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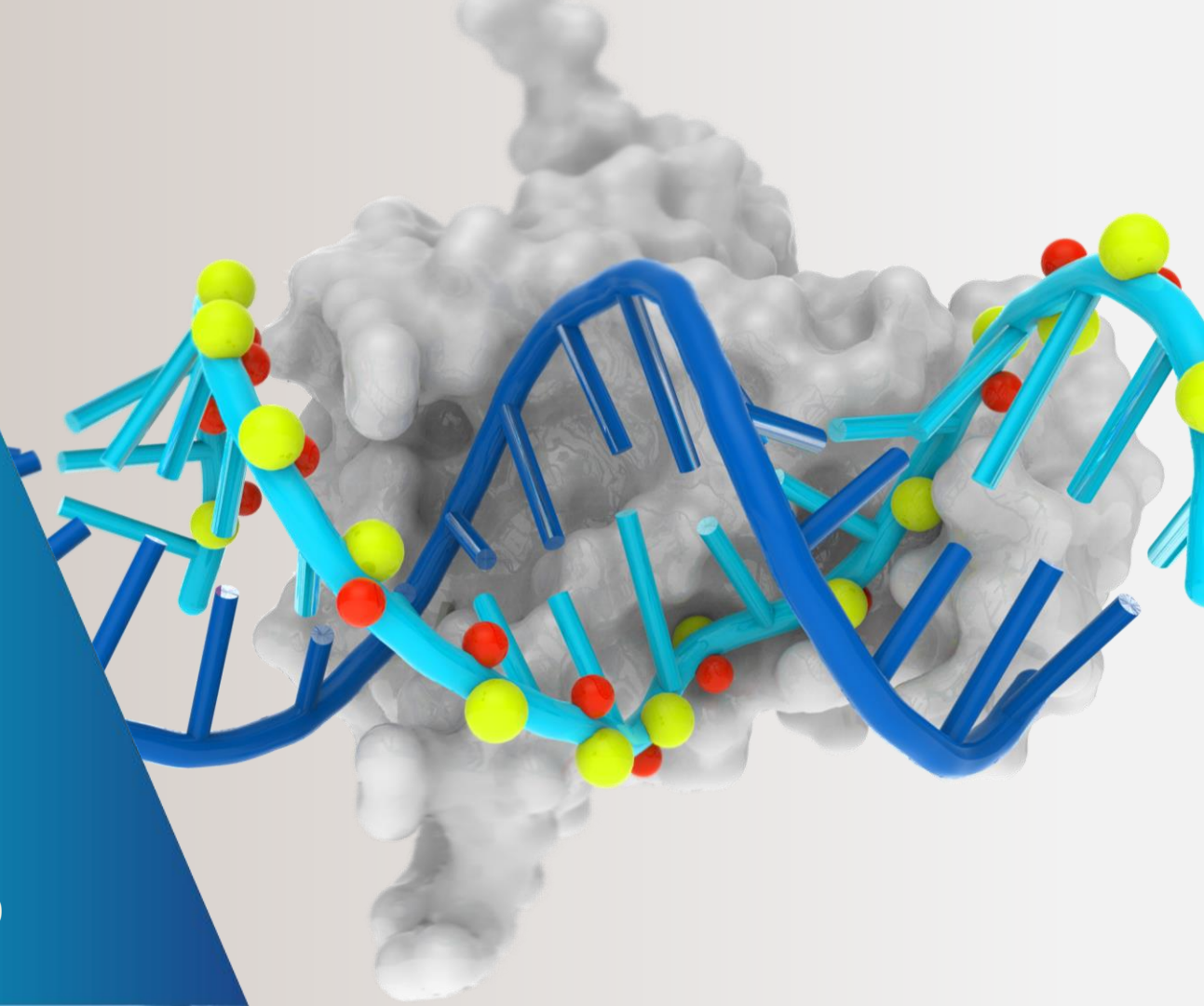
Analyst & Investor Research Webcast

August 25, 2020



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.

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Today's speakers

Paul Bolno, MD, MBA
President and CEO

Vision & Strategy

Chandra Vargeese, PhD
Chief Technology Officer

PRISM Platform Update

ADAR Editing

Kenneth Rhodes, PhD
SVP, Therapeutics Discovery

Neurology Pipeline

C9orf72 Program

Conclusion and Q&A

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Vision and Strategy

Paul Bolno, MD, MBA
President and CEO

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Wave Life Sciences

Building a fully integrated genetic medicines company

VISION

We envision a future in which the diagnosis of a genetically-defined disease leads to effective and available treatment, providing patients and their families the ability to realize a brighter future

MISSION

Apply innovative nucleic acid chemistry and deep biological insights to develop transformative medicines for millions of people living with devastating conditions

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Wave Life Sciences

Building a fully integrated genetic medicines company

Opportunity

- >6,000 genetically defined diseases
- Increases in genetic testing
- Greater understanding of genetic drivers of disease and definition at molecular level

Many diseases beyond the reach of existing treatments

Unlocking the genetic medicine opportunity

- **Evolution of PRISM**
  - Stereochemistry
  - New ADAR editing modality
  - Advances in oligonucleotide design
- **Addressing genetic mutations at RNA level**
  - Regulate dose and frequency
  - Avoid permanent off-target effects

Leveraging PRISM to derive insights from chemistry and apply them to biology

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PRISM platform designed to achieve four goals

- **Enable multiple modalities**
  Silencing, Splicing, ADAR editing
- **Ability to optimize pharmacology**
  Potency, Exposure, Durability
- **Target engagement across key tissues**
- **Scalable and cost-effective manufacturing**

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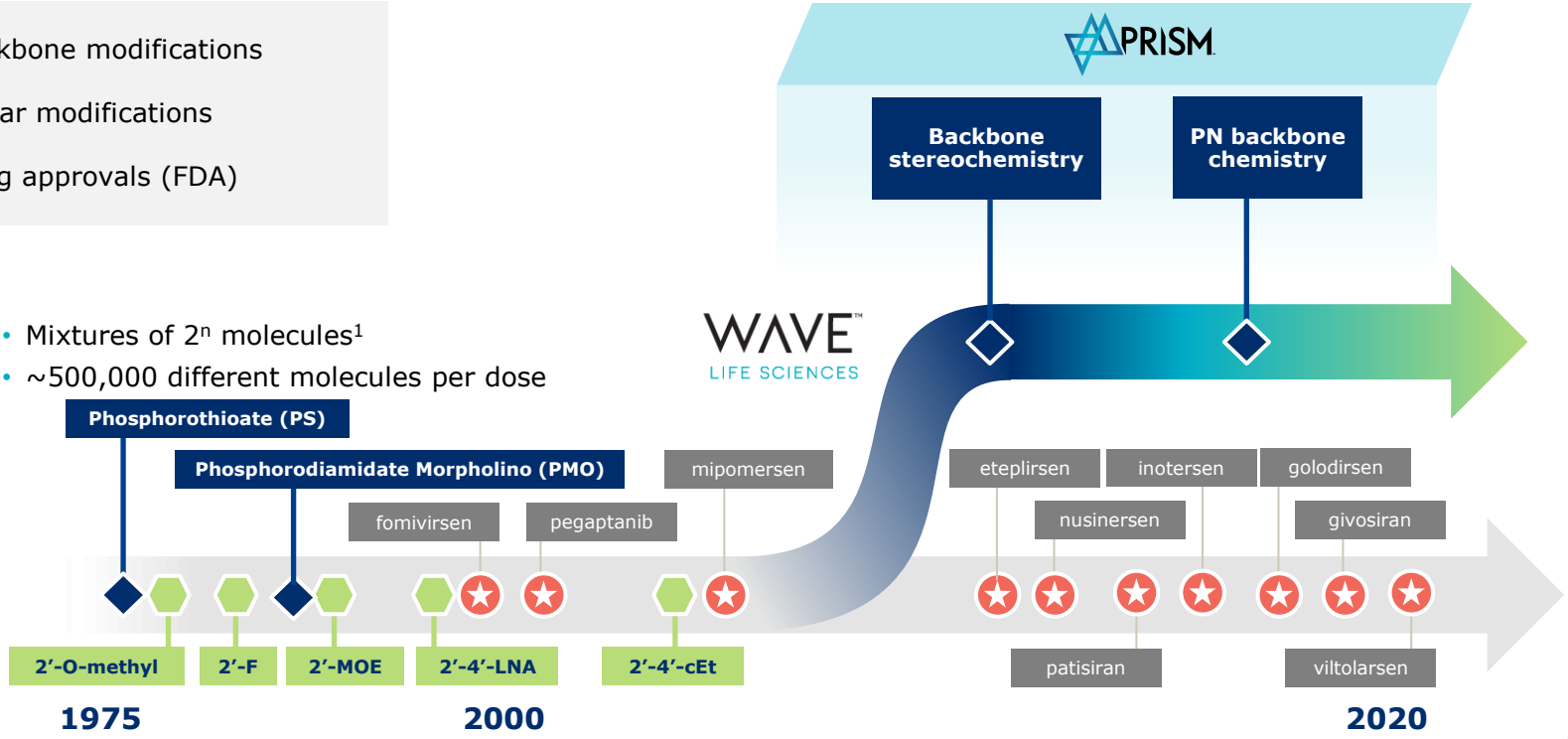
PRISM has unlocked novel and proprietary advances in oligonucleotide design

- Backbone modifications
- Sugar modifications
- Drug approvals (FDA)

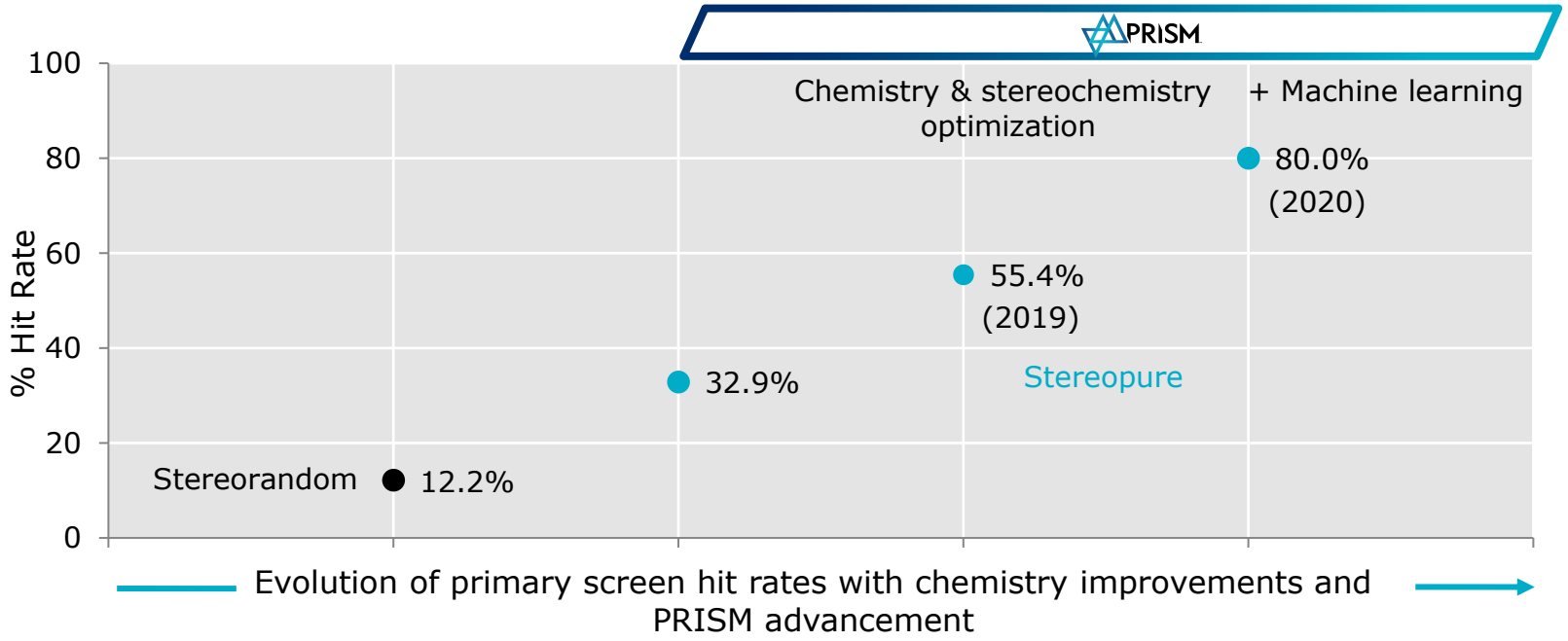
- Mixtures of 2^n molecules[1]
- ~500,000 different molecules per dose



[1]n=number of chiral centers

PRISM platform advancements

Primary screen hit rates in neurons far above industry standard hit rates



All screens used iPSC-derived neurons; Data pipeline for improved standardization. Hit rate = % of oligonucleotides with target knockdown greater than 50%. Each screen contains >100 oligonucleotides.

Today: Building a fully integrated genetic medicines company focused on neurology

Central nervous system

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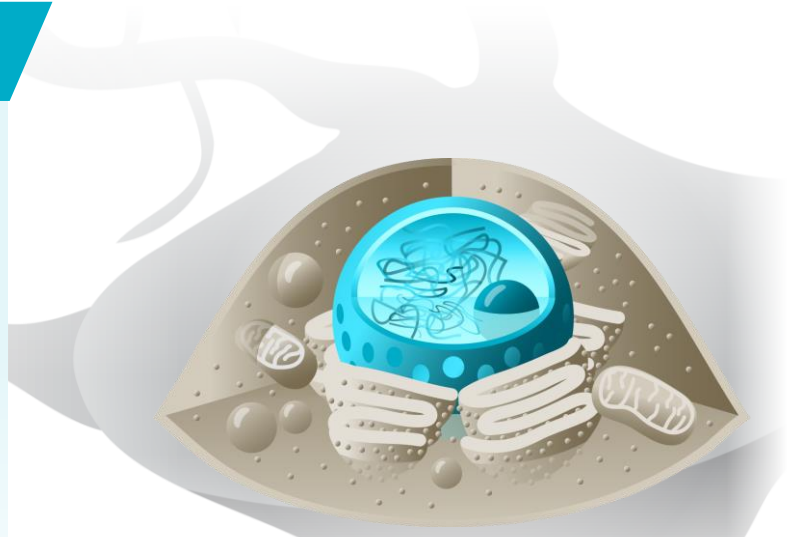
<2 years exclusivity remaining in collaboration

Committed cash: at least $60M in research support over 4 years

Potential additional cash inflows:

Category 1 programs	Category 2 programs
Six programs: HD (SNP1, SNP2, SNP3) C9-ALS, C9-FTD SCA3	**Up to six preclinical targets†** (Alzheimer's, Parkinson's, other CNS disorders)
Milestones, global 50:50 profit split	**>$1B in precommercial milestones & royalties**



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†During a four-year term, Wave and Takeda may collaborate on up to six preclinical targets at any one time.
ALS: Amyotrophic lateral sclerosis; FTD: Frontotemporal dementia; SCA3: Spinocerebellar ataxia 3

Looking ahead: Building a fully integrated genetic medicines company focused on neurology

Neurology pipeline expansion

- Employing new chemistries and modalities to expand wholly-owned neurology pipeline
- ADAR editing to access new target classes and new pathways
- PRISM enables access to larger set of potential indications than other existing platforms

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Leveraging platform discovery research to build out areas of potential new biology

Opportunities outside of neurology

- Hepatic diseases
- Ophthalmology
- Muscle diseases
- Additional therapeutic areas

