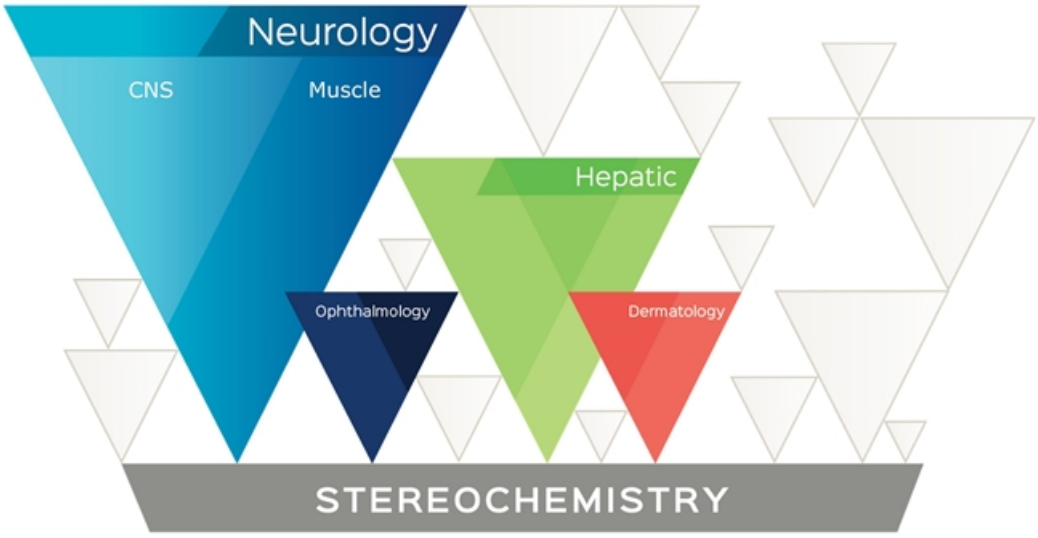
Neurodegenerative movement disorders
- Parkinson's disease
- Progressive supranuclear palsy

Neurodegenerative dementias
- Alzheimer's disease

Developmental diseases
- Fragile X
- Batten disease

Neurophysiology/ neuropsychiatry/pain
- Epilepsy
- Schizophrenia

Broad platform relevance across therapeutic areas



WAVE LIFE SCIENCES

Building the optimal, stereopure medicine

STANDARD OLIGONUCLEOTIDE APPROACHES

Pharmacologic properties include >500,000 permutations in every dose

↓

Impact:
Unreliable therapeutic effects
Unintended off-target effects

WAVE RATIONAL DESIGN

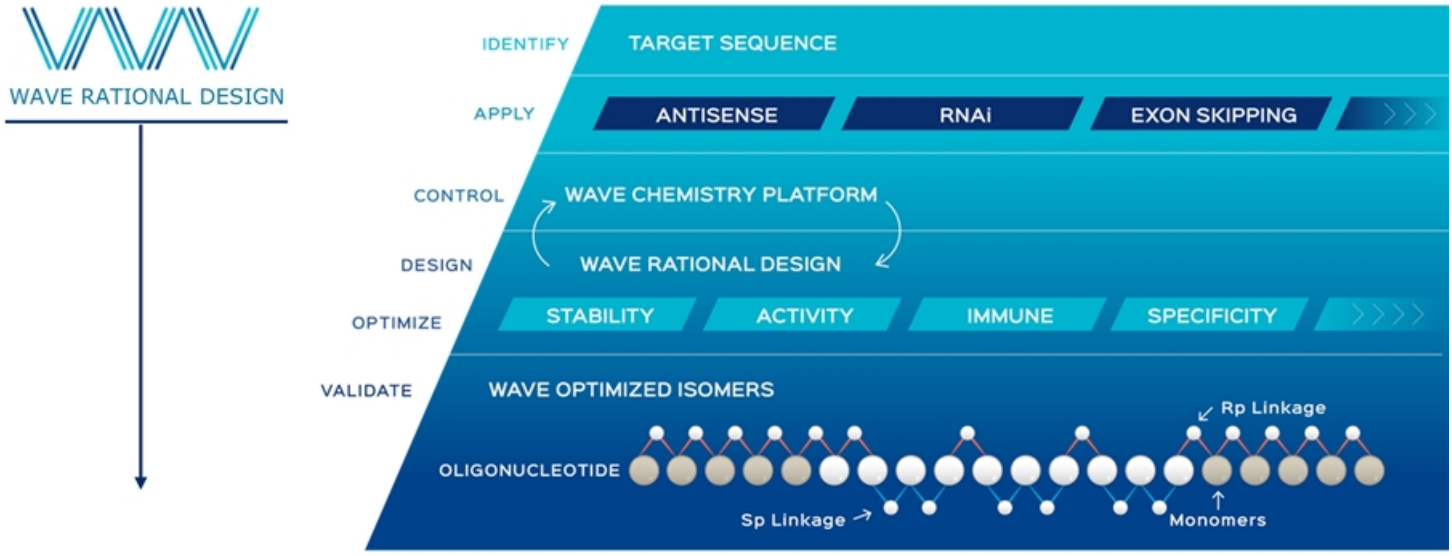
Stereochemistry enables precise control, ability to optimize critical constructs into one defined and consistent profile

↓

Impact:
Potential for safer, more effective, targeted medicines that can address difficult-to-treat diseases

WAVE LIFE SCIENCES

Creating a new class of oligonucleotides

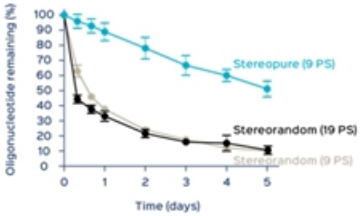


Source: Iwamoto N, et al. Control of phosphorothioate stereochemistry substantially increases the efficacy of antisense oligonucleotides. Nature Biotechnology. 2017.

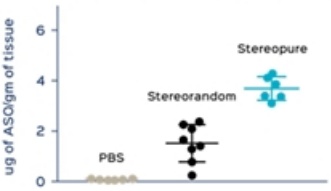
Chemistry may optimize medicines across multiple dimensions

Improved Stability

Stability of stereopure molecules with reduced PS content (liver homogenate)

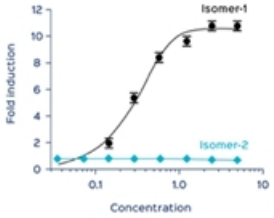


Oligonucleotide exposure (spinal cord)

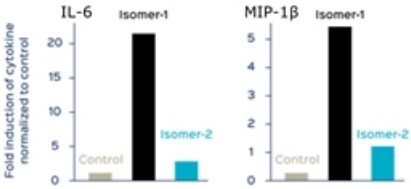


Controlled Immunogenicity

Human TLR9 activation assay with 5mC modified CpG containing MOE gapmer

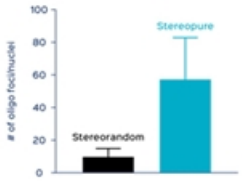


Cytokine induction in human PBMC assay

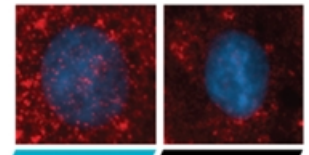


Enhanced Delivery

Stereochemistry enables enhanced delivery of oligonucleotides



Uptake without transfection agent between a stereopure and stereorandom oligonucleotide



Gymnotic uptake of ASOs:18h differentiating myoblasts

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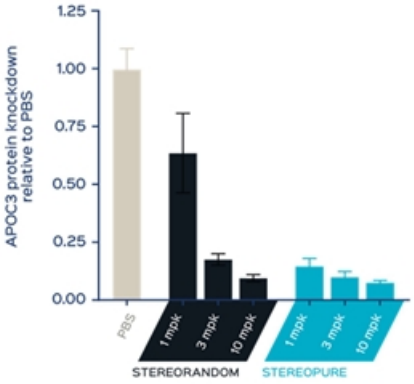
Data represented in this slide from in vitro studies. Experimental conditions: Human TLR9 assay – Source: Ohto U, et al. Structural basis of CpG and inhibitory DNA recognition by Toll-like receptor 9, Nature 520, 702-705, 2015. Intracellular trafficking assay – Cells were washed and fixed and oligos were detected by viewRNA assay and visualized on immunofluorescence microscope with deconvolution capabilities. Z-stacks were taken to eliminate artifacts.

