Selective Mutant Huntingtin Lowering for People With Huntington's Disease

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December 12, 2020

Forward looking statements

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Wave Life Sciences

We are a genetic medicines company focused on delivering transformational therapies for people with serious, genetically-defined diseases

- Unique approach to Huntington's disease research
- Selectively lower mutant huntingtin protein while leaving the healthy huntingtin protein relatively intact
- Currently have two candidates in clinical development and expect to have three candidates in clinical development in 2021

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Committed to HD Community

THERAPEUTIC AREA	TARGET	DISCOVERY	PRECLINICAL	CLINICAL
Huntington's disease	**WVE-120101** mHTT SNP1		**Phase 1b/2a and OLE**	
	WVE-120102 mHTT SNP2		**Phase 1b/2a and OLE**	
	WVE-003 mHTT SNP3			

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Commitment is our bridge to innovation

Listening, **learning**, and **partnering** with the community

Inspired by a strong and resilient patient and caregiver community

Aspiring to transform the lives of people living with serious genetic diseases

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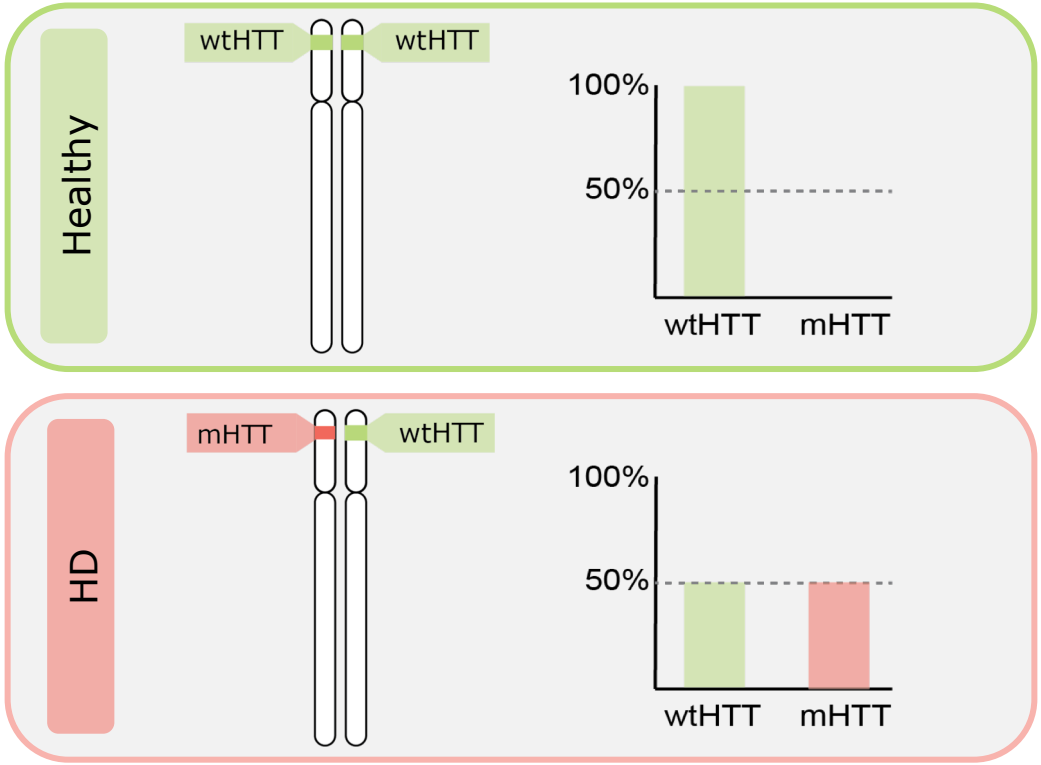
Our approach to HD:

Selective Lowering of Mutant Huntingtin (mHTT) Protein

Both loss of healthy huntingtin and gain of mutant huntingtin occur in HD



Saudou F, Humbert S. Neuron. 2016 Mar 2;89(5):910-26.

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Huntingtin protein is important for healthy brain function

Maintain health and survival of neurons (cells of the brain)

Support response to stress

Regulate communication

Circulate fluids to provide nutrients and eliminate waste

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Saudou F, Humbert S. Neuron. 2016 Mar 2;89(5):910-26.