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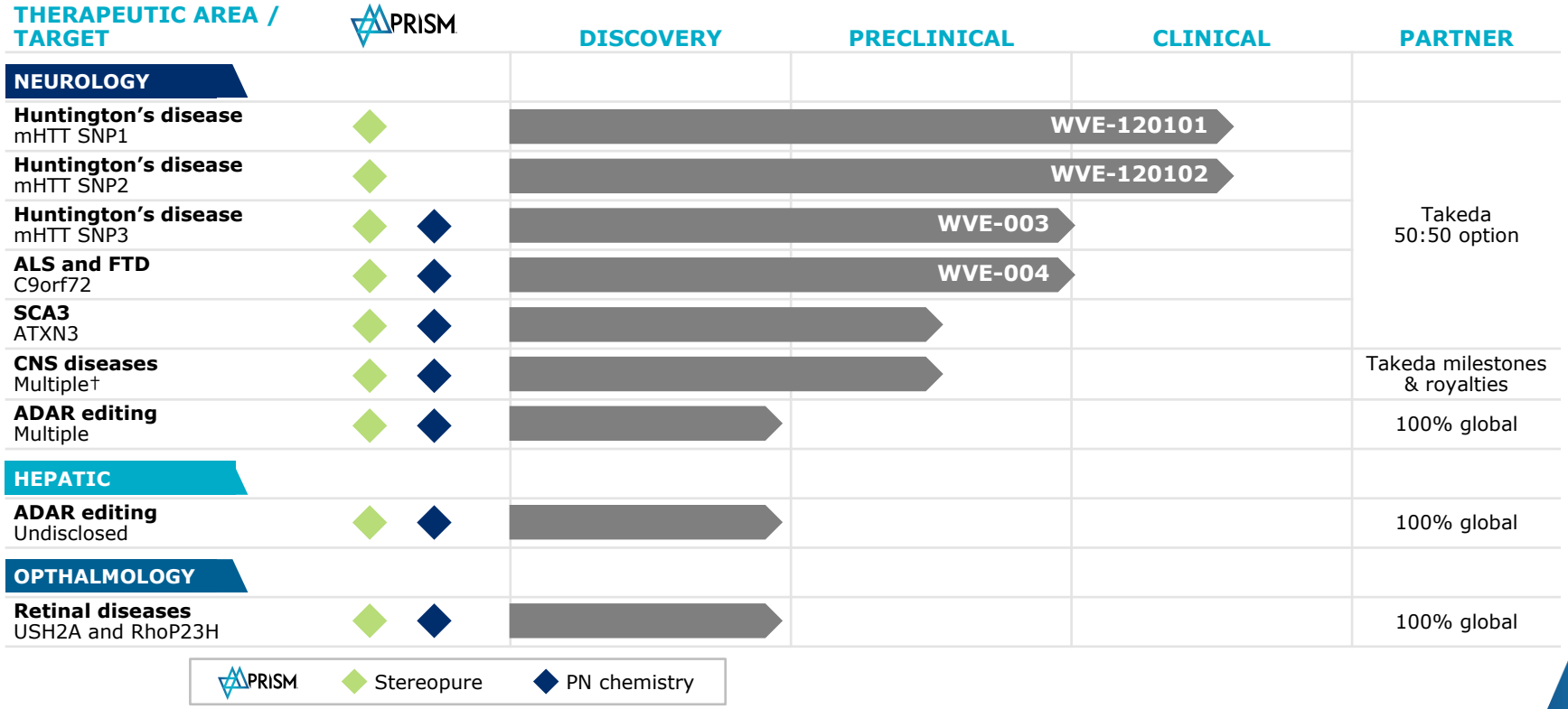
Innovative pipeline led by neurology programs



†During a four-year term, Wave and Takeda may collaborate on up to six preclinical targets at any one time.
ALS: Amyotrophic lateral sclerosis; FTD: Frontotemporal dementia; SCA3: Spinocerebellar ataxia 3 CNS: Central nervous system

Wave Life Sciences: Redefining the potential of RNA therapeutics in neurology

Well positioned to drive near-term value from PRISM

- Four global clinical neurology programs expected next year, with multiple data readouts by 2022
- Positioned to deliver multiple clinical trial applications over the next three years
- Leveraging platform to bring new neurology targets, including editing targets in CNS, to clinic
- Collaborations to unlock further value

PRISM

- Continuous learning
- Platform engine delivering new targets

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PRISM Platform Update

Chandra Vargeese, PhD
Chief Technology Officer

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PRISM platform enables rational drug design

Sequence

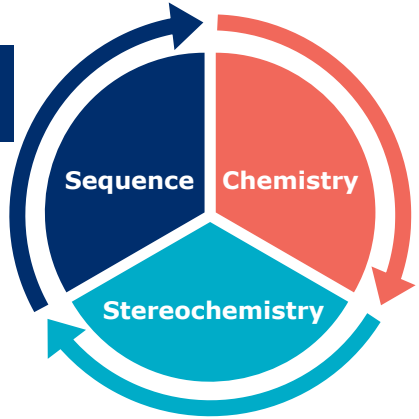
B: bases

A, T, C, mC, G, U,
other modified bases

Stereochemistry

Chiral control of
any stereocenter

5′ modifications,
backbone modifications



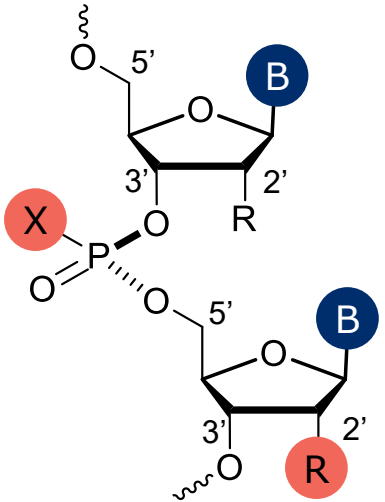
Chemistry

R: 2′ modifications

OMe, MOE, F,
other modifications

X: backbone chemistry

Phosphodiester (PO),
phosphorothioate (PS),
other backbone
modifications



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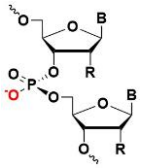
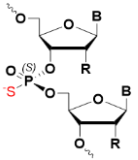
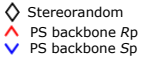
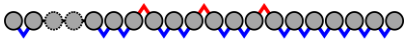
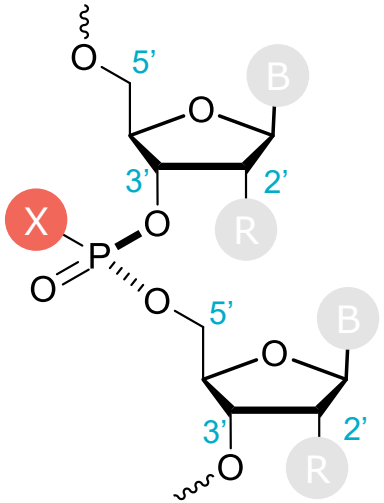
PRISM

Focused on backbone chemistry modifications amenable to all modalities

Backbone linkages

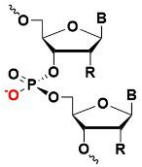
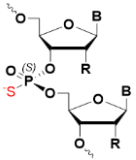
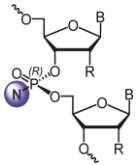
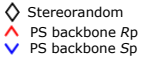
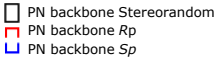
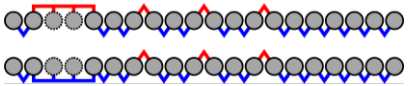
	PO	PS
Backbone modification (X)	Phosphodiester 	Phosphorothioate 
Stereochemistry	Not chiral	Chiral 
Charge	Negative	Negative
Depiction		
PRISM backbone modifications	PO/PS	

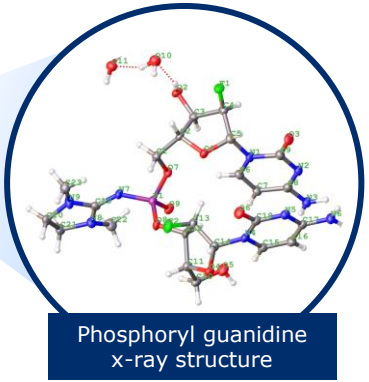


Molecule structure illustrative of backbone modification patterns

Expanding repertoire of backbone modifications with novel PN backbone chemistry

Backbone linkages

	PO	PS	PN
Backbone modification (X)	Phosphodiester 	Phosphorothioate 	Phosphoramidate diester 
Stereochemistry	Not chiral	Chiral 	Chiral 
Charge	Negative	Negative	Neutral
Depiction			
PRISM backbone modifications	PO/PS		
	PO/PS/PN		



Phosphoryl guanidine x-ray structure

Molecule structure illustrative of backbone modification patterns

Across many modalities, PN chemistry enhances potency, exposure, and durability

Modality		Pharmacology	
Silencing	• Efficient engagement of RNase H or Ago2	Potency	• Target knockdown, splicing or editing
Splicing	• Efficient uptake in the cell nucleus	Exposure	• In the right tissues, cells and cellular compartments
Editing	• Efficient engagement of ADAR	Durability	• Enabling infrequent administration

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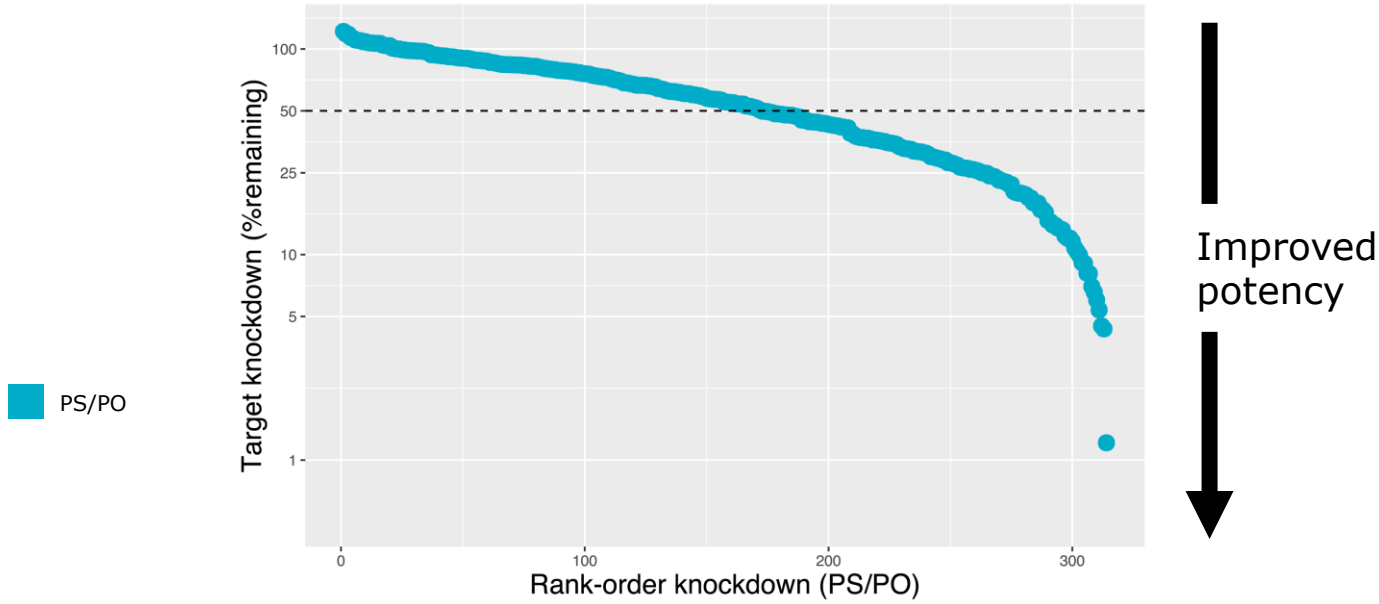
PRISM

Screen of stereopure PS/PO molecules ranked by potency

Target knockdown *in vitro* in neurons

In vitro knockdown of PS/PO containing compounds

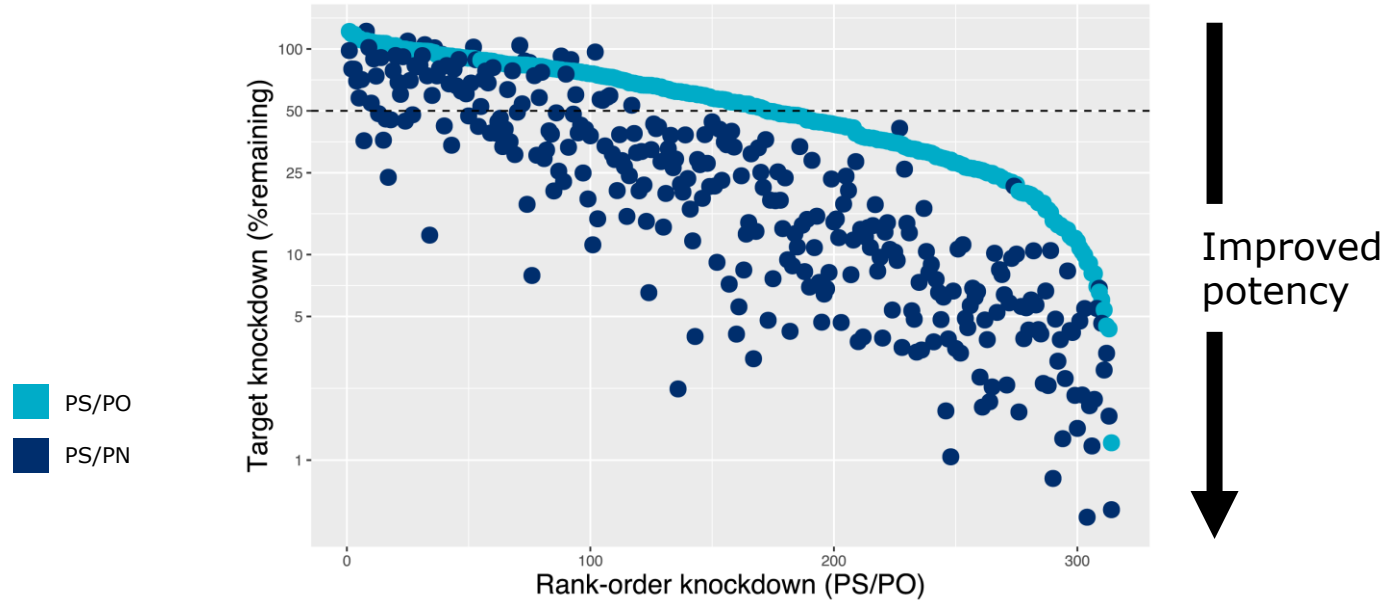


Experiment was performed in iPSC-derived neurons *in vitro*; target mRNA levels were monitored using qPCR against a control gene (HPRT1) using a linear model equivalent of the ΔΔCt method (referred to as "delta-delta Ct")

Rational design using PN chemistry backbone modification increases potency on average