Stereochemistry is applicable across modalities

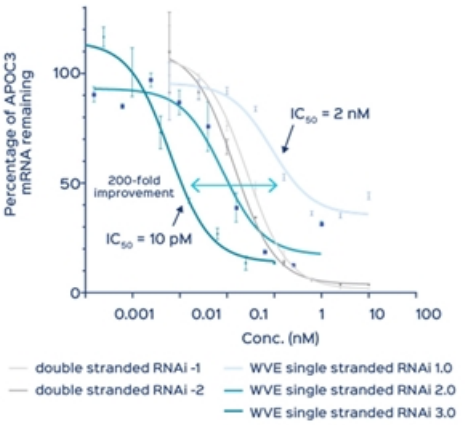
Antisense

In vivo potency and durability
(APOC3 transgenic mice, day 15)



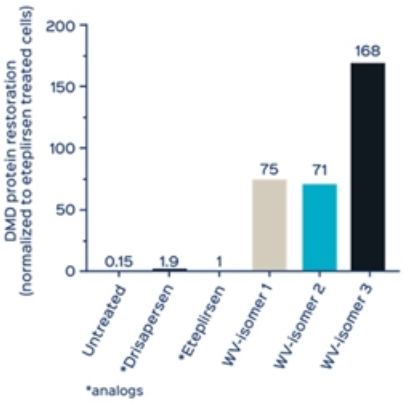
RNAi

200 Fold Higher Potency from
Original ssRNAi Designs



Exon skipping

71-168 Fold Increase in
Protein Restoration *
Compared to Eteplirsen



Stereochemistry allows for novel approaches to previously difficult diseases and inaccessible targets

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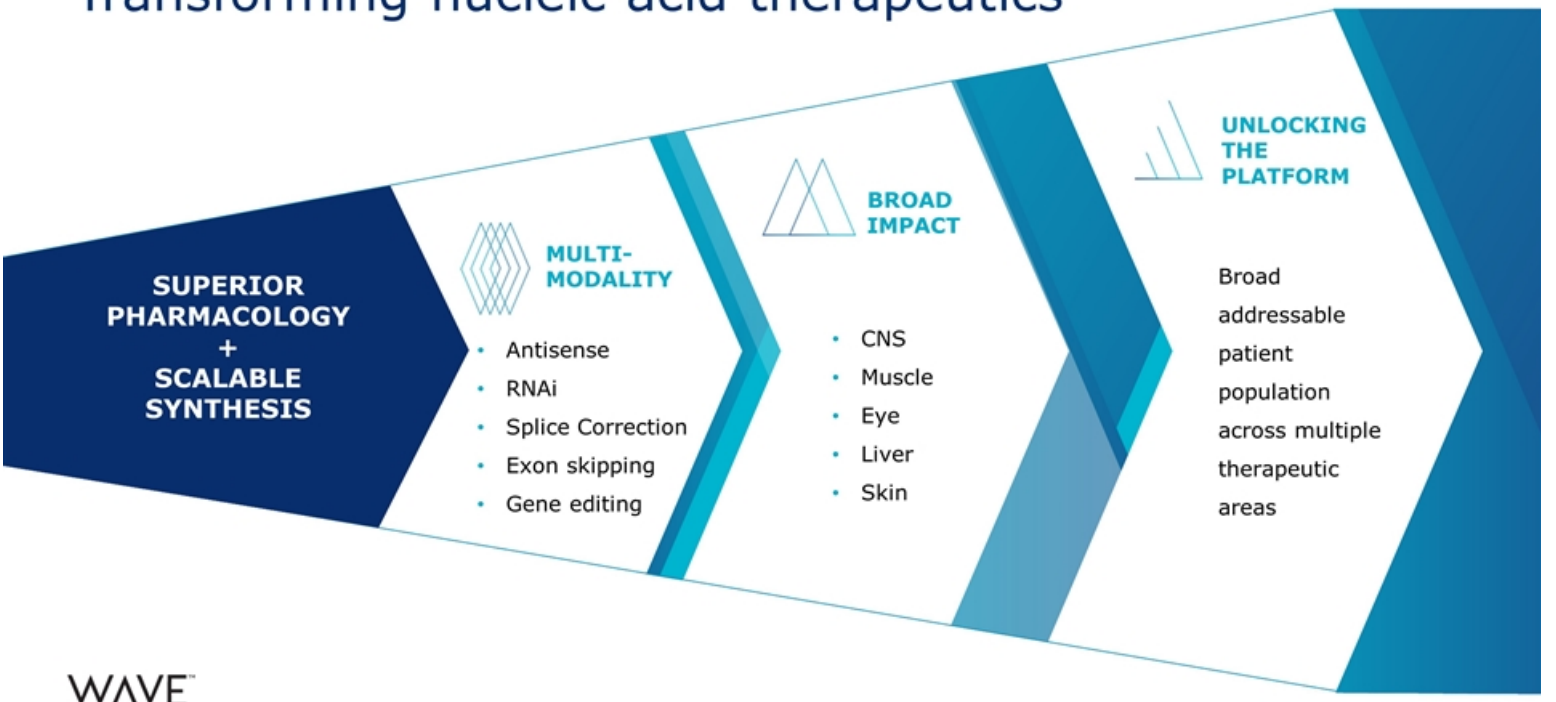
Transforming nucleic acid therapeutics



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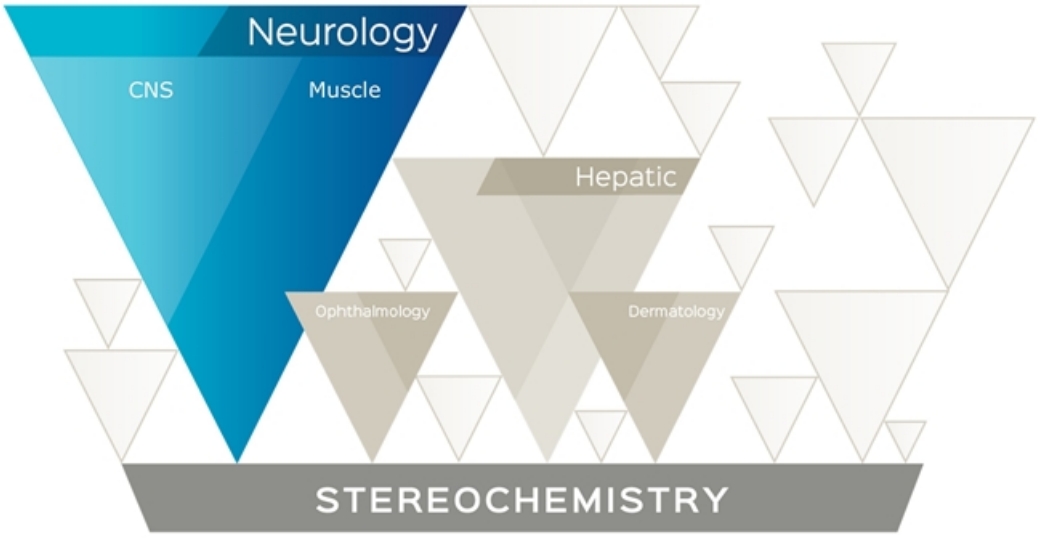
Neurology