Objectives of selective mutant huntingtin lowering approach to Huntington's disease

- **Slow the progression** of HD
- Selectively **lower mutant huntingtin** protein while potentially **preserving healthy huntingtin**
- Potentially **enable treatment earlier** in the course of HD

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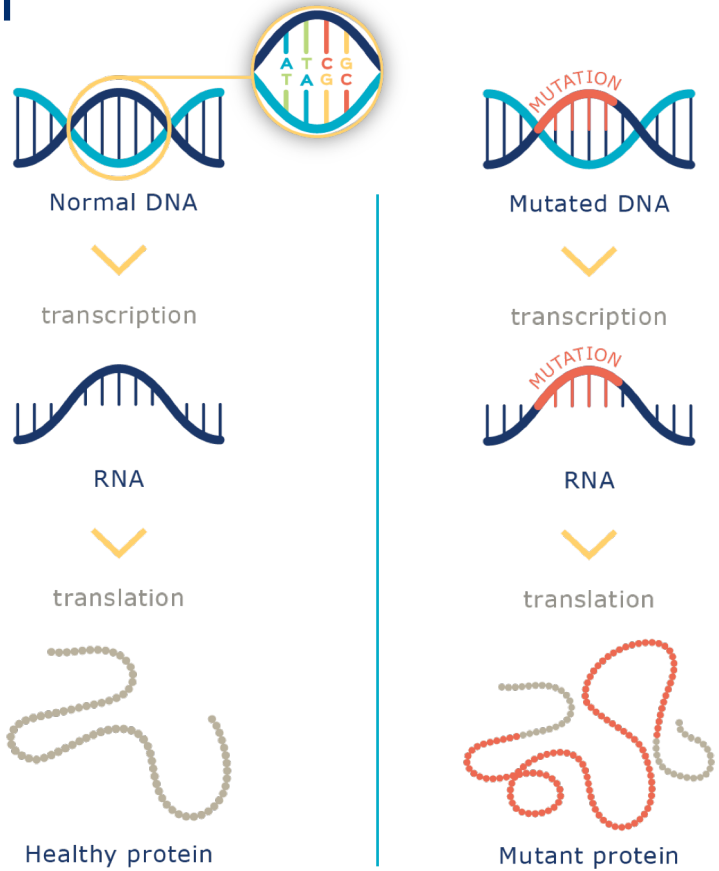
Antisense oligonucleotides (ASOs) enable reversible targeting of mHTT



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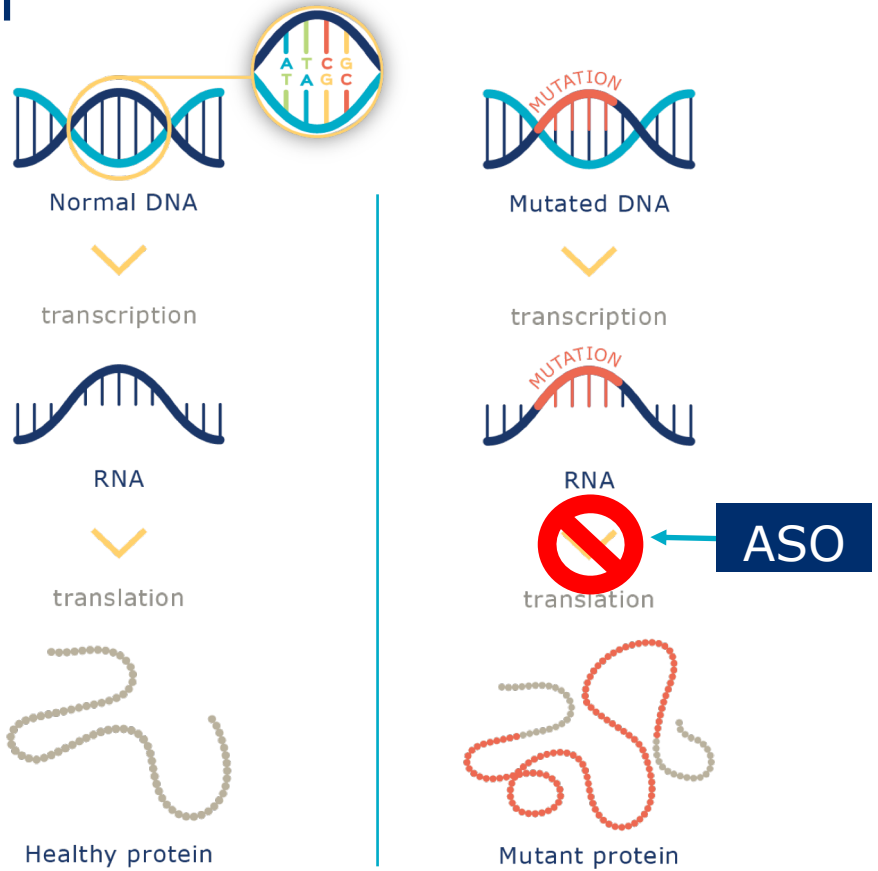