Target knockdown *in vitro* in neurons

In vitro knockdown of PS/PO containing compounds compared to PS/PN compounds

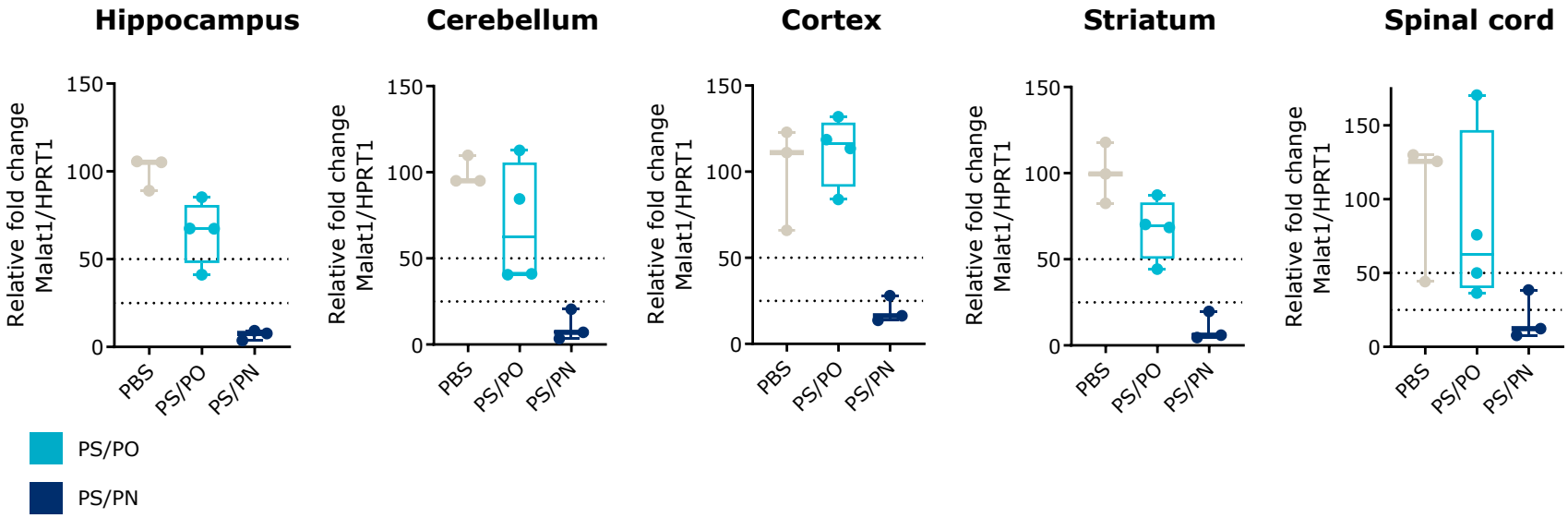


Experiment was performed in iPSC-derived neurons *in vitro*; target mRNA levels were monitored using qPCR against a control gene (HPRT1) using a linear model equivalent of the ΔΔCt method (referred to as "delta-delta Ct")

PN chemistry increases durability across CNS tissues

Silencing | Potency
Splicing | Exposure
Editing | Durability

Malat1 knockdown at 10 weeks in CNS (100 µg)

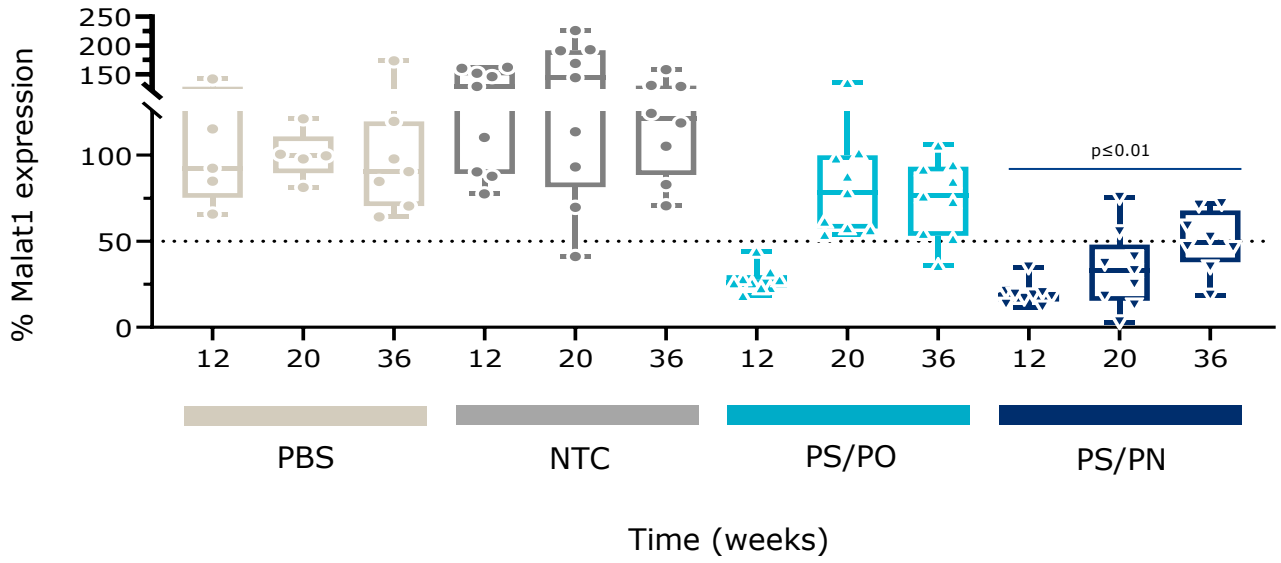


Mice received a single 100 ug ICV injection (n=3 per group). Relative fold-change in MALAT1 expression is shown for the indicated tissues 10-weeks post-dose. MALAT1 expression levels are normalized to Hprt1. PBS, phosphate buffered saline

Durable Malat1 knockdown through 9 months with PN chemistry

Silencing | Potency
Splicing | Exposure
Editing | Durability

~50% Malat1 knockdown at 36 weeks in the posterior of the eye

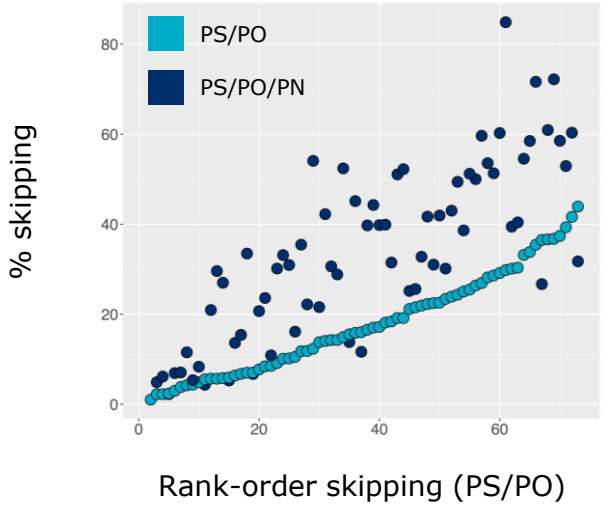


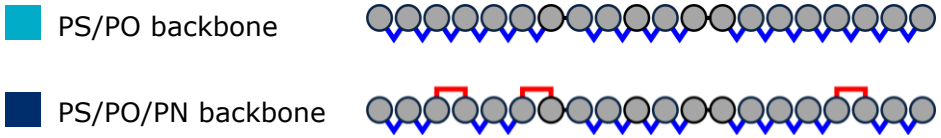
Compound or PBS (1 x 50 ug IVT) was delivered to C57BL6 mice. Relative percentage of Malat1 RNA in the posterior of the eye (retina, choroid, sclera) to PBS-treated mice is shown at 12, 20 and 36 weeks post-single injection. PBS = phosphate buffered saline; NTC= chemistry matched non-targeting control

Improved exon skipping with PN chemistry

Exon skipping plotted for compounds with same sequence

In vitro skipping efficiency of PS/PO containing compounds compared to PS/PO/PN compounds





- Exon skipping compounds have same sequence
- PS / PO / PN oligonucleotides have three PN backbone modifications

PS *Rp* | PS *Sp* | PO | PN *Rp*

DMD patient-derived myoblasts treated with PS/PO or PS/PO/PN stereopure oligonucleotide under free-uptake conditions. Exon-skipping efficiency evaluated by qPCR.

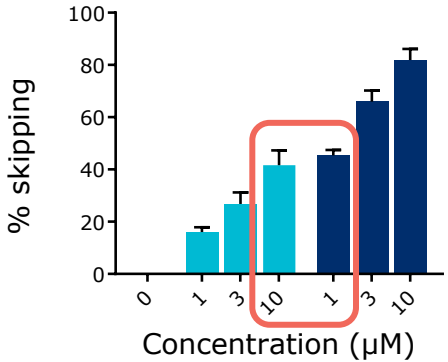
PN chemistry improves potency and increases cellular uptake in myoblasts

Silencing | Potency
Splicing | Exposure
Editing | Durability

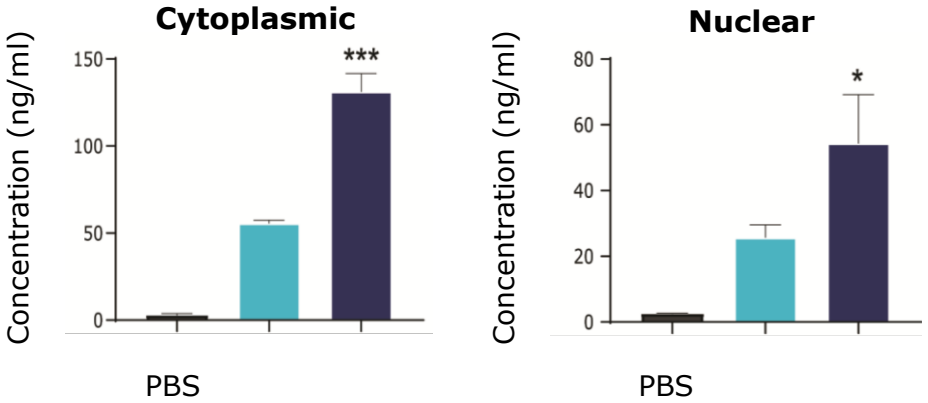
PS/PO backbone

PS/PO/PN backbone

DMD mRNA skipping (Exon 23, H2K mouse myoblasts)



Cellular uptake (H2K mouse myoblasts)



Left: Cultured H2K myoblasts treated with increasing concentrations of PS/PO or PS/PO/PN stereopure oligonucleotide under free-uptake conditions. Skipping efficiency evaluated by TaqMan assay. Right: Cultured H2K cells treated with 0.5 uM oligonucleotide. Uptake quantified in cytoplasmic and nuclear extracts by hybridization ELISA. **: P ≤ 0.01, ***: P ≤ 0.001

PS *Rp* | PS *Sp* | PO | PN *Rp*

DKO model to assess PN chemistry on survival

MDX mouse

	Protein	Pathology
✓	Utrophin	Mild No decrease in survival
×	Dystrophin	

Utrophin knockout

	Protein	Pathology
×	Utrophin	None
✓	Dystrophin	

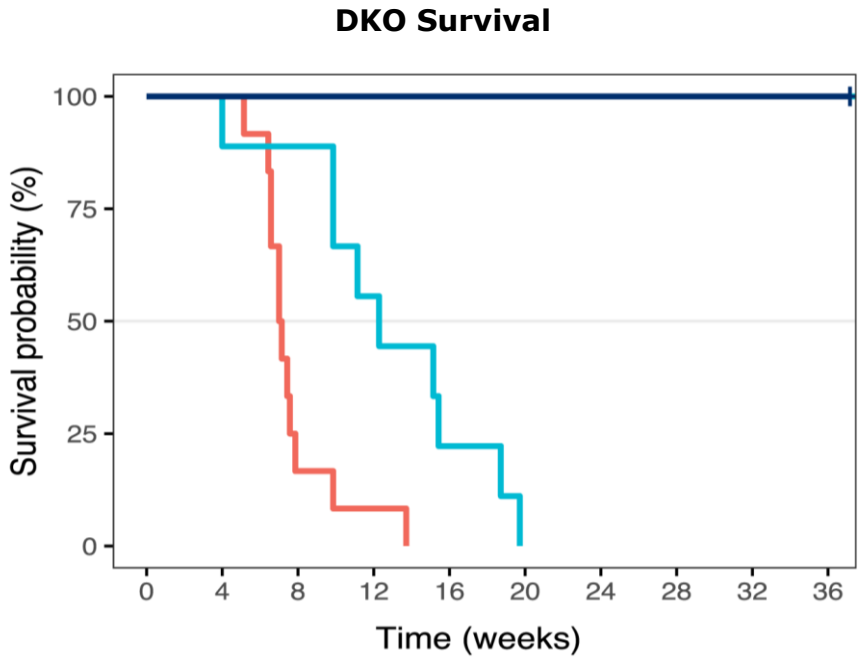
Double knockout mouse (DKO)

	Protein	Pathology
×	Utrophin	Severe muscular dystrophy Premature death
×	Dystrophin	

DKO model generation and in vivo studies were performed by our collaborator Professor Matthew Wood at the University of Oxford; DKO PS/PO/PN and DKO PS/PO oligonucleotides have same sequence

Step-change in survival observed in DKO model using PN chemistry

Silencing | Potency
Splicing | Exposure
Editing | Durability



Study completion: DKO PS/PO/PN mice sacrificed for further analyses

PS/PO/PN, QW 150 mpk weekly

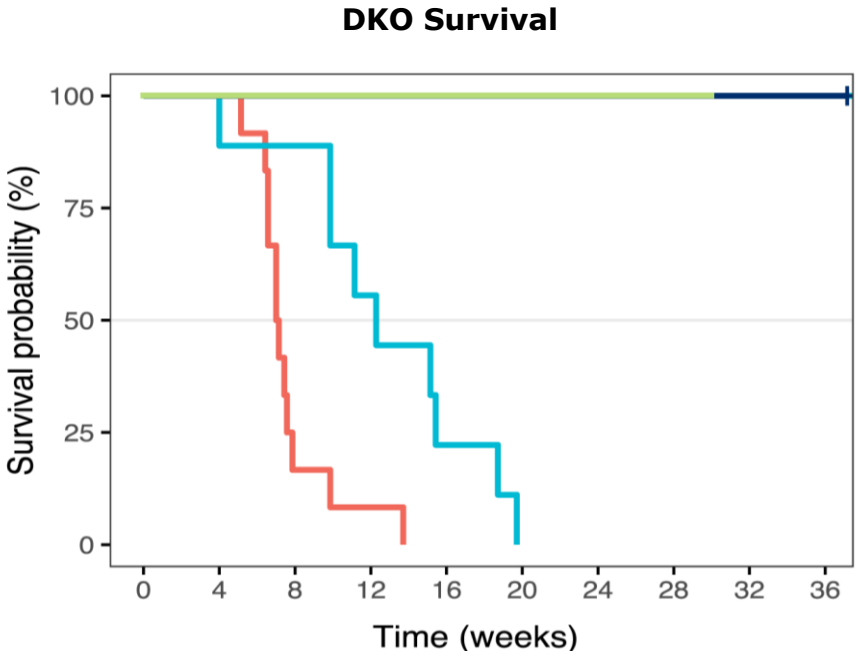
PS/PO, QW 150 mpk weekly

PBS

Mdx/utr-/- mice received weekly subQ 150 mpk dose of PS/PO or PS/PO/PN stereopure oligonucleotide beginning at postnatal day 10. Age-matched *mdx/utr-/-* littermates were treated with PBS, and *mdx* mice were not treated. Mice with severe disease were euthanized. DKO: PS/PO/PN n=8, PS/PO n=9, PBS n=12

Similar survival trend observed with 75% less total dose

Silencing | Potency
Splicing | Exposure
Editing | Durability



PS/PO/PN, Q2W 75 mpk bi-weekly*

PS/PO/PN, QW 150 mpk weekly

PS/PO, QW 150 mpk weekly

PBS

*Ongoing study at (50%) reduced dose and frequency (bi-weekly vs. weekly)

Mdx/utr-/- mice received weekly subQ 150 mpk dose of PS/PO or PS/PO/PN stereopure oligonucleotide beginning at postnatal day 10. Age-matched *mdx/utr-/-* littermates were treated with PBS, and *mdx* mice were not treated. Mice with severe disease were euthanized. DKO: PS/PO/PN 75 mpk n=9; PS/PO/PN 150 mpk n=8, PS/PO n=9, PBS n=12