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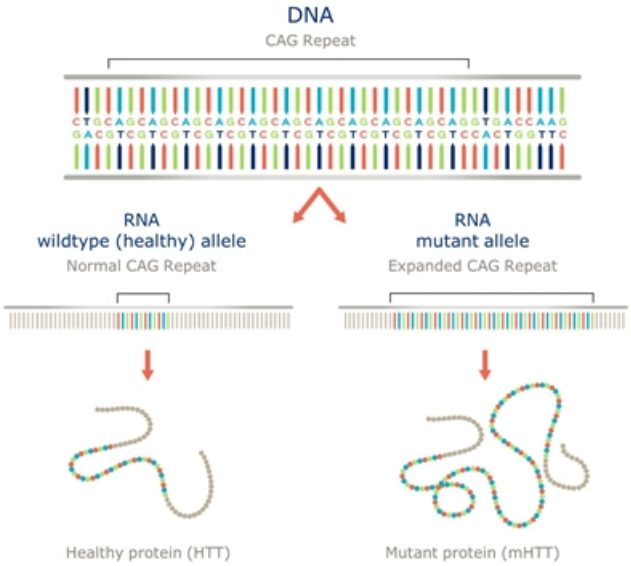
Huntington's Disease

Huntington's Disease: a hereditary, fatal disorder

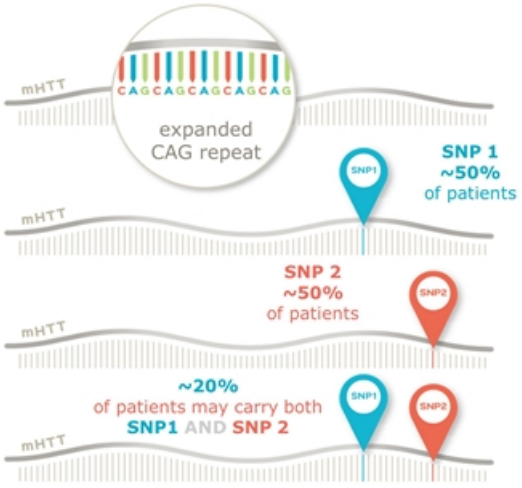
- Autosomal dominant disease, characterized by cognitive decline, psychiatric illness and chorea; fatal
- No approved disease-modifying therapies
- Expanded CAG triplet repeat in HTT gene results in production of mutant huntingtin protein (mHTT); accumulation of mHTT causes progressive loss of neurons in the brain
- Wildtype (healthy) HTT protein critical for neuronal function; suppression may have detrimental long-term consequences
- 30,000 people with Huntington's disease in the US; another 200,000 at risk of developing the condition



Sources: Auerbach W, et al. Hum Mol Genet. 2001;10:2515-2523. Dragatsis I, et al. Nat Genet. 2000;26:300-306. Leavitt BR, et al. J Neurochem. 2006;96:1121-1129. Nasir J, et al. Cell. 1995;81:811-823. Reiner A, et al. J Neurosci. 2001;21:7608-7619. White JK, et al. Nat Genet. 1997;17:404-410. Zeitlin S, et al. Nat Genet. 1995;11:155-163. Carroll JB, et al. Mol Ther. 2011;19:2178-2185.

Wave approach: novel, allele-specific silencing

- Utilize association between single nucleotide polymorphisms (SNPs) and genetic mutations to specifically target errors in genetic disorders, including HD.
- Allele-specificity possible by targeting SNPs associated with expanded long CAG repeat in mHTT gene
- Approach aims to lower mHTT transcript while leaving healthy HTT relatively intact
- Potential to provide treatment for up to 70% of HD population (either oligo alone could address approximately 50% of HD population)



Total: Due to overlap, an estimated **~70%** of the total HD patient population carry SNP 1 and/or SNP 2

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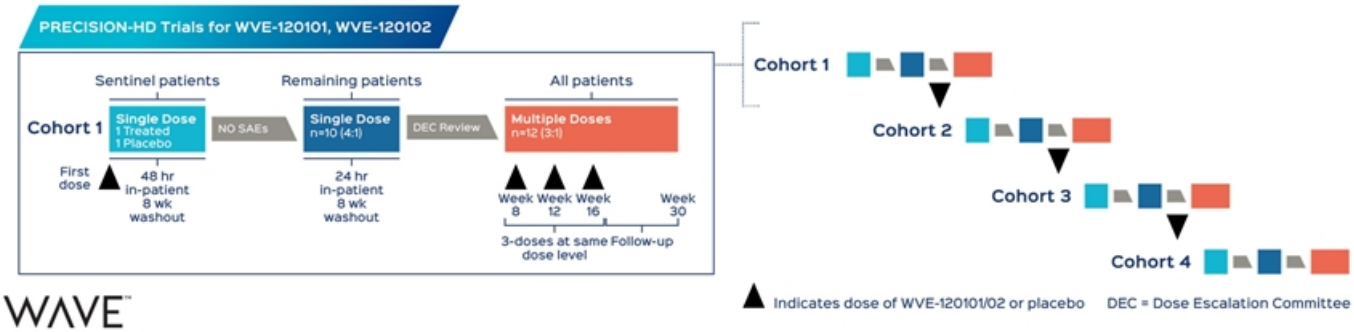
Source: Kaye, et al. Personalized gene silencing therapeutics for Huntington disease. Clin Genet 2014: 86: 29–36

Two simultaneous Phase 1b/2a clinical trials

- Two parallel global placebo-controlled multi-ascending-dose trials for WVE-120101, WVE-120102
- Primary objective: assess safety and tolerability of intrathecal doses in early manifest HD patients
- Additional objectives: exploratory pharmacokinetic, pharmacodynamic, clinical and MRI endpoints
- Blood test to determine presence of SNP 1 or SNP 2 done at pre-screening
- Approximately 50 patients per trial
- Key inclusion criteria: age ≥25 to ≤65, stage I or II HD
- Top line data anticipated 1H 2019



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Mutant huntingtin: a powerful, novel biomarker

- Novel immunoassay allows for quantification of mutant huntingtin, the cause of HD
- Level of mHTT detected is associated with time to onset, increased with disease progression, and predicts diminished cognitive and motor dysfunction
- Assay currently being utilized in clinical studies

Novel approach enables precise measurement of target engagement and effect

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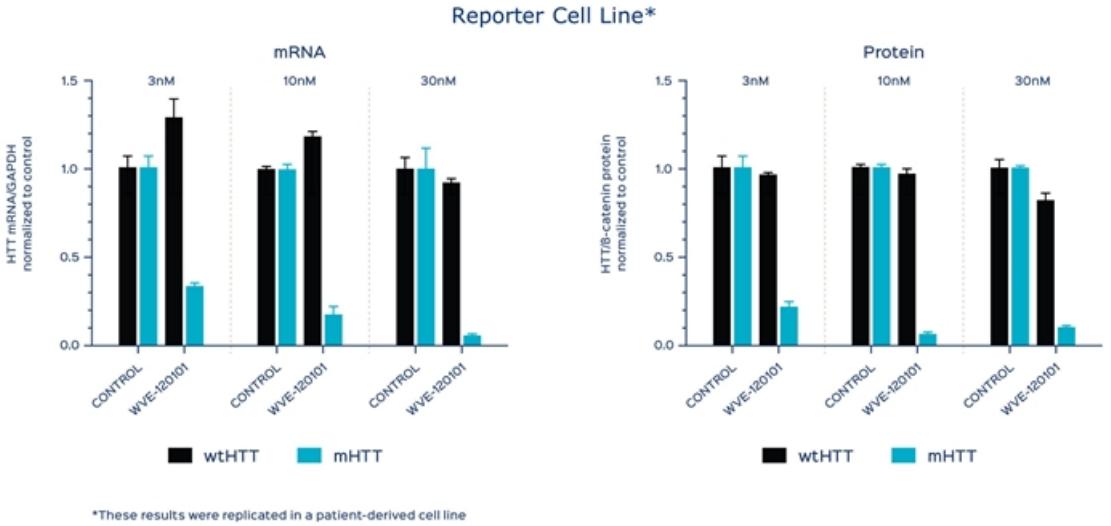
Source: Wild E, et al. Quantification of mutant huntingtin protein in cerebrospinal fluid from Huntington's disease patients. J. Clin. Invest. 2015:125:1979–1986. Edward Wild, MA MB BChir PhD MRCP Principal Investigator at UCL Institute of Neurology and Consultant Neurologist at the National Hospital for Neurology and Neurosurgery, London