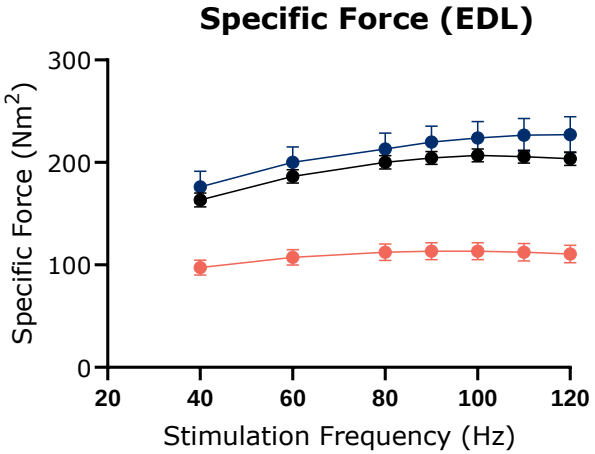
Restoration of wild-type muscle function using PS/PO/PN compound

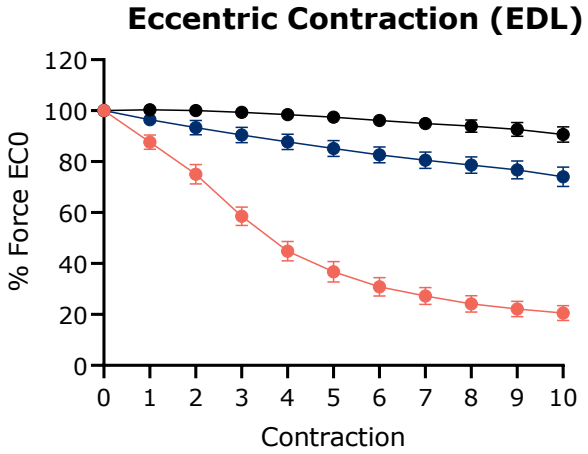
Silencing | Potency
Splicing | Exposure
Editing | Durability

Wild-type (6 week old)

DKO / PBS (6 week old)

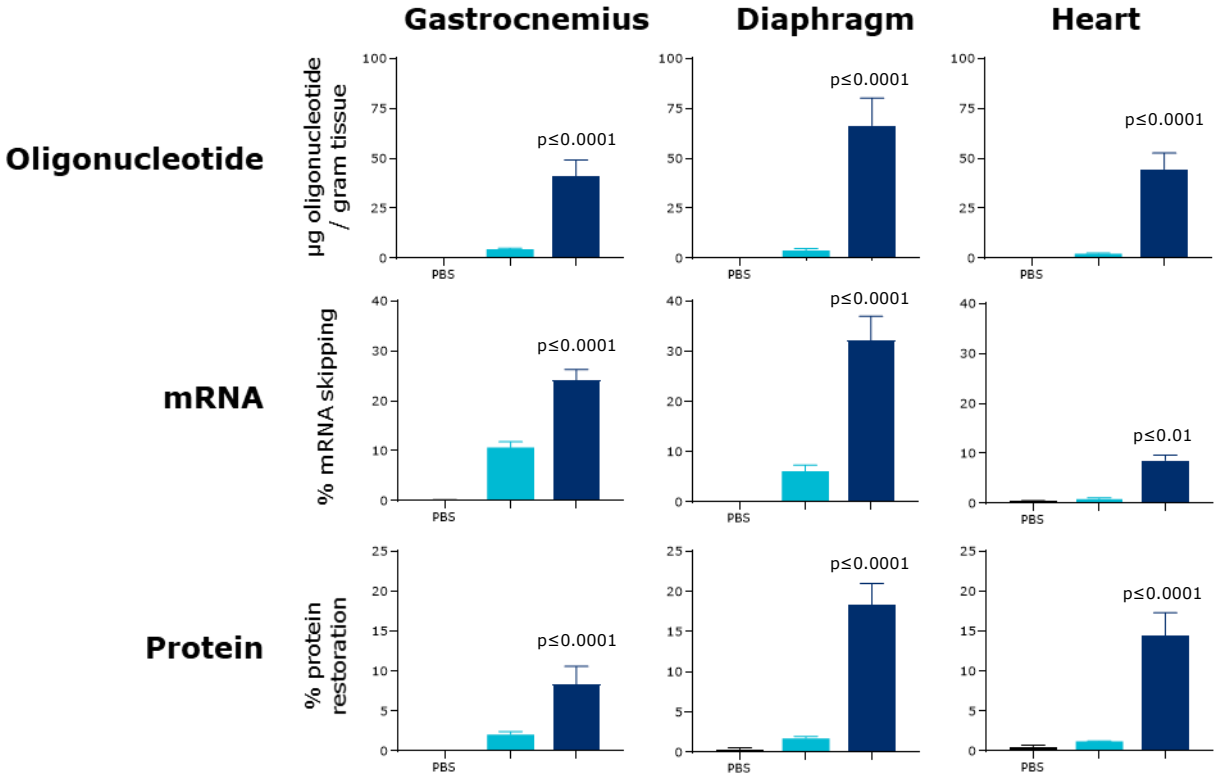
DKO PS/PO/PN, QW 150mpk (38-41 week old)





Mdx/utr-/- mice received weekly subQ 150 mpk dose of PS/PO/PN stereopure oligonucleotide beginning at postnatal day 10. Age-matched *mdx/utr-/-* littermates were treated with PBS, and *wild-type C57BL10* mice were not treated. Electrophysiology to measure specific force and eccentric contraction performed at Oxford University based on Goyenvalle et al., 2010 Mol Therapy 18(1), 198-205.

PN chemistry improves exposure and target engagement in key tissues

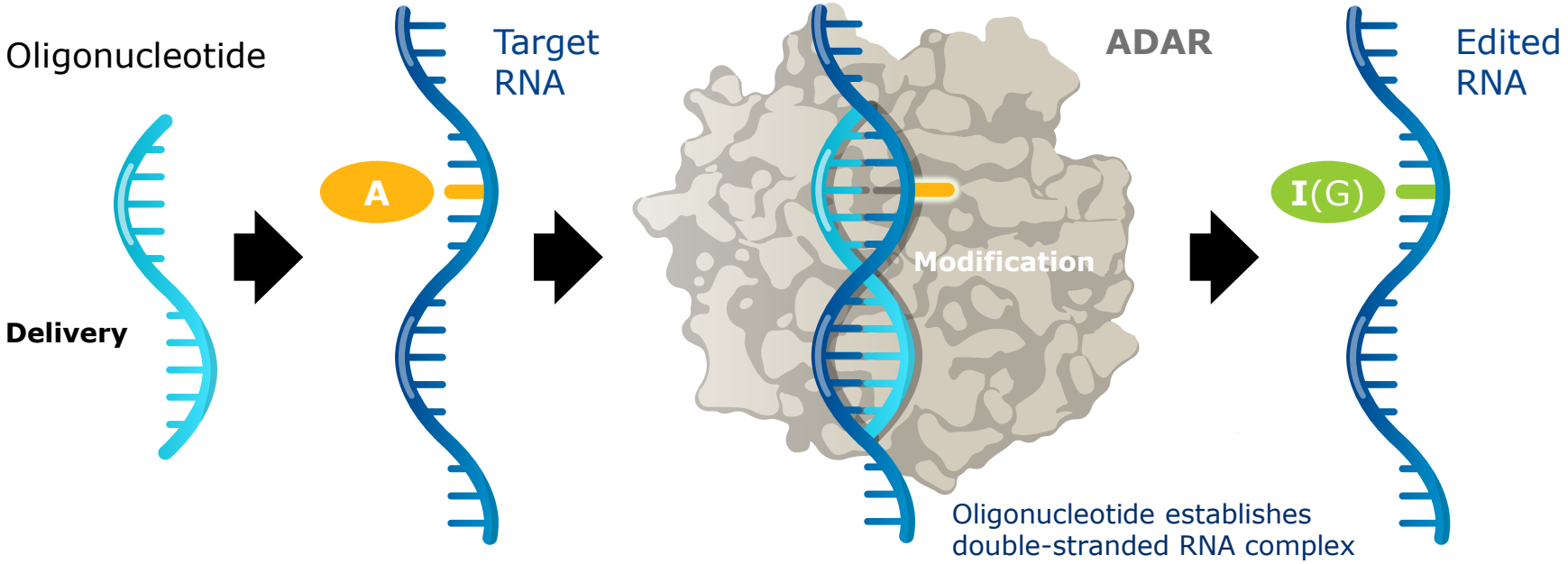


PS/PO

PS/PO/PN

6x weekly 75 mg/kg subcutaneous doses; Sample collected 2 days after last dose

PRISM platform has unlocked ADAR editing



- **A**-to-**I** editing is one of most common post-transcriptional modifications
- ADAR is ubiquitously expressed across tissues, including liver and CNS

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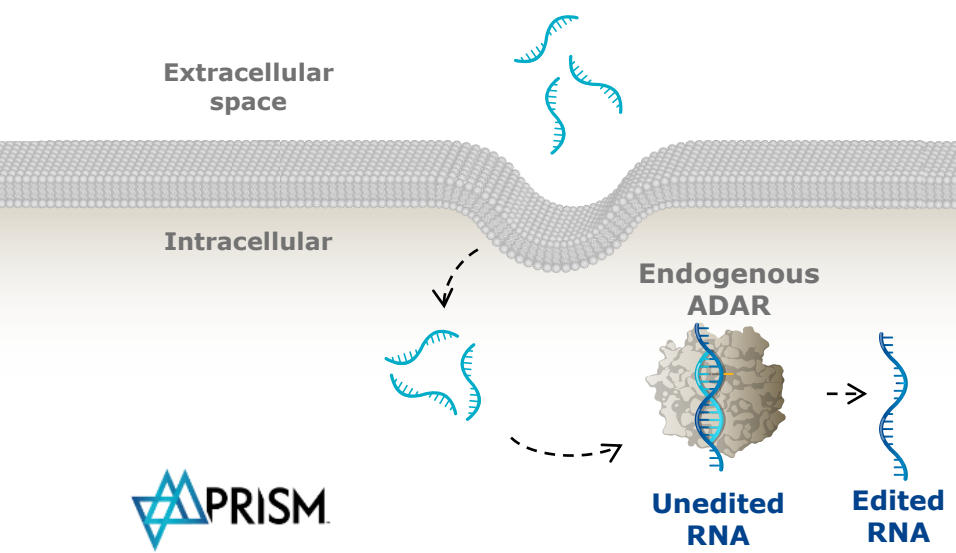
Nishikura, K. A-to-I editing of coding and non-coding RNAs by ADARs. Nat. Rev. Mol. Cell Biol. 2016; Picardi, E. *et al.* Profiling RNA editing in human tissues: towards the inosinome Atlas. *Scientific reports* **5**, 14941, doi:10.1038/srep14941 (2015).

PRISM enables practical approach to RNA editing without need for viruses or exogenous protein

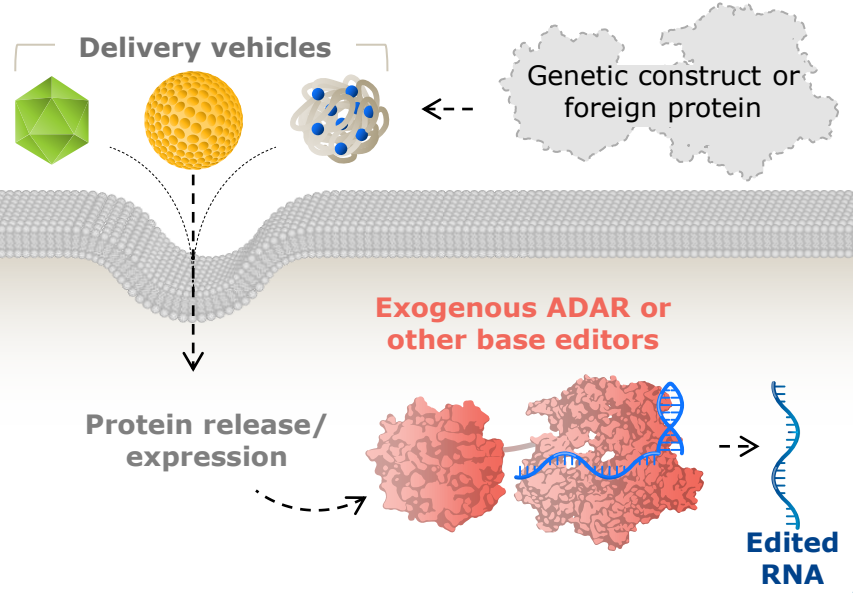
Wave ADAR-editing Oligonucleotides



PRISM

- ✓No delivery vehicle required
- ✓No exogenous proteins necessary
- ✓Potential for reduced off-target effects

Alternative Base-Editing Systems



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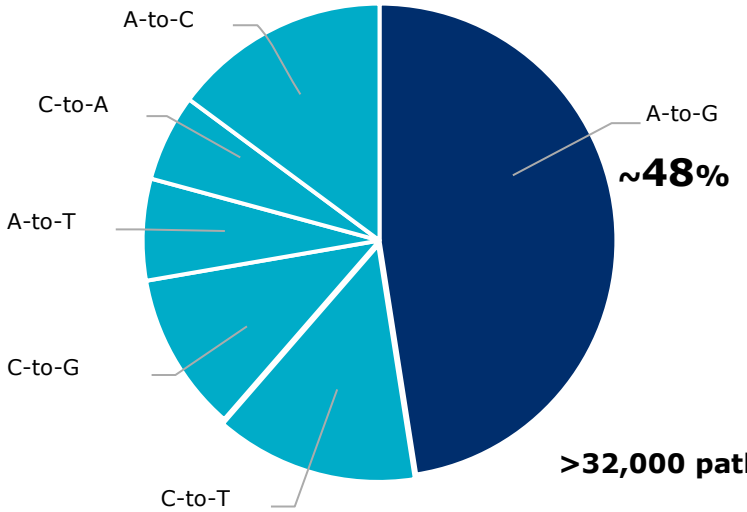
ADAR amenable diseases represent a sizeable opportunity

Pathogenic human SNPs by base pair corrections



- Nearly half of known human genetic pathogenic SNPs are G-to-A mutations
- Tens of thousands of potential disease variants A-to-I(G) editing could target[1]

>32,000 pathogenic human SNPs[2]

SNP: single nucleotide polymorphism A: Adenosine I: Inosine G: Guanosine
[1]ClinVar database [2]Gaudeli NM et al. *Nature* (2017).