Selective reduction of mHTT mRNA & protein



*These results were replicated in a patient-derived cell line

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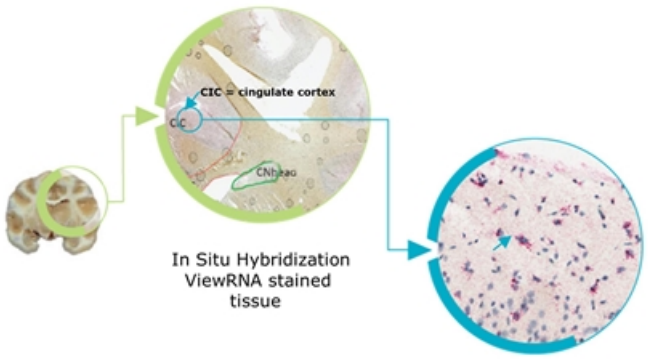
Demonstrated delivery to brain tissue

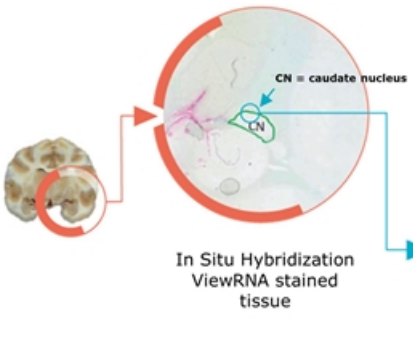
- WVE-120101 and WVE-120102 distribution in cynomolgus non-human primate brain following intrathecal bolus injection



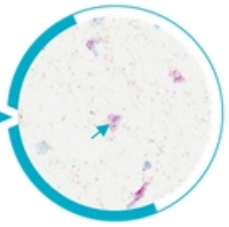
In Situ Hybridization ViewRNA stained tissue

Red dots are WVE-120101 oligonucleotide.

Arrow points to nuclear and perinuclear distribution of WVE- 120101 in cingulate cortex



In Situ Hybridization ViewRNA stained tissue



Red dots are WVE-120102 oligonucleotide.

Arrow points to nuclear and perinuclear distribution of WVE-120102 in caudate nucleus

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CIC = cingulate cortex.
CN = caudate nucleus.

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Duchenne Muscular Dystrophy (DMD)

DMD: a progressive, fatal childhood disorder

- Fatal, X-linked genetic neuromuscular disorder characterized by progressive, irreversible loss of muscle function, including heart and lung
- Genetic mutation in dystrophin gene prevents the production of dystrophin protein, a critical component of healthy muscle function
- Symptom onset in early childhood; one of the most serious genetic diseases in children worldwide
- Current disease modifying treatments have demonstrated minimal dystrophin expression and clinical benefit has not been established
- Impacts 1 in every 3,500 newborn boys each year; 20,000 new cases annually worldwide

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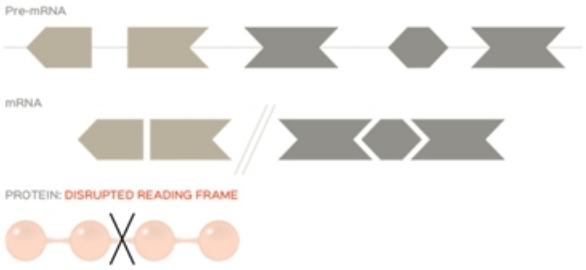
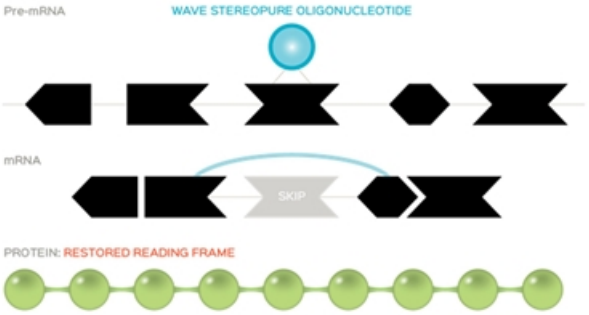
Wave approach:
meaningful restoration of dystrophin production through exon skipping

- Meaningful restoration of dystrophin production is expected to result in therapeutic benefit
- Exon-skipping antisense approaches may enable production of functional dystrophin protein
- Initial patient populations are those amenable to Exon 51 and Exon 53 skipping

Dysfunctional splicing (Disease)



Exon skipping (Potential Remedy)



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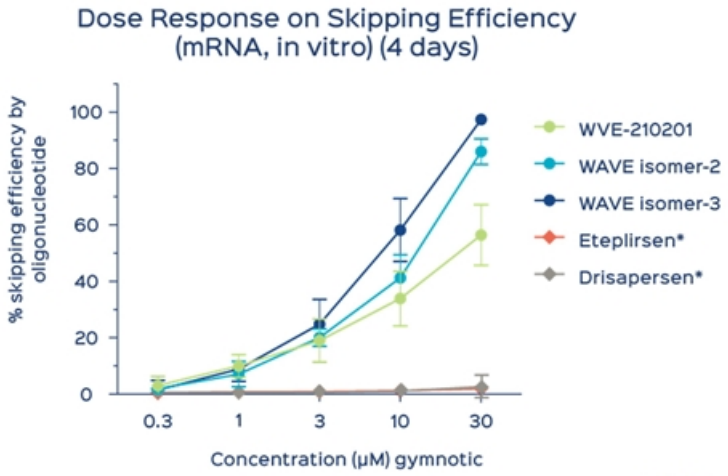
Exon 51: WVE-210201 clinical program

- WVE-210201 Phase 1 clinical trial initiated November 2017
  - Design: Multicenter, double-blind, placebo-controlled, single ascending dose study with I.V. administration
  - Primary endpoint: Safety and tolerability
  - Inclusion criteria: ages 5 to 18, amenable to exon 51 skipping
    - Ambulatory and non-ambulatory boys eligible, including those previously treated with eteplirsen (following appropriate washout period)
  - Readout expected Q3 2018
  - Planned open-label extension (OLE) with muscle biopsy and ≥2-years of follow-up
- WVE-210201 planned efficacy study
  - Design: Double-blind, placebo-controlled, multi-dose study assessing dystrophin expression and clinical outcomes
  - Measurement of dystrophin via standardized Western Blot
  - Interim analysis of dystrophin expression in muscle biopsies
  - Efficacy readout anticipated 2H 2019
- Exploring intravenous and subcutaneous formulations for WVE-210201

Exon 51: improved skipping efficiency

- RNA skipping determined by quantitative RT-PCR
- Wave isomers demonstrated a dose-dependent increase in skipping efficiency
- Free uptake at 10uM concentration of each compound with no transfection agent
- Same foundational stereopure chemistry for Wave isomers; individually optimized to assess ideal profile