RNA editing opens many new therapeutic applications

Restore protein function

- Fix nonsense and missense mutations that cannot be splice-corrected
- Remove stop mutations
- Prevent protein misfolding and aggregation

Examples:

Recessive or dominant genetically defined diseases

Modify protein function

- Alter protein processing (e.g. protease cleavage sites)
- Protein-protein interactions domains
- Modulate signaling pathways

Examples:

Ion channel permeability

Protein upregulation

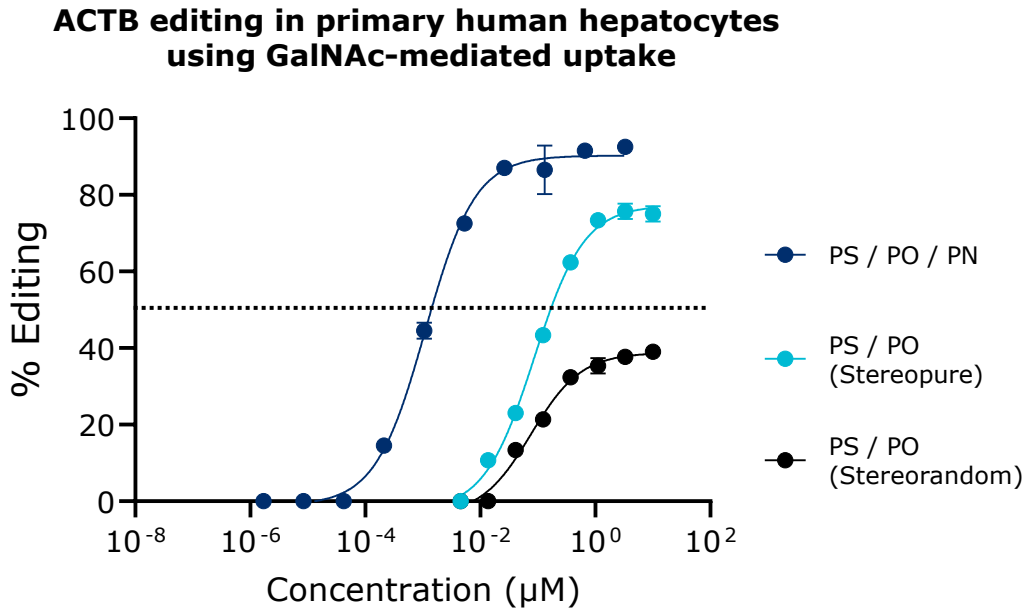
- miRNA target site modification
- Modifying upstream ORFs
- Modification of ubiquitination sites

Examples:

Haploinsufficient diseases

PN chemistry improves editing efficiency

PN backbone modification increased both potency and editing efficiency *in vitro*

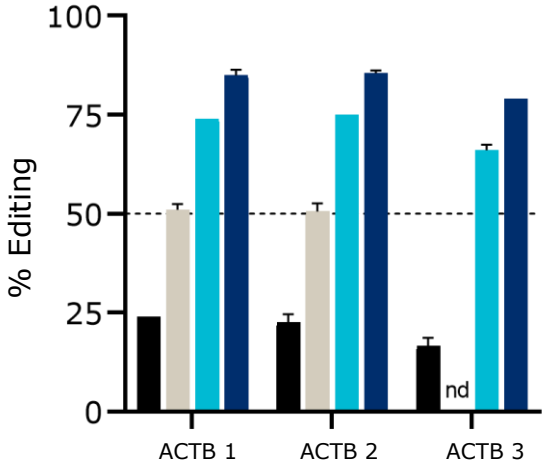


Data from independent experiments; Total RNA was harvested, reverse transcribed to generate cDNA, and the editing target site was amplified by PCR and quantified by Sanger sequencing

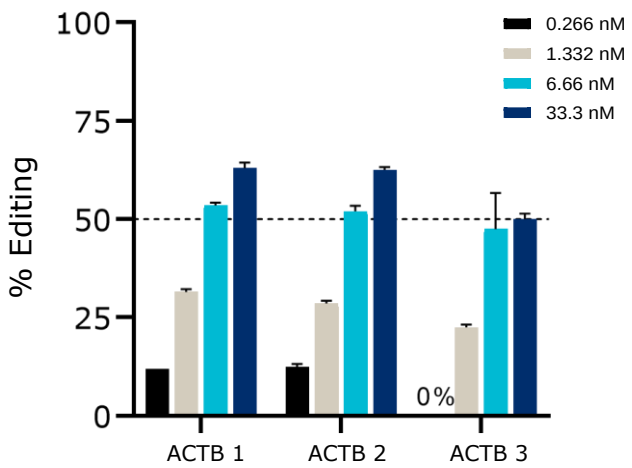
Significant ADAR editing demonstrated *in vitro* in NHP and primary human hepatocytes

ACTB GalNAc-conjugated oligonucleotides with stereopure PN chemistry modification

In vitro dose-response human hepatocytes



In vitro dose-response NHP hepatocytes



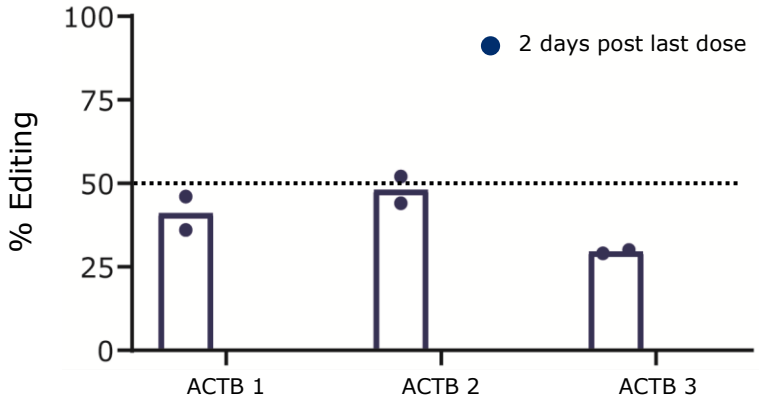
NHP: non-human primate; ACTB: Beta-actin; nd= not determined
Total RNA was harvested, reverse transcribed to generate cDNA, and the editing target site was amplified by PCR.

Efficient ADAR editing translated *in vivo* in non-human primate study

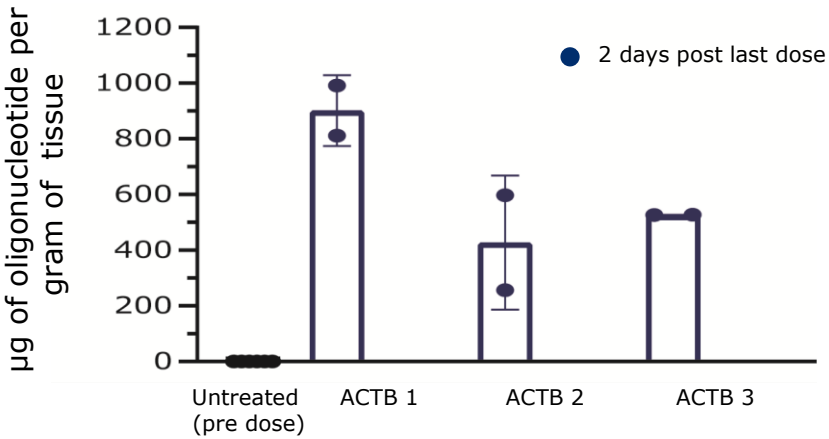
Silencing | Potency
Splicing | Exposure
Editing | Durability

Up to 50% editing efficiency observed at Day 7, 2 days post last dose

In vivo editing in NHP following subcutaneous administration



Oligonucleotide quantification in NHP following subcutaneous administration



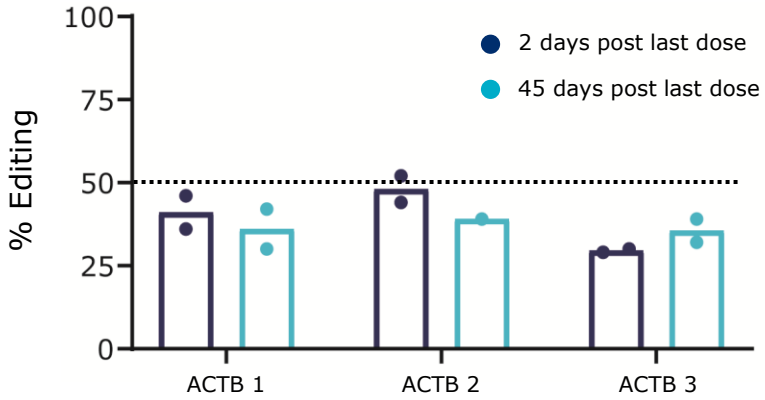
NHP: non-human primate; ACTB: Beta-actin; Left: 5mg/kg SC: Day 1,2,3,4,5; Liver Biopsy for mRNA (ACTB Editing) & eASO Exposure: Day 7

Sustained editing *in vivo* in non-human primates after 45 days

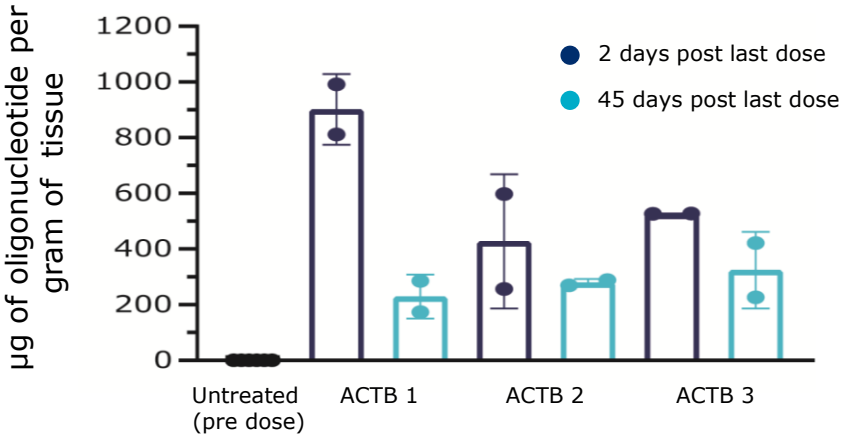
Silencing | Potency
Splicing | Exposure
Editing | Durability

Substantial and durable editing out to at least Day 50, 45 days post last dose

In vivo editing in NHP following subcutaneous administration



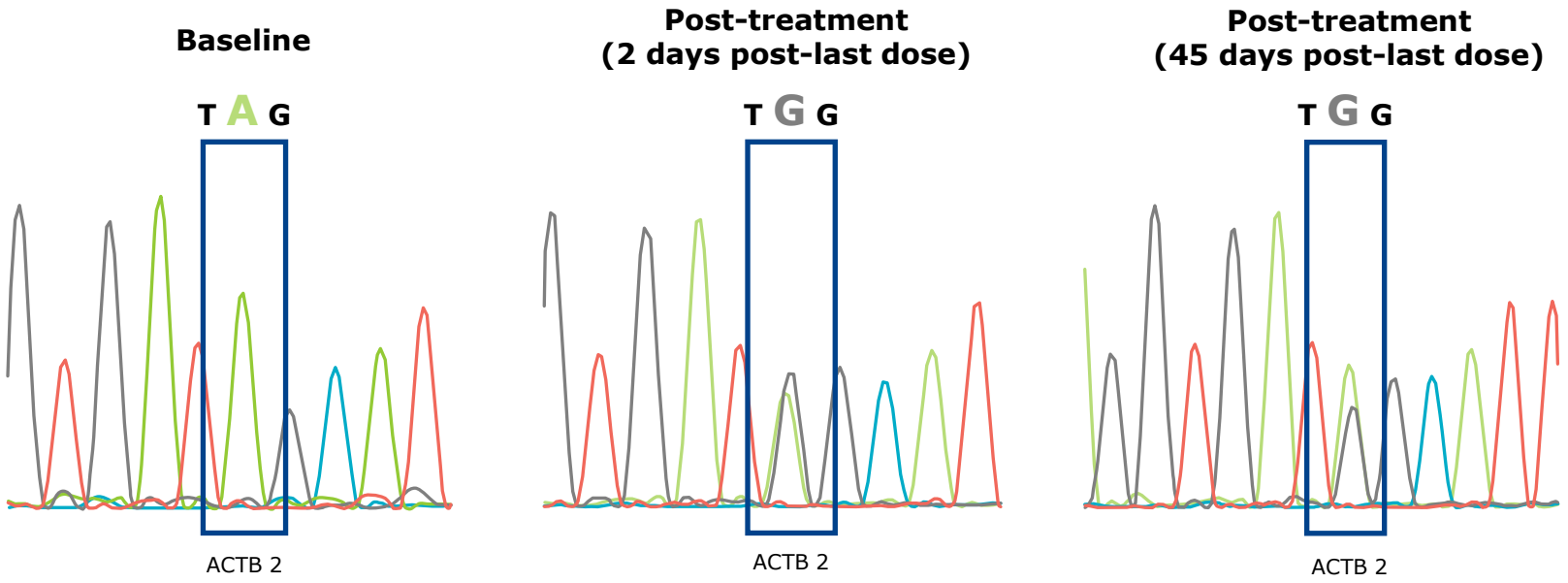
Oligonucleotide quantification in NHP following subcutaneous administration



NHP: non-human primate; ACTB: Beta-actin; Left: 5mg/kg SC: Day 1,2,3,4,5; Liver Biopsy for mRNA (ACTB Editing) & eASO Exposure: Day 7

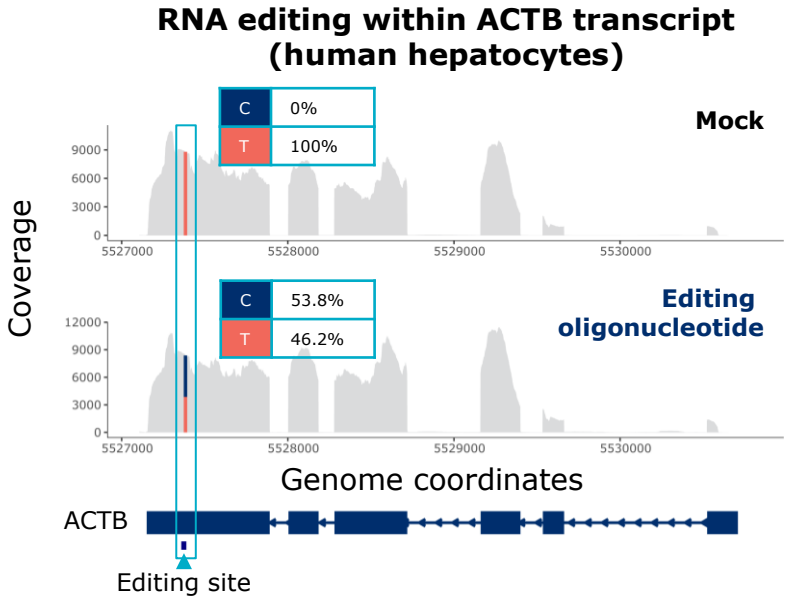
Sustained editing *in vivo* in non-human primates after 45 days

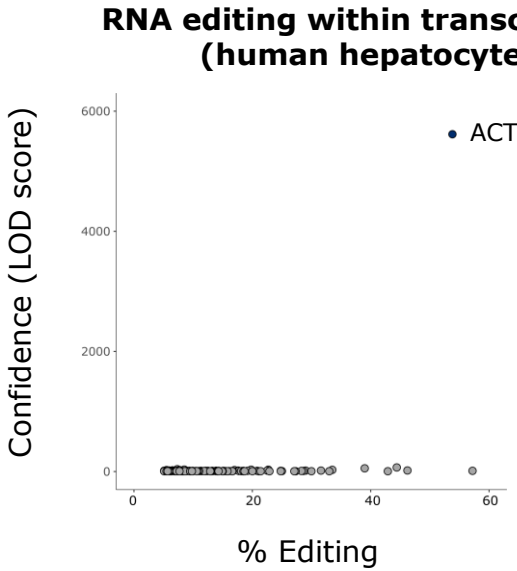
Efficient and potent editing of ACTB demonstrated with Sanger sequencing



% Editing quantified from Sanger sequencing using EditR program.