*analogs

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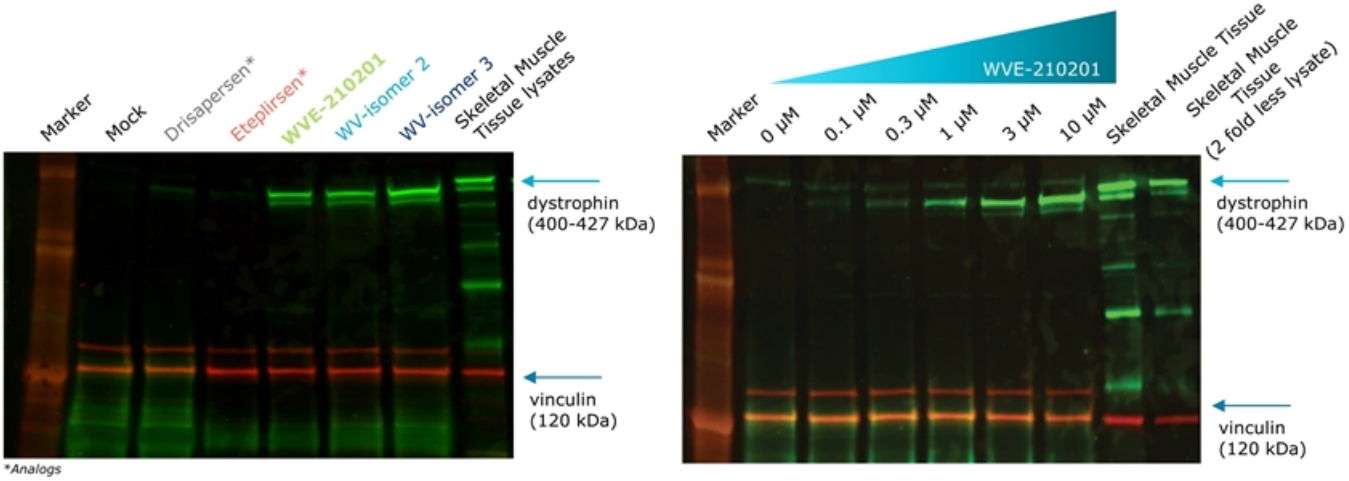
Exon 51: increased dystrophin restoration



Dystrophin protein restoration in vitro *was quantified to be between* ***50-100% of normal*** *skeletal muscle tissue lysates, as compared to about 1% by drisapersen and eteplirsen analogs*

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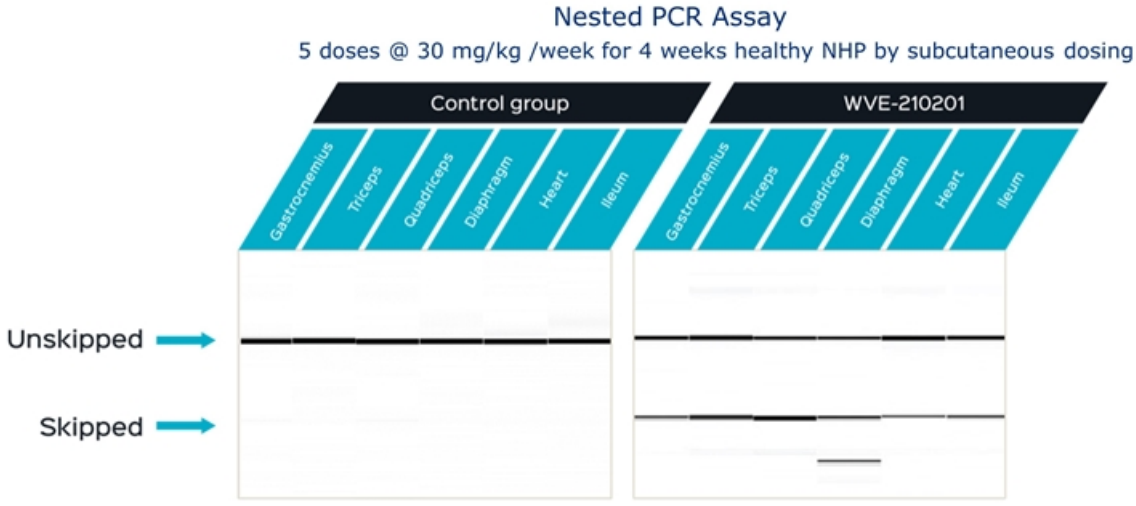
Experimental conditions: DMD protein restoration by Western Blot in patient-derived myotubes with clear dose effect. Free uptake at 10uM concentration of each compound with no transfection agent

Exon 51: target engagement in healthy non-human primate



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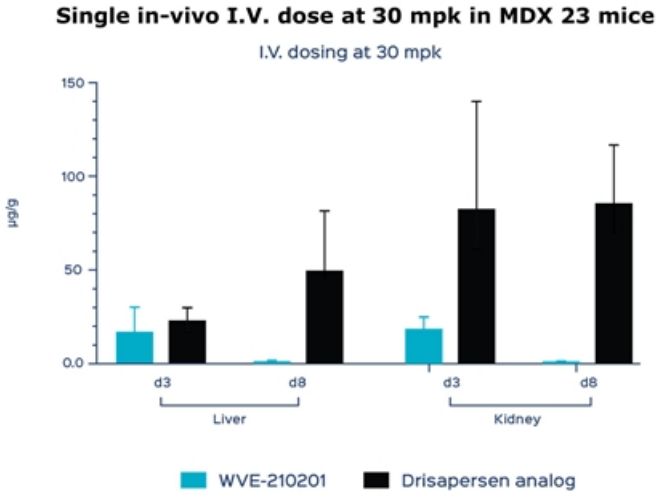
Experimental conditions: Muscle tissues were collected 2 days after the last dose and fresh frozen. Total RNAs were extracted with phenol/chloroform and converted to cDNA using high capacity kit. Nested PCR assay was performed and analyzed by fragment analyzer.

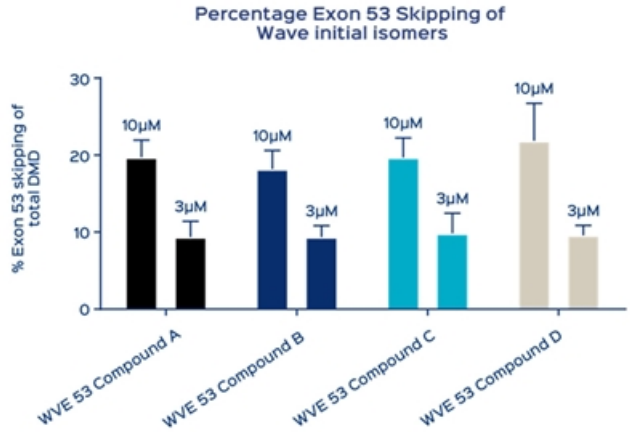
Exon 51: no apparent tissue accumulation observed

- Standard oligonucleotides tend to accumulate in liver and kidney
- Wave rationally designed oligonucleotides optimized to allow compound to clear more effectively
- WVE-210201 demonstrated wide tissue distribution in dose dependent fashion
- No apparent accumulation observed after multiple doses



Experimental description: Oligo quantifications in tissues were performed using hybridization ELISA assay

Exon 53:
Stereopure lead molecules advancing toward candidate



- RNA skipping determined by quantitative RT-PCR
- Free uptake at 10uM and 3uM concentration of each compound with no transfection agent
- Current published clinical dystrophin levels achieved for Exon 53 are ~1%

Early Exon 53 data suggests initial skipping efficiency around 20% pre-optimization

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C9orf72

Amyotrophic Lateral Sclerosis (ALS)

Frontotemporal Dementia (FTD)

C9orf72: a critical genetic risk factor

- C9orf72 gene provides instructions for making protein found in various tissues, with abundance in nerve cells in the cerebral cortex and motor neurons
- C9orf72 genetic mutations are the strongest genetic risk factor found to date for the more common, non-inherited (sporadic) forms of Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD); GGGGCC repeat drives the formation and accumulation of dipeptide repeat proteins that accumulate in brain tissue
- First pathogenic mechanism identified to be a genetic link between familial (inherited) ALS and FTD
- Most common mutation identified associated with familial ALS and FTD
- Availability of dipeptide biomarker in CSF has potential to accelerate drug development

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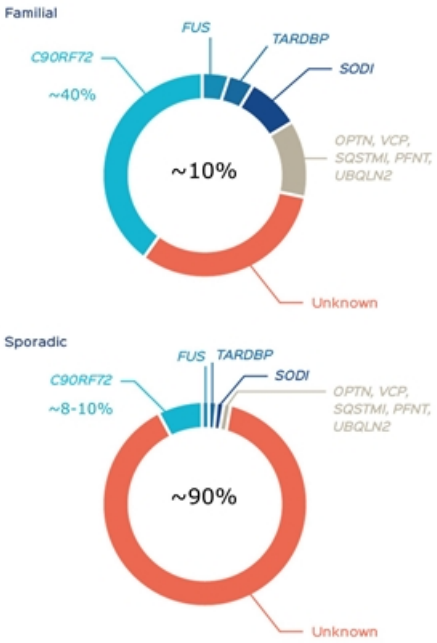
Amyotrophic lateral sclerosis

- Neurodegenerative disease characterized by the progressive degeneration of motor neurons in the brain and spinal cord
- Affects approximately 15,000-20,000 people in the US with a median survival of 3 years
- C9orf72 is present in approximately 40% of familial ALS and 8-10% of sporadic ALS; currently the most common demonstrated mutation related to ALS, far more so than SOD1 or TDP-43
- Pathogenic transcripts of the C9orf72 gene contain hundreds to thousands of hexanucleotide repeats compared to 2-23 in wild-type transcripts; dominant trait with high penetrance

Initiation of clinical study expected 4Q '18



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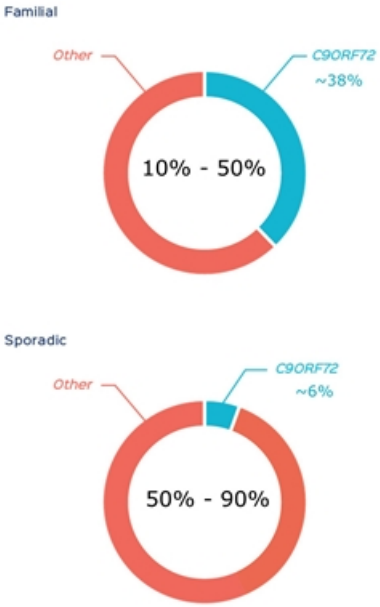
Source: State of play in amyotrophic lateral sclerosis genetics Alan E Renton, Adriano Chiò & Bryan J. Traynor Nature Neuroscience 17, 17–23 (2014) doi:10.1038/nn.3584

Frontotemporal dementia

- Progressive neuronal atrophy with loss in the frontal and temporal cortices characterized by personality and behavioral changes, as well as gradual impairment of language skills
- Affects approximately 55,000 people in the US
- Second most common form of early-onset dementia after Alzheimer's disease in people under the age of 65
- Up to 50% of FTD patients have a family history of dementia, many inheriting FTD as an autosomal dominant trait with high penetrance
- Pathogenic transcripts of the C9orf72 gene contain hundreds to thousands of hexanucleotide repeats compared to 2-23 in wild-type transcripts

Initiation of clinical study expected 4Q '18



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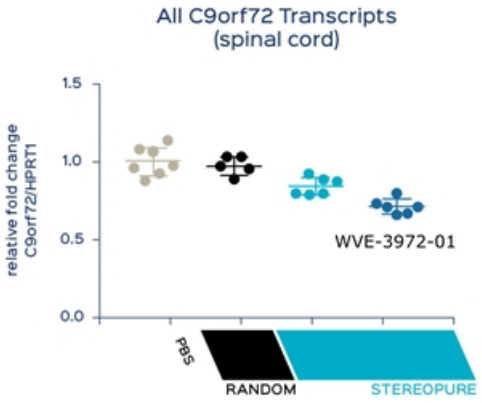
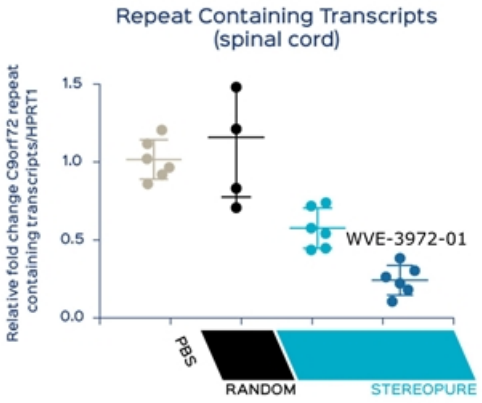
Sources: Familial aggregation in frontotemporal dementia, M. Stevens, MD; C.M. et al, Neurology 1998. Frequency of the C9orf72 hexanucleotide repeat expansion in patients with amyotrophic lateral sclerosis and frontotemporal dementia: a cross-sectional study. Elisa Majounie et al Lancet Neurology March 9, 2012 DOI:10.1016/S1474-4422(12)70043-1

Selective silencing in vivo of expanded C9orf72 repeat transcripts

- Wave has developed a series of highly optimized antisense compounds which selectively silence the repeat containing transcript in C9orf72 transgenic mice
- These compounds show target engagement across cell types and regions of the nervous system critically implicated in ALS





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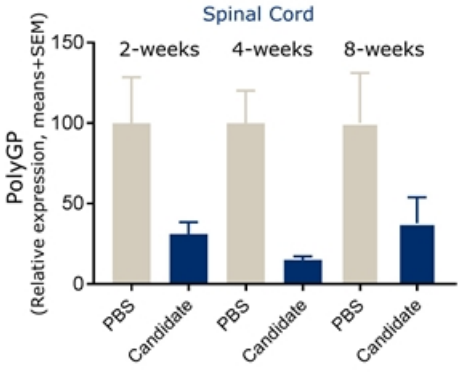
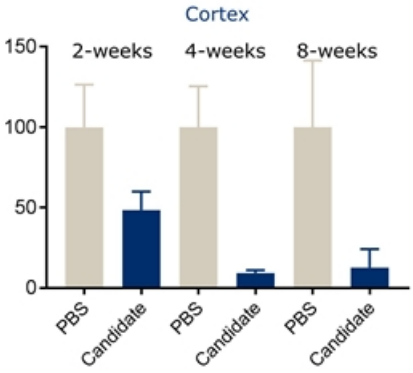
Experimental description: Samples were analyzed using quantitative PCR (Taqman assay)

Durable reduction of dipeptides and RNA foci in vivo

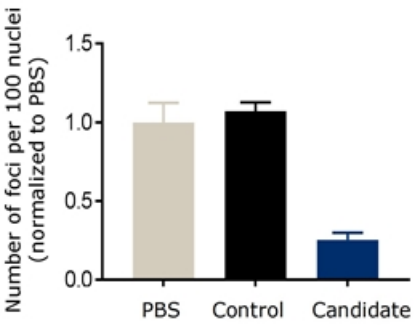
- Wave's candidate (WVE-3972-01) demonstrates durable reduction of dipeptides and reductions in RNA foci
- Data is consistent across blinded studies in independent laboratories (collaboration with Professor Bob Brown, U. Mass)

Durable reduction of dipeptide in vivo





Reductions in RNA foci in vivo (8 weeks)



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Spinocerebellar ataxia type 3

Spinocerebellar ataxia type 3

- Also known as Machado-Joseph disease
- Rare, hereditary, progressive neurodegenerative disorder that results in a lack of muscle control and coordination in upper and lower extremities; gradually leads to paralysis and loss of ability to speak or swallow
- Life expectancy is 10-20 years from symptom onset
- Prevalence: 1-2 in 100,000 people; most common dominantly inherited form of ataxia, representing 20% to 50% of all SCAs
- Expanded CAG repeat in *ATXN3* gene results in mutant ATXN3 protein that causes widespread neuronal loss in brain and spinal cord