ADAR editing is highly specific

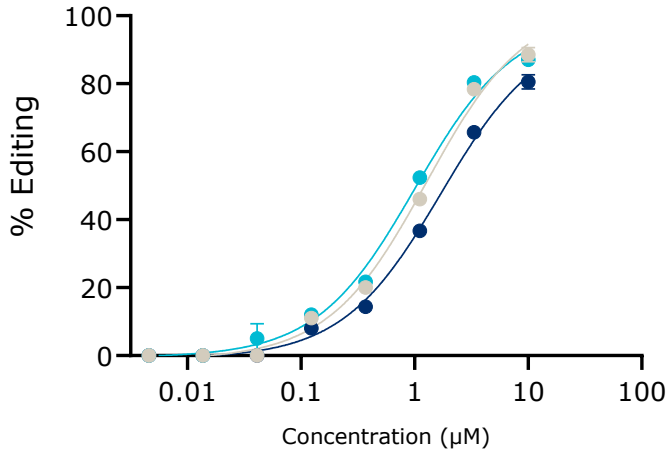




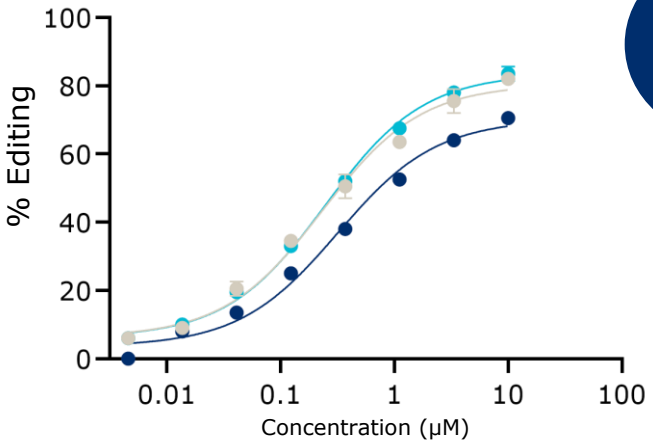
Human hepatocytes were dosed with 1um oligonucleotide, 48 hours later RNA was collected and sent for RNA sequencing. RNAseq conducted using strand-specific libraries to quantify on-target ACTB editing and off-target editing in primary human hepatocytes; plotted circles represent sites with LOD>3

Efficient and potent editing observed in neurons and astrocytes

ACTB editing in iCell Neurons



ACTB editing in human iCell Astrocytes



EC50: ~200-250nM

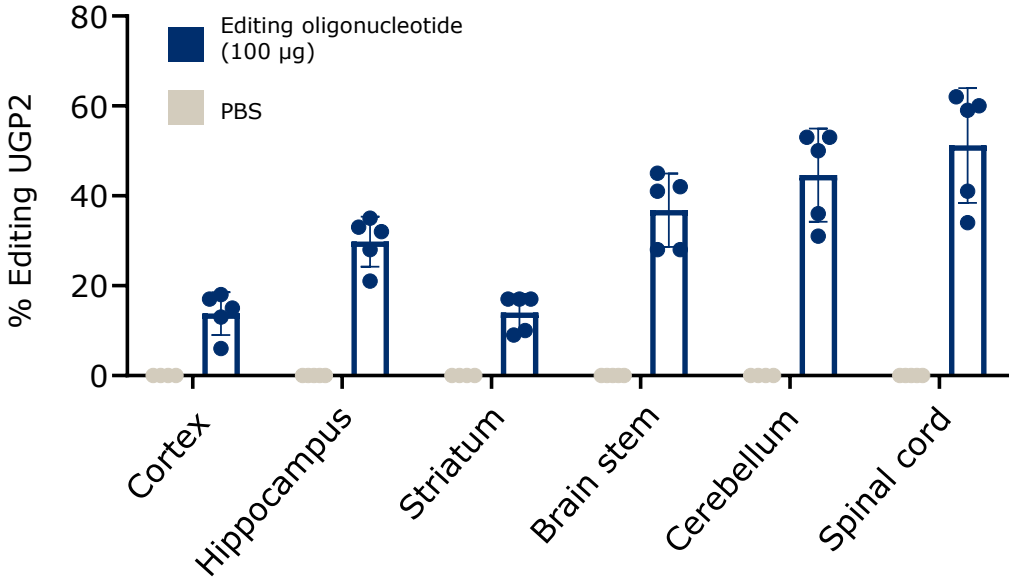
Compound 1 (PS / PN)
Compound 2 (PS / PN)
Compound 3 (PS / PN)

Gymnotic uptake; Total RNA was harvested, reverse transcribed to generate cDNA, and the editing target site was amplified by PCR and quantified by Sanger sequencing

Opening the door to ADAR editing in CNS

First *in vivo* study in proprietary transgenic model yields efficient editing across all tissues

In vivo CNS editing in proprietary hADAR transgenic mouse (1 week)



hADAR: human ADAR; UGP2: Glucose Pyrophosphorylase 2; CNS: central nervous system; Editing observed across all tested tissues of human-ADAR-transgenic mice by ICV injection. 5 mice in each group were injected with PBS or a single 100uG dose on day 0. Animals were necropsied on day 7. RNA was harvested and editing measured by Sanger sequencing.

Continued evolution of PRISM platform

Sustained investment has yielded novel modality and pharmacology advances

- PN chemistry is a novel backbone chemistry modification
  - Preclinical data demonstrates PN chemistry can enhance potency, durability and exposure across three modalities (silencing, splicing, editing)

- Platform innovations have unlocked ADAR editing modality
  - Efficient and durable editing demonstrated *in vivo* in NHPs
  - Expect to announce first ADAR editing program in a hepatic indication in 2020

- Moving ADAR editing quickly into neurology
  - Editing demonstrated in neurons and astrocytes *in vitro* and across CNS tissue types *in vivo* in first transgenic human ADAR mouse study
  - Ongoing work to unlock new neurology targets with ADAR editing

Neurology Pipeline & C9orf72 Program

Kenneth Rhodes, PhD
SVP, Therapeutics Discovery

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Focus on neurological diseases

- Neurological diseases represent one of the greatest medical challenges of our time
- PRISM can deliver oligonucleotide drug candidates that directly address the genetic drivers of neurologic diseases
- PRISM-derived oligonucleotides access neurons and glia without need for transfection, encapsulation or other modifications
- The range of modalities offered by PRISM (silencing, splicing and ADAR editing), unlocks therapeutic opportunities in a broad range of neurological diseases

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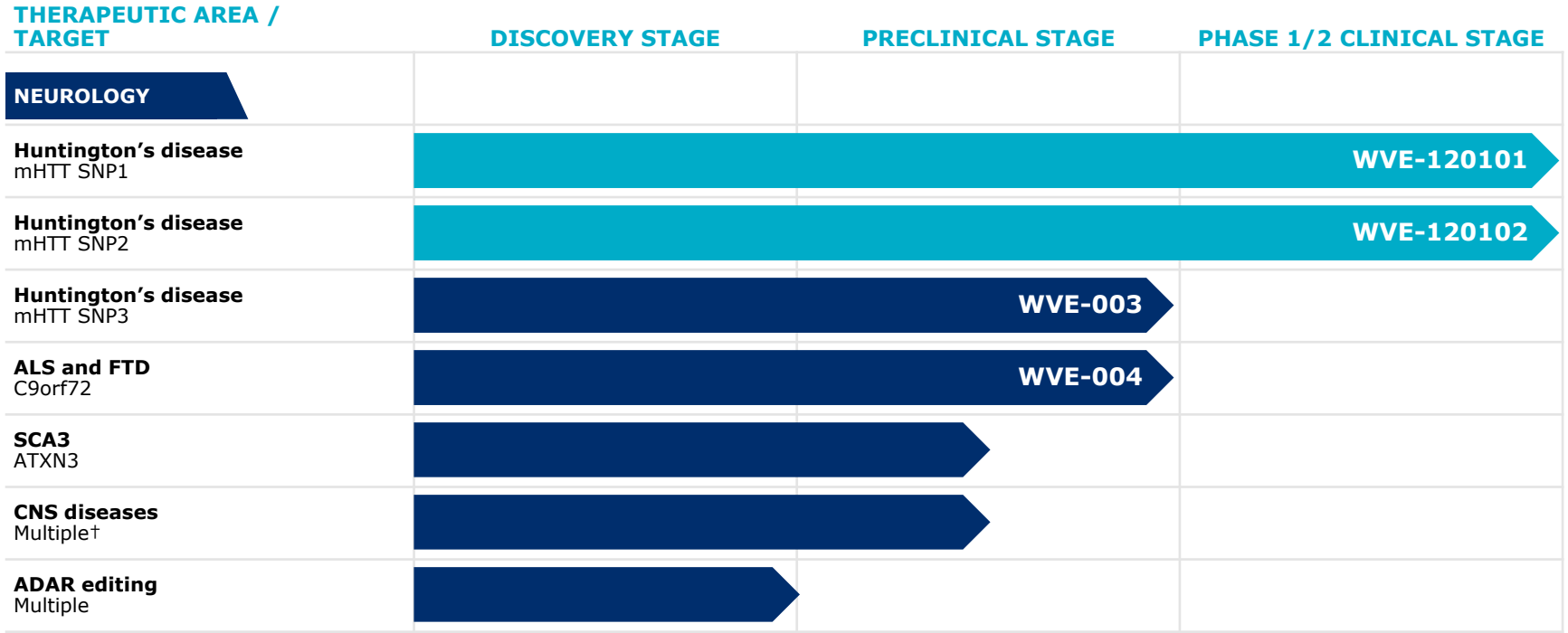
Diverse pipeline of disease-modifying therapies



†During a four-year term, Wave and Takeda may collaborate on up to six preclinical targets at any one time.
ALS: Amyotrophic lateral sclerosis; FTD: Frontotemporal dementia; SCA3: Spinocerebellar ataxia 3 CNS: Central nervous system.

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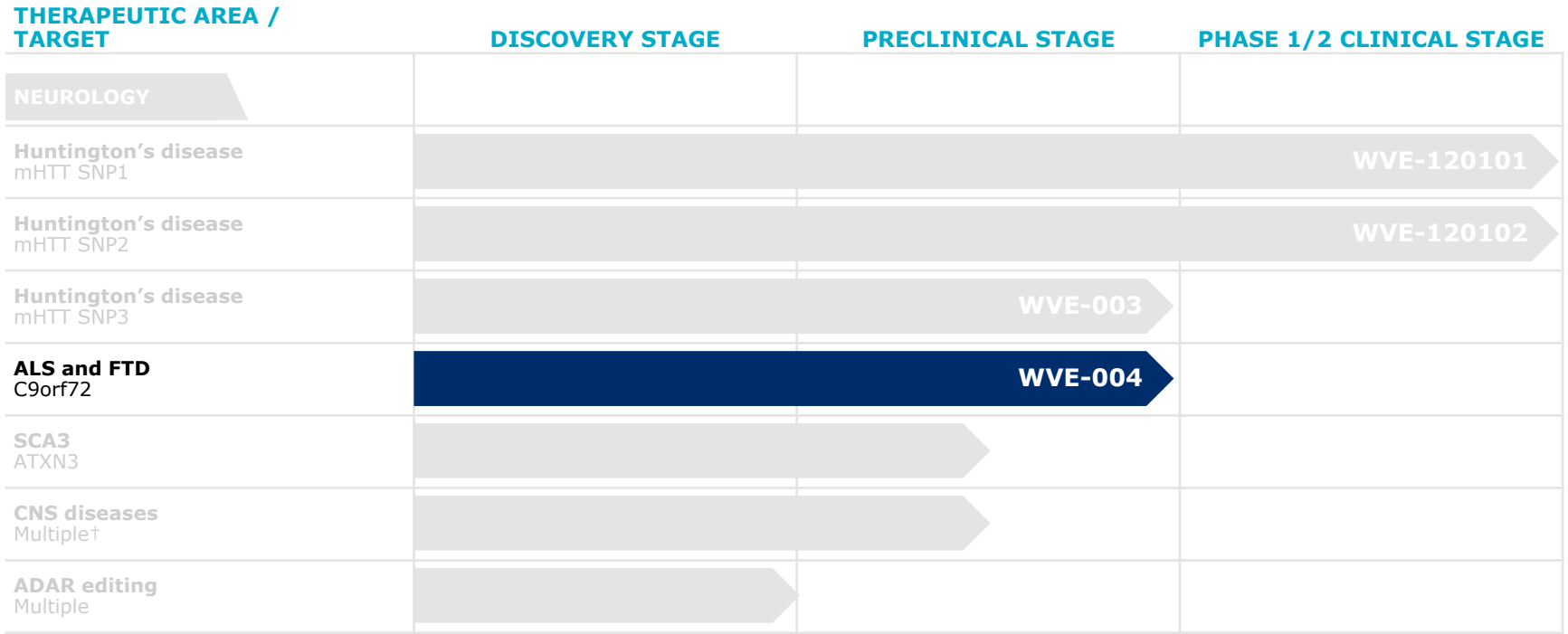
WVE-004: C9orf72 program for ALS and FTD



†During a four-year term, Wave and Takeda may collaborate on up to six preclinical targets at any one time.
ALS: Amyotrophic lateral sclerosis; FTD: Frontotemporal dementia; SCA3: Spinocerebellar ataxia 3 CNS: Central nervous system.

C9-ALS and C9-FTD: Manifestations of a clinical spectrum

	Disease	C9 specific US population	Mean disease duration	Standard of care
C9-ALS	• Fatal neurodegenerative disease • Progressive degeneration of motor neurons in brain and spinal cord	~2,000	3.1 years	Significant unmet need despite two approved therapies
C9-FTD	• Progressive neuronal atrophy in frontal/temporal cortices • Personality and behavioral changes, gradual impairment of language skills	~10,000	6.4 years	No approved disease modifying therapies

Two devastating diseases with a shared genetic basis

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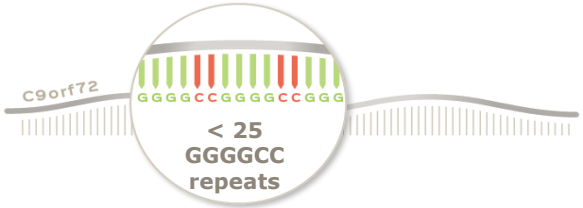
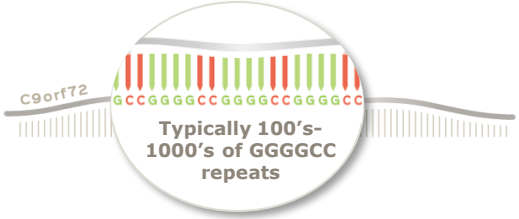
ALS: Amyotrophic lateral sclerosis; FTD: Frontotemporal dementia
Sources: Cammack et al, Neurology, October 2019. Moore et al, Lancet Neurology, February 2020

C9orf72 repeat expansions: A critical genetic driver of ALS and FTD

Normal (non-expanded) Allele



Expanded Allele



- C9orf72 hexanucleotide repeat expansions (GGGGCC) are the strongest known risk factor for sporadic and inherited forms of Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD)
- The C9orf72 repeat expansions also lead to accumulation of repeat-containing transcripts, nuclear sequestration of RNA binding proteins and synthesis of toxic dipeptide-repeat (DPR) proteins
- The C9orf72 repeat expansions lead to reduced expression of wild-type C9orf72 and to cellular changes that reduce neuronal viability