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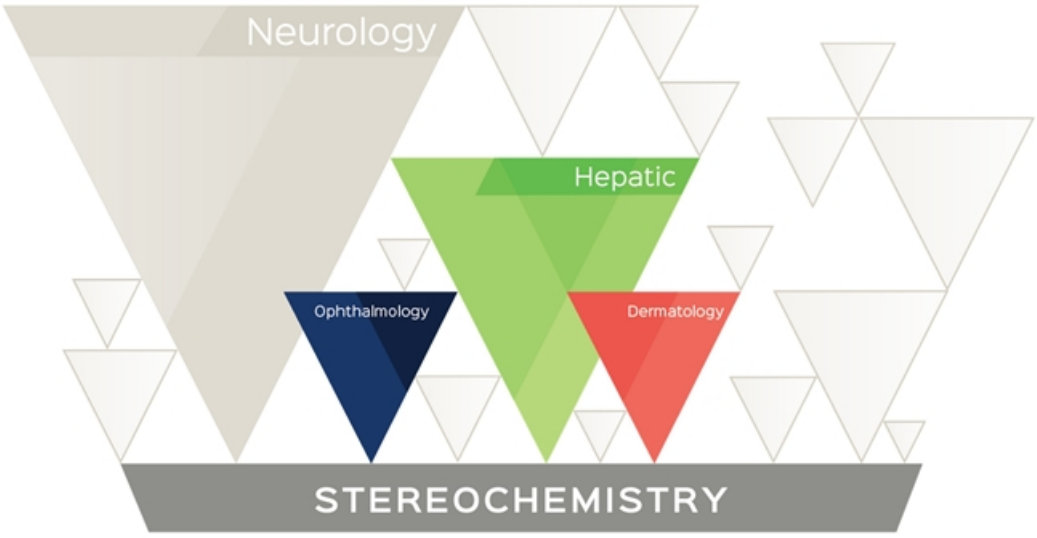
Source: Paulson H. Machado-Joseph disease/spinocerebellar ataxia type 3. Handb Clin Neurol 103, 437—449 (2012).
National Institute of Health. Spinocerebellar ataxia 3. Accessed at: https://ghr.nlm.nih.gov/condition/spinocerebellar-ataxia-type-3 on February 15, 2018

Emerging areas



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Pfizer hepatic collaboration

- Initiated May 2016
- Exploring targets across modalities, including ASO and ssRNAi
- Up to 5 hepatic-metabolic programs
  - 3 targets declared; APOC3, 2 undisclosed
  - Option to declare 2 additional targets
- Access to Pfizer's hepatic targeting technology
  - Potentially increasing potency beyond GalNAc
  - Freedom to leverage beyond collaboration targets

40

$M upfront payment

871

$M in potential milestone payments and royalties

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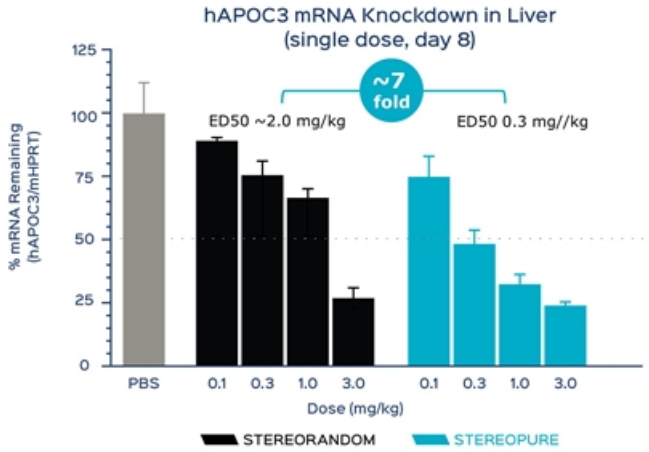
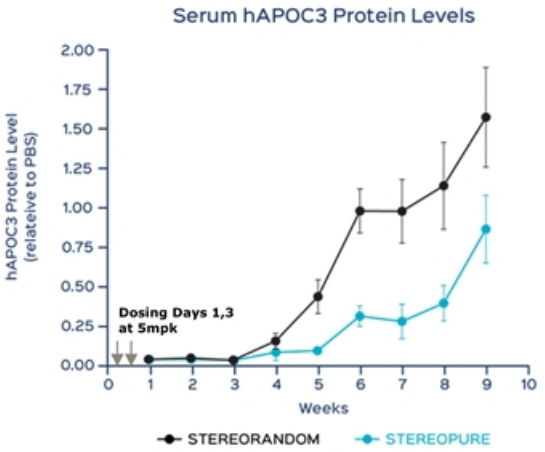
Stereopure ASOs: improved in vivo potency, extended duration

- Potency equivalent to state-of-the-art GalNAc conjugated double strand RNAi (ED50 0.3 mg/kg)
- Demonstrated increase in durability over GalNAc conjugated stereorandom





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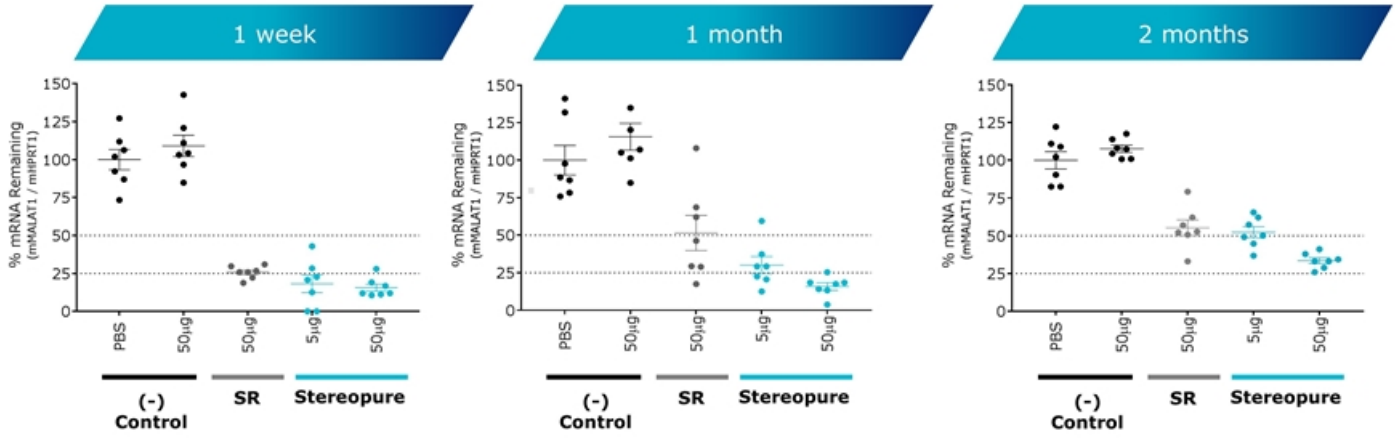
Experimental description: Male human APOC3 transgenic mice were dosed with APOC3 ASOs with indicated doses. APOC3 mRNA quantification in the liver was performed using Taqman assay specific for hAPOC3. For protein analysis, plasma samples were collected weekly and analyzed by ELISA assay specific to human APOC3 protein.