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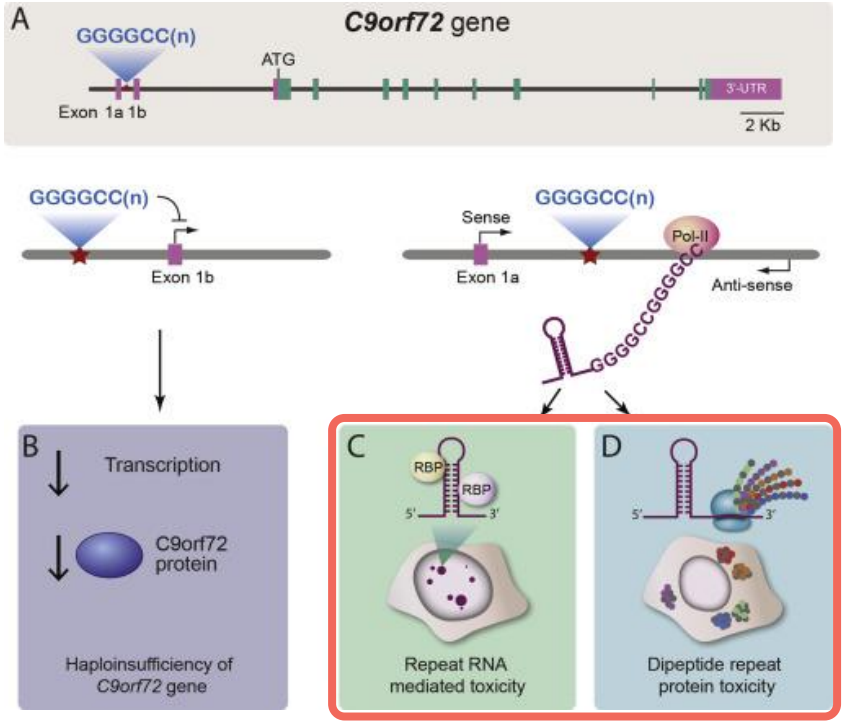
Sources: DeJesus-Hernandez et al, Neuron, 2011. Renton et al, Neuron, 2011. Zhu et al, Nature Neuroscience, May 2020

C9orf72 repeat expansions: Mechanisms of cellular toxicity

- C9-ALS and C9-FTD may be caused by multiple factors:
  - Insufficient levels of C9orf72 protein
  - Accumulation of repeat-containing RNA transcripts
  - Accumulation of aberrantly translated DPR proteins
- Recent evidence suggests lowering C9orf72 protein exacerbates DPR-dependent toxicity

Variant-selective targeting could address multiple potential drivers of toxicity

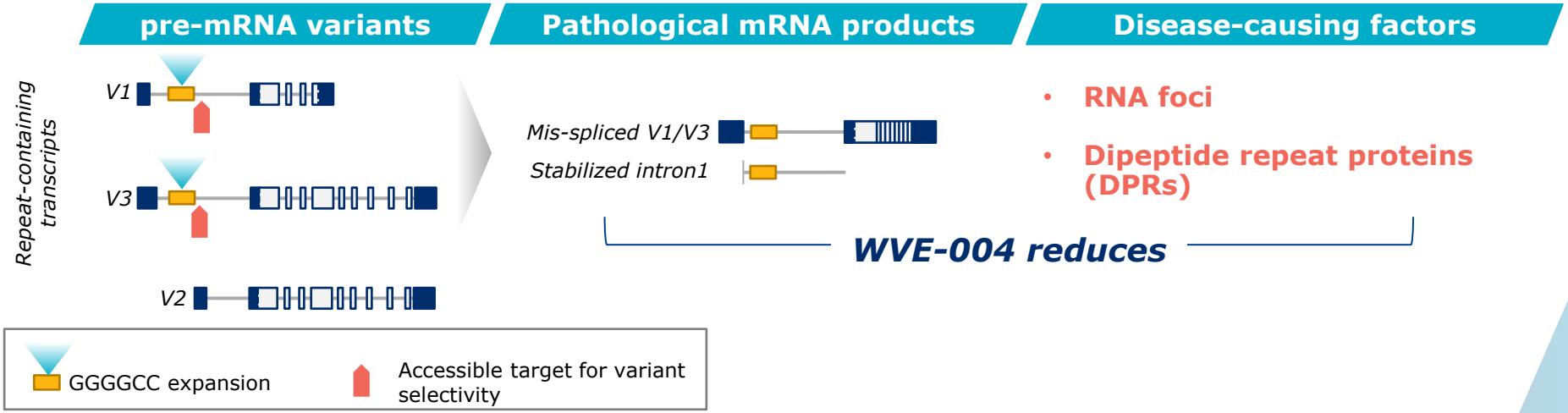


Targeted by Wave ASOs

Sources: Gitler et al, Brain Research, September 2016. Zhu et al, Nature Neuroscience, May 2020

C9orf72 targeting strategy spares C9orf72 protein

- Normal C9orf72 allele produces three mRNA transcripts (~80% are V2, ~20% are V1 and V3)
- **Pathological allele** with expanded repeat leads to **healthy V2** and **pathological V1 and V3** transcript by-products



Wave C9orf72 candidate targets only V1 and V3 transcripts, sparing V2 transcripts and healthy C9orf72 protein

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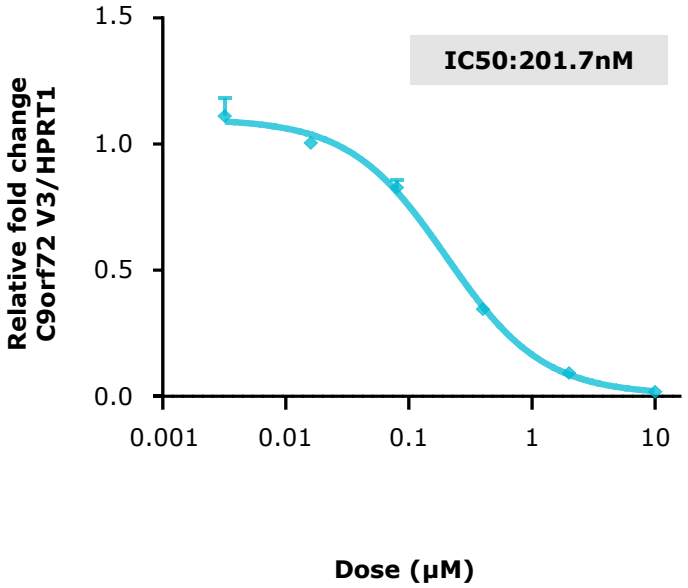
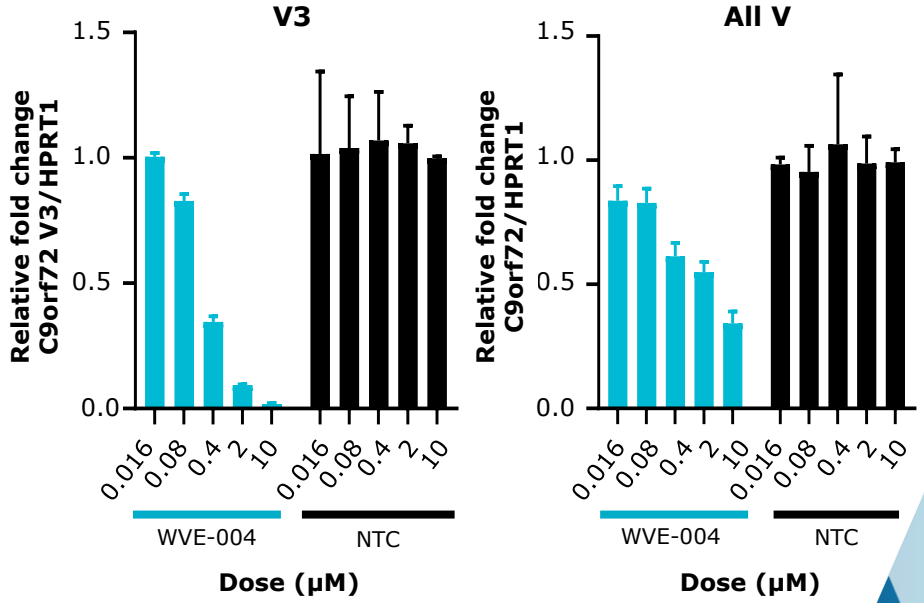
WVE-004: Potent and selective knockdown of repeat-containing transcripts *in vitro*

In vitro activity in C9 patient-derived neurons



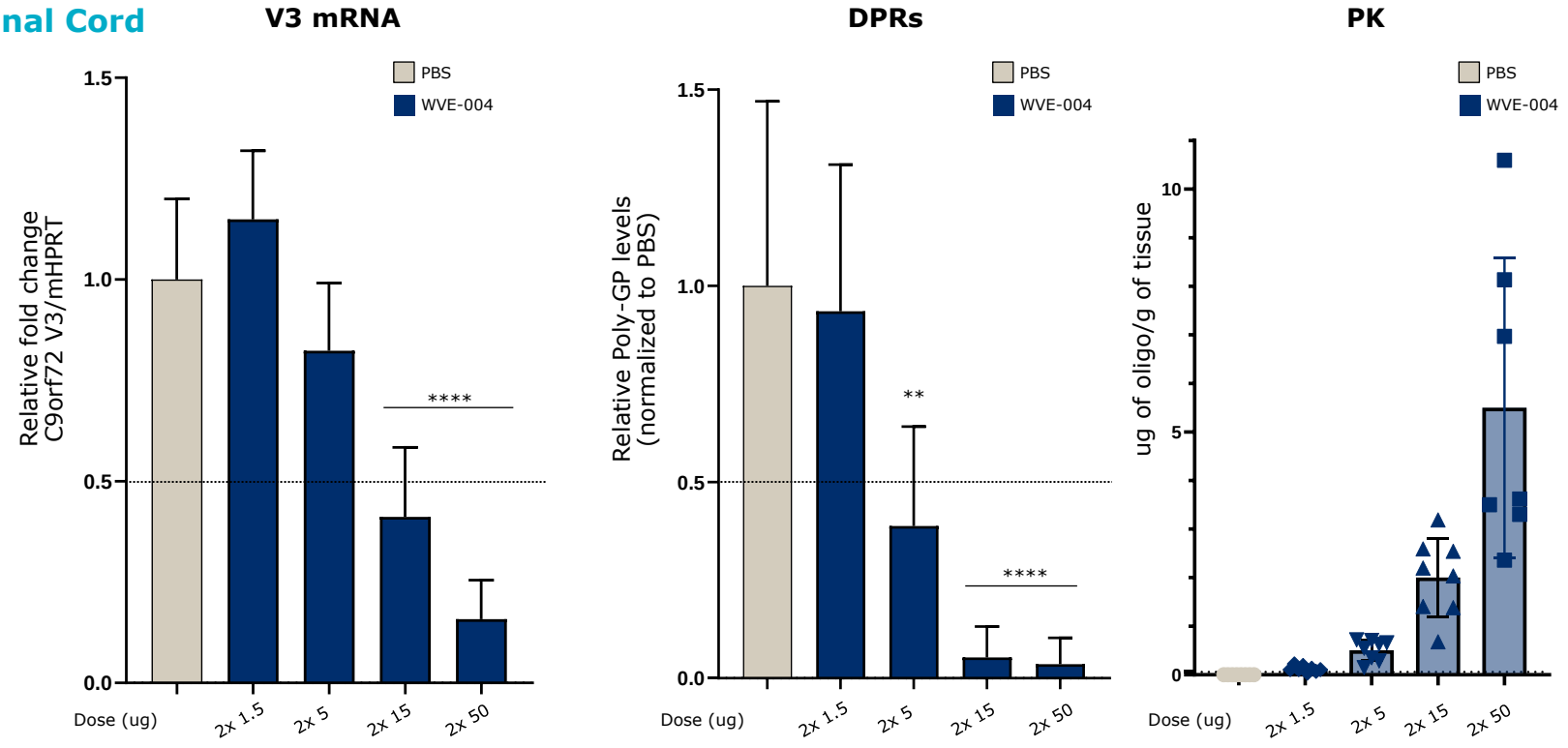
In vitro selectivity in C9 patient-derived neurons



C9 patient-derived motor neurons were treated with C9orf72 candidate and NTC under gymnotic conditions up to 10uM. Taqman qPCR assays were used to evaluating V3 and all V transcripts. NTC- non-targeting control.

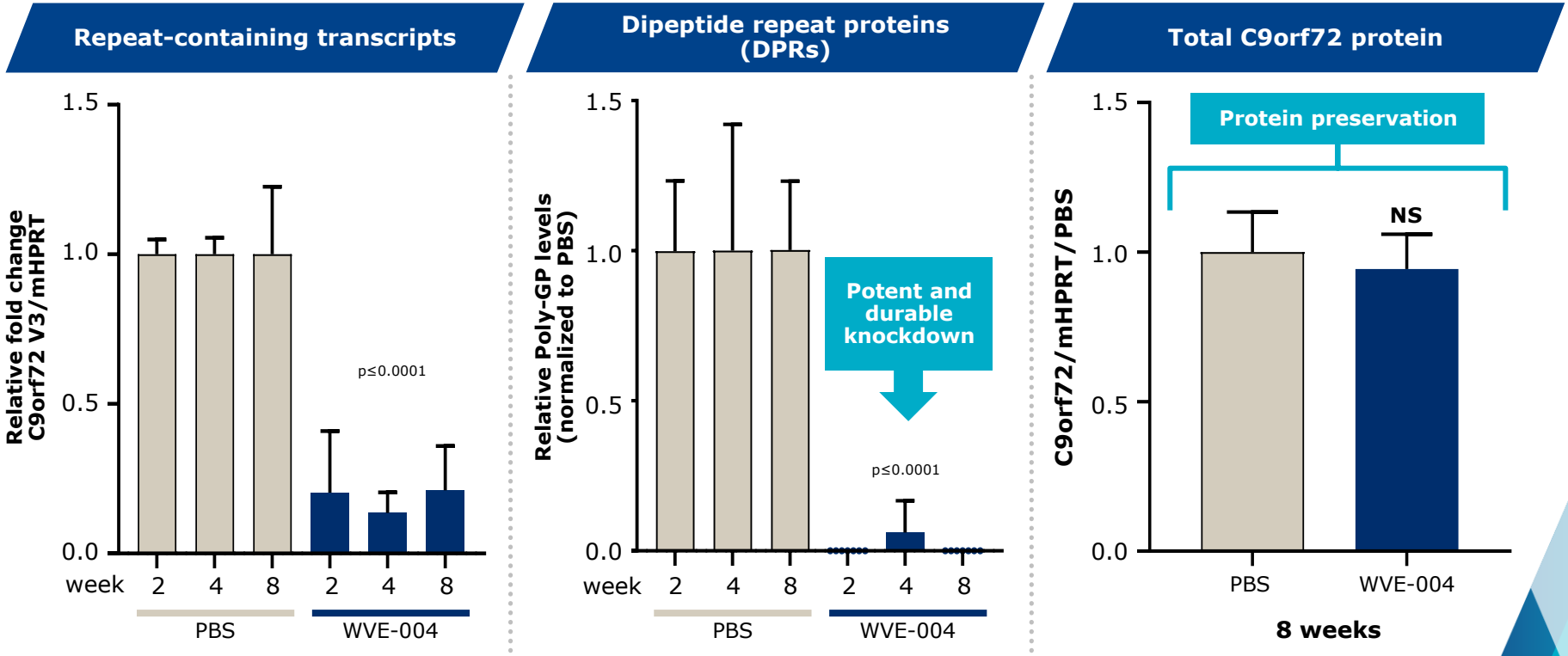
WVE-004 shows dose dependent knockdown of V3 mRNA and DPRs in C9 transgenic mouse model

Spinal Cord



C9 BAC transgenic mice were administered two times with PBS, 1.5ug, 5ug, 15ug or 50ug of WVE-004 on day 0 and day 7. Mice were euthanized 6 weeks after first injection. Taqman qPCR assay used to evaluate V3 transcripts. MSD assay used to detect ploy-GP protein. Hybridization Elisa used to detect ASO exposure. **: P ≤ 0.01, ***: P ≤ 0.001, ****: P ≤ 0.0001; DPR: dipeptide repeat protein; PK: pharmacokinetics

WVE-004: Potent and selective knockdown of repeat transcripts and DPRs in spinal cord



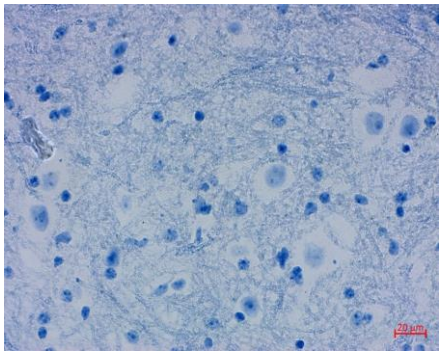
Experimental description: 2 x 50 ug on day 0 and day 7 dosed ICV; mRNA Samples were analyzed using quantitative PCR (Taqman assay), Dipeptide repeat proteins were measured by Poly-GP MSD assay. Protein samples were measured by Western Blot. NS: not significant

WVE-004 reaches target brain regions and cell types *in vivo*

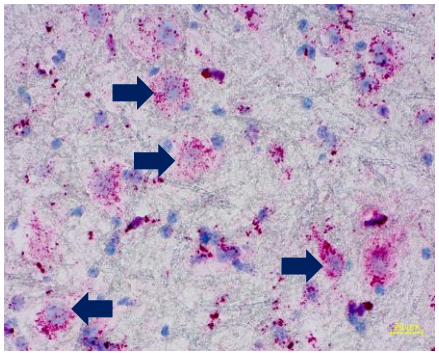
In situ hybridization of WVE-004 in spinal cord and cortex at 8 weeks

Spinal cord

PBS Control

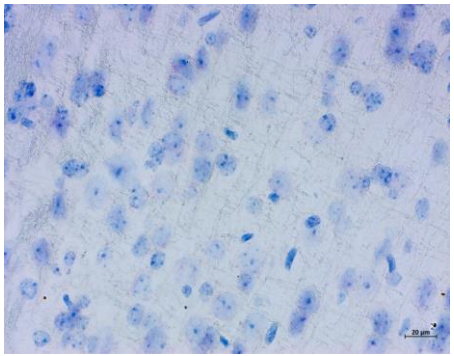


WVE-004

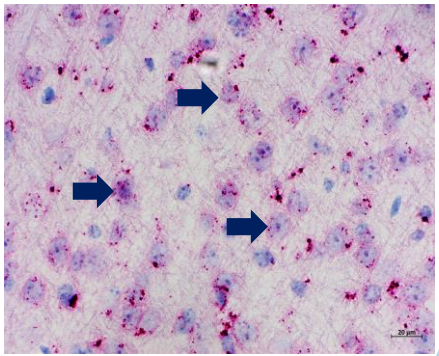


Cortex

PBS Control

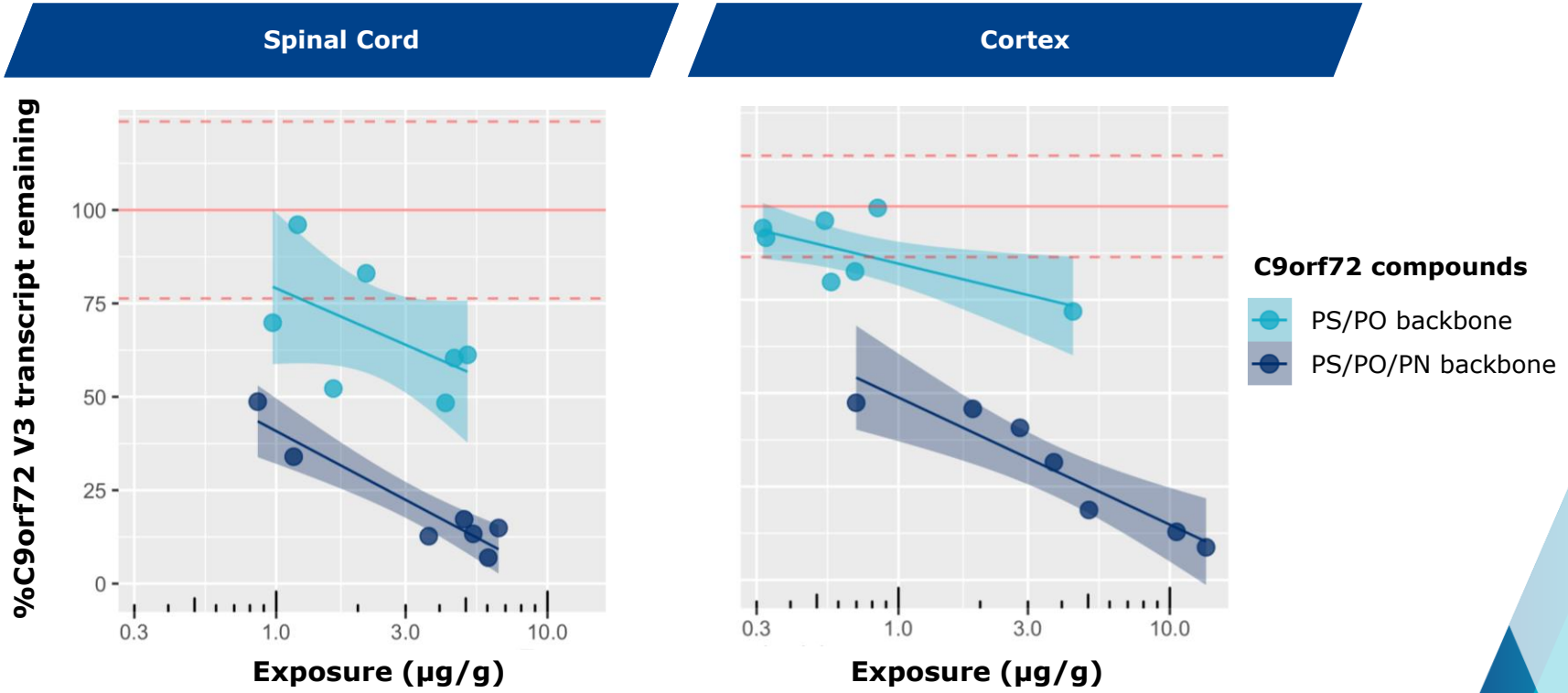


WVE-004



In situ hybridization: Red - ViewRNA for WVE-004; Blue – Hematoxylin. 40X magnification.
C9 BAC transgenic mice were administered PBS or 50 ug of WVE-004, ICV, on day 0 and day 7. Mice were euthanized at 8 weeks after the first injection.

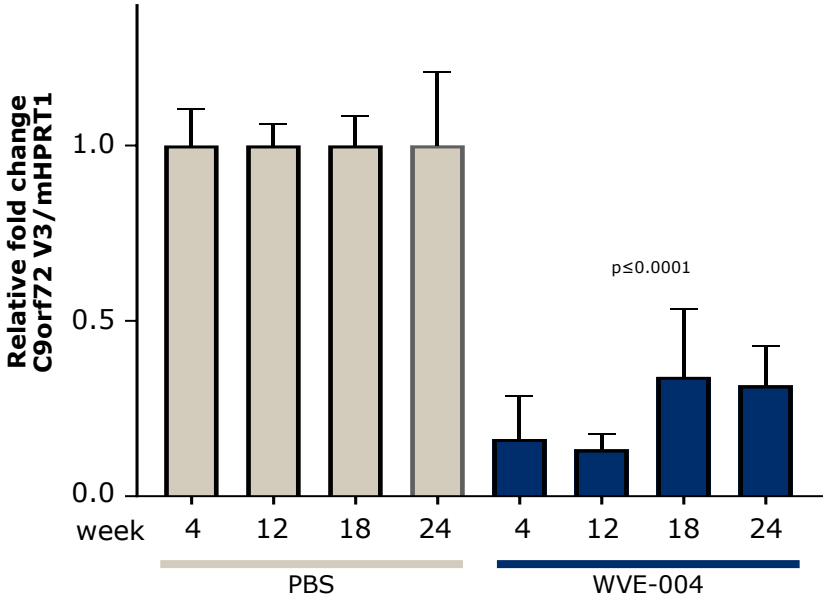
PN backbone chemistry: Improved potency among C9orf72-targeting oligonucleotides *in vivo*



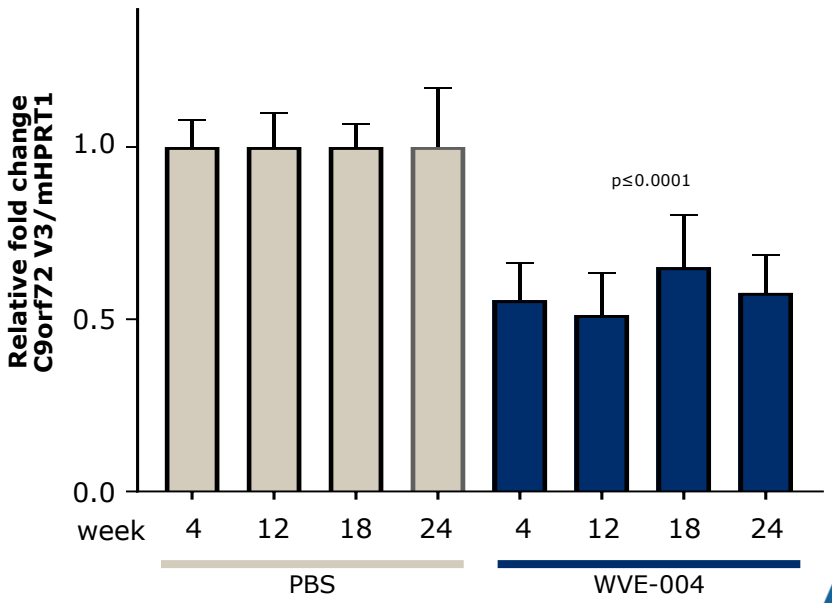
Mice received 2 x 50 ug ICV doses on days 0 & 7; mRNA from spinal cord and cortex quantified by PCR (Taqman assay) 8 weeks later. Oligonucleotide concentrations quantified by hybridization ELISA. Graphs show robust best fit lines with 95% confidence intervals (shading) for PK-PD analysis.

Durable knockdown of repeat transcripts *in vivo* after 6 months in spinal cord and cortex

Spinal cord



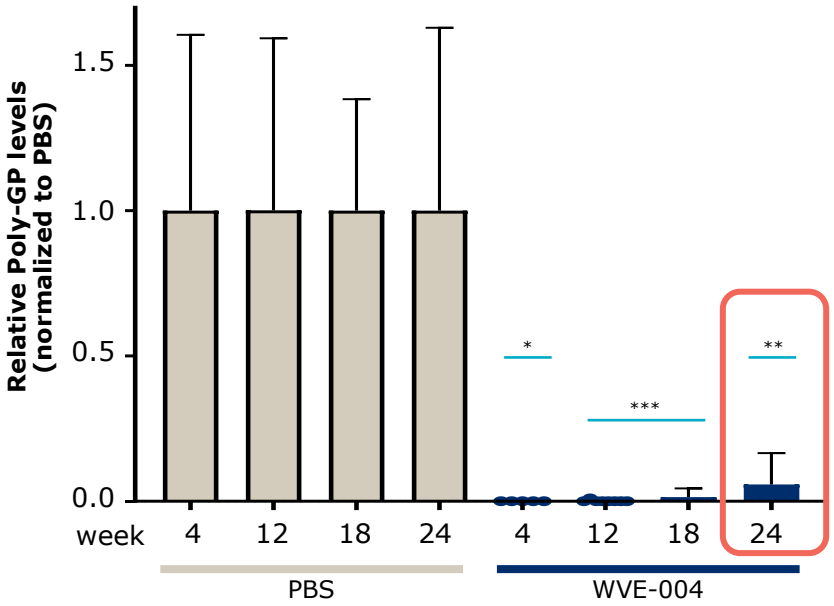
Cortex



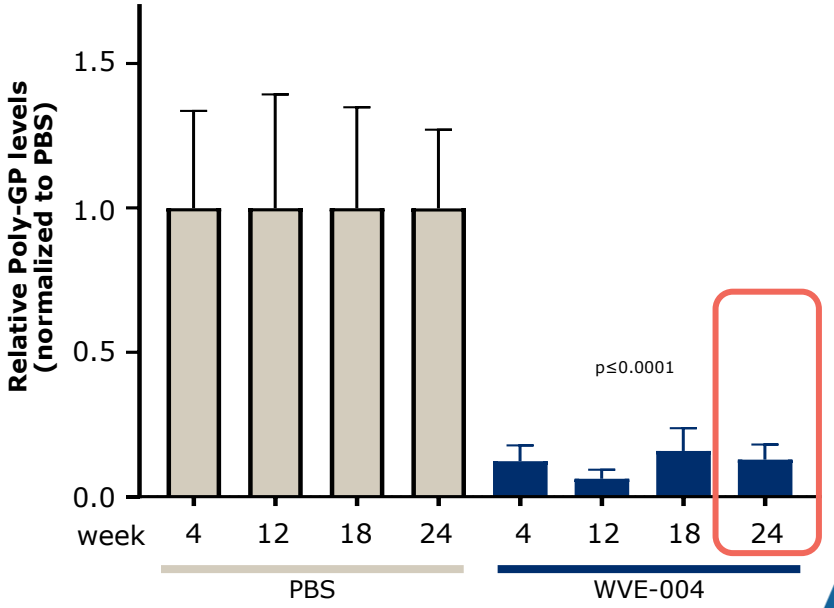
Experimental description: 2 x 50 ug on day 0 and day 7 dosed ICV; mRNA Samples were analyzed using quantitative PCR (Taqman assay)

Durable knockdown of DPRs *in vivo* after 6 months in spinal cord and cortex

Spinal cord



Cortex



Experimental description: 2 x 50 ug on day 0 and day 7 dosed ICV; Dipeptide repeat proteins were measured by Poly-GP MSD assay.
*: p≤ 0.05 **: P ≤ 0.01, ***: P ≤ 0.001

WVE-004 proof-of-concept study to include both ALS and FTD patients

- Patients with documented C9orf72 expansion and confirmed ALS or FTD diagnosis
- Single and multiple ascending doses to be explored
- Safety and tolerability
- Pharmacodynamic effects on key biomarkers while on treatment
  - PolyGP
  - NfL
- Key exploratory clinical outcome measures
  - ALSFRS-R and CDR-FTLD

CTA submission expected in 4Q 2020

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CTA: clinical trial application; NfL: neurofilament light chain; ALSFRS: Amyotrophic Lateral Sclerosis Functional Rating Scale; CDRFTLD: Clinical Dementia Scale – frontotemporal lobar degeneration

PRISM platform enables further pipeline expansion in neurology

PRISM modalities

- Silencing
- Editing
- Splicing

PRISM evolution

- Stereochemistry
- PN backbone chemistry

Wave & Takeda CNS programs

- Multiple Category 2 programs ongoing†
- Novel PN chemistry an important tool

Unlocking new targets in neurological diseases

Focus on genetically validated mechanisms and diseases with high unmet need

†During a four-year term, Wave and Takeda may collaborate on up to six preclinical targets at any one time.

Conclusion

Paul Bolno, MD, MBA
President and CEO

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Wave Life Sciences: Redefining the potential of RNA therapeutics in neurology

Well positioned to drive near-term value from PRISM

- Four global clinical neurology programs expected next year, with multiple data readouts by 2022
- Positioned to deliver multiple clinical trial applications over the next three years
- Leveraging platform to bring new neurology targets, including editing targets in CNS, to clinic
- Collaborations to unlock further value

PRISM

- Continuous learning
- Platform engine delivering new targets

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Q&A

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Analyst & Investor Research Webcast

August 25, 2020