Stereopure ASOs: improved in vivo potency, extended duration

Back of the eye



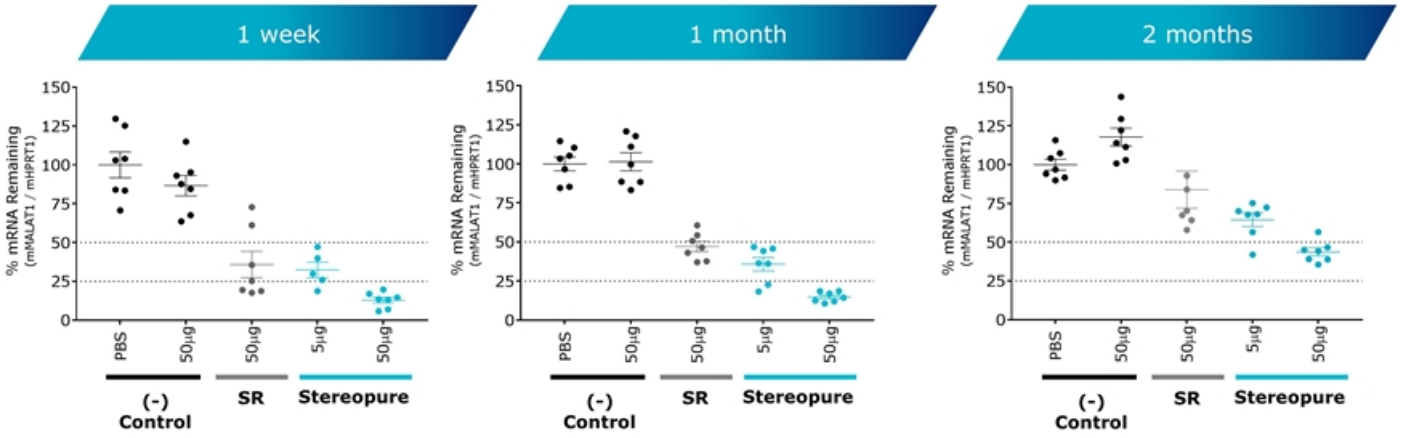
10X lower dose of stereopure oligo is more potent than stereorandom oligo

WAVE LIFE SCIENCES

Experimental description: Single intravitreal injection to mouse eye on day 1.

Stereopure ASOs: improved in vivo potency, extended duration

Front of the eye



10X lower dose of stereopure oligo is more potent than stereorandom oligo

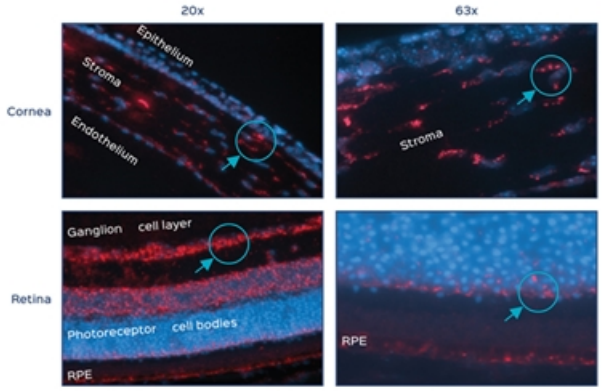
WAVE LIFE SCIENCES

Experimental description: Single intravitreal injection to mouse eye on day 1.

Distribution and target engagement

Ophthalmology

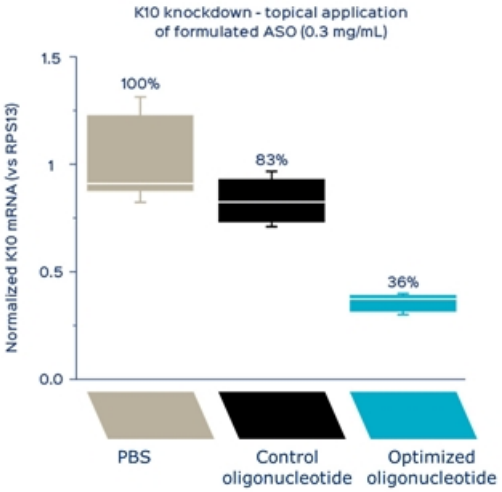
Distribution of oligonucleotide to key cellular Compartments following intravitreal injection in murine eye



Red dots = Oligonucleotides

Dermatology

Target engagement following topical administration on human skin explant model



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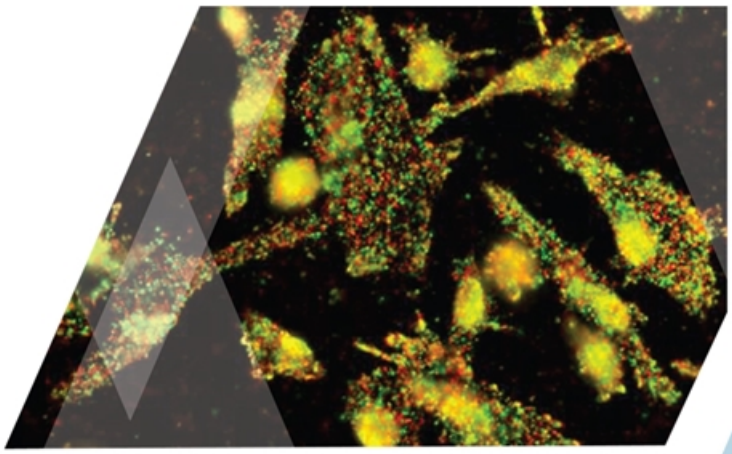
Enabling technologies: enhancing stereopure platform

READCOOR

- Collaboration leverages ReadCoor's proprietary FISSEQ (Florescent In-Situ Sequencing) platform designed to provide critical spatial data by combining next generation sequencing and three-dimensional imaging
- Developing a registry of brain cell network maps
- Advancing chemistry for targeted delivery to the brain



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Scalable nucleic acid synthesis

- Oligonucleotide synthesis capacity ranging from high throughput to large scale GMP production
- 90,000 square foot facility
- Ability to continue to meet synthesis demands of growing portfolio and increase control and visibility of product supply chain
- Comparable yield and cost-of-goods to standard stereorandom oligonucleotides
- Industry standard equipment with no biological processing required
- GMP manufacturing capacity potentially available to partners

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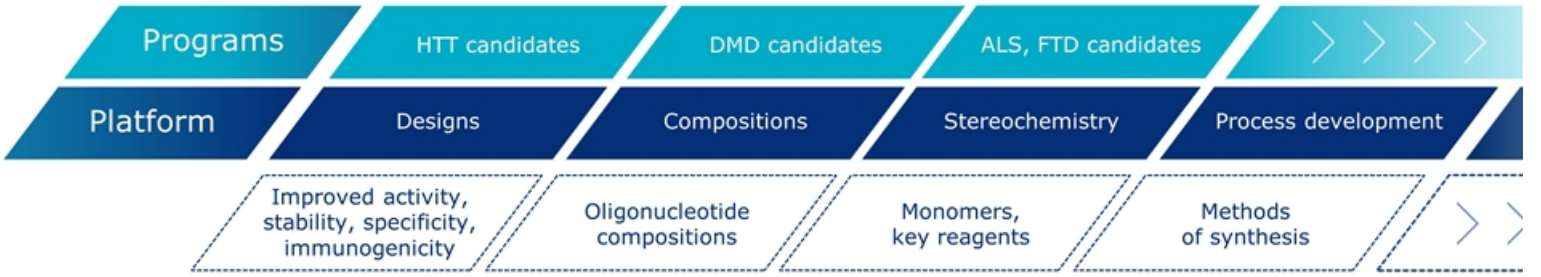
Secure patent and intellectual property position



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Wave catalysts

- **Q3 2018: data expected in DMD from Phase 1 trial for WVE-210201**
  - Initiated clinical trial in DMD (Exon 51) November 2017
  - WVE-210201 is the first stereopure oligonucleotide targeting Exon 51 with potential to be best-in-class
  - Interim dystrophin readout from planned efficacy and open label extension trials expected in 2H 2019

- **Q4 2018: clinical trials expected to initiate in ALS and FTD for WVE-3972-01**
  - WVE-3972-01 is designed to target the pathogenic allele of the C9orf72 gene
  - In vivo animal data demonstrate potent, sustained and preferential knockdown of toxic biomarkers associated with ALS and FTD

- **1H 2019: data expected in HD from Phase 1b/2a trials for WVE-120101 and WVE-120102**
  - Initiated two clinical trials in HD July 2017
  - Potential to be first two allele-specific disease-modifying therapies selectively lowering mHTT
  - Received U.S. orphan drug designation for WVE-120101 and WVE-120102

- **Q1 2019: clinical trial expected to initiate for next DMD program (Exon 53)**

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Realizing the potential of nucleic acid therapeutics