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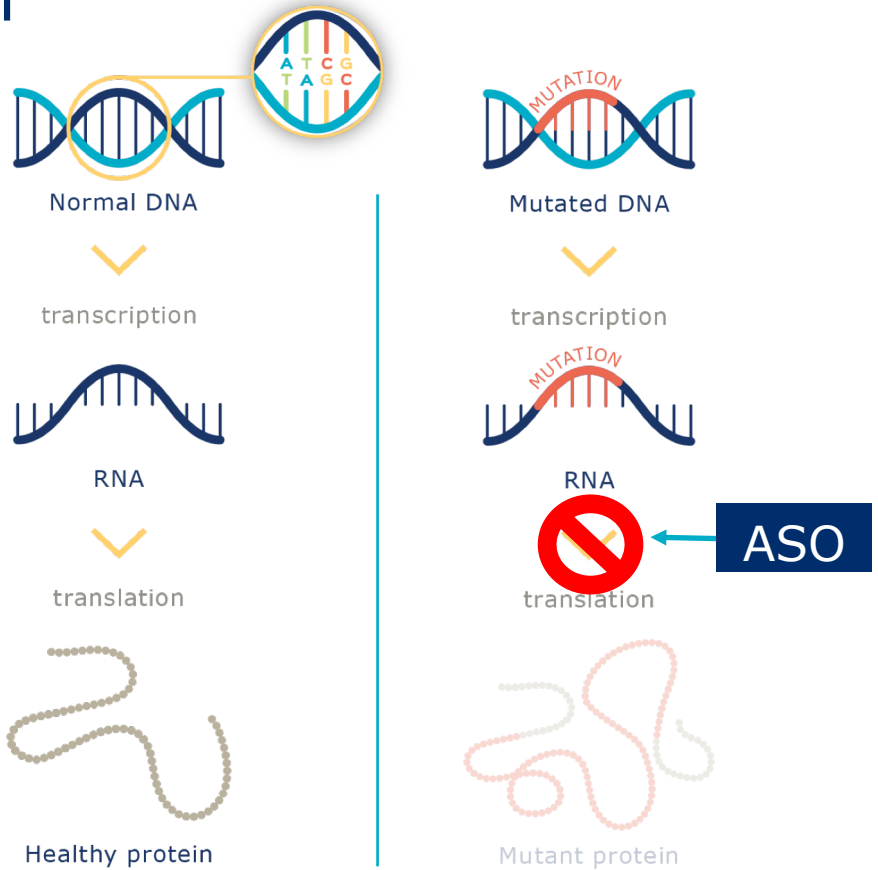

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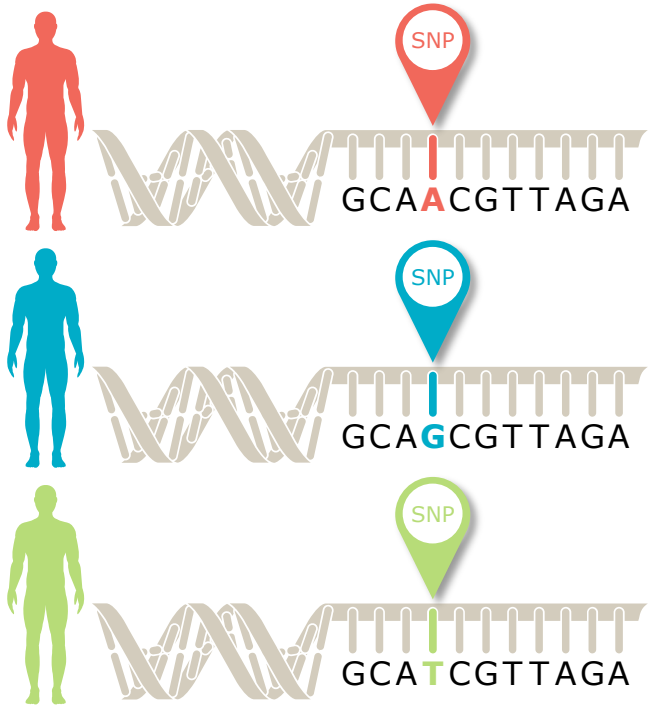
SNPs enable selective targeting of mutant huntingtin protein

- SNPs are normally-occurring variations in DNA where ONE letter at a specific location is different
  - Located in specific spots in our DNA—**like a pin on a map**
- Certain SNPs are more frequently found on the mutant HTT copy (or allele) than the healthy copy
- The association between SNPs and mutant HTT makes it possible to selectively target mutant HTT in order to preserve healthy HTT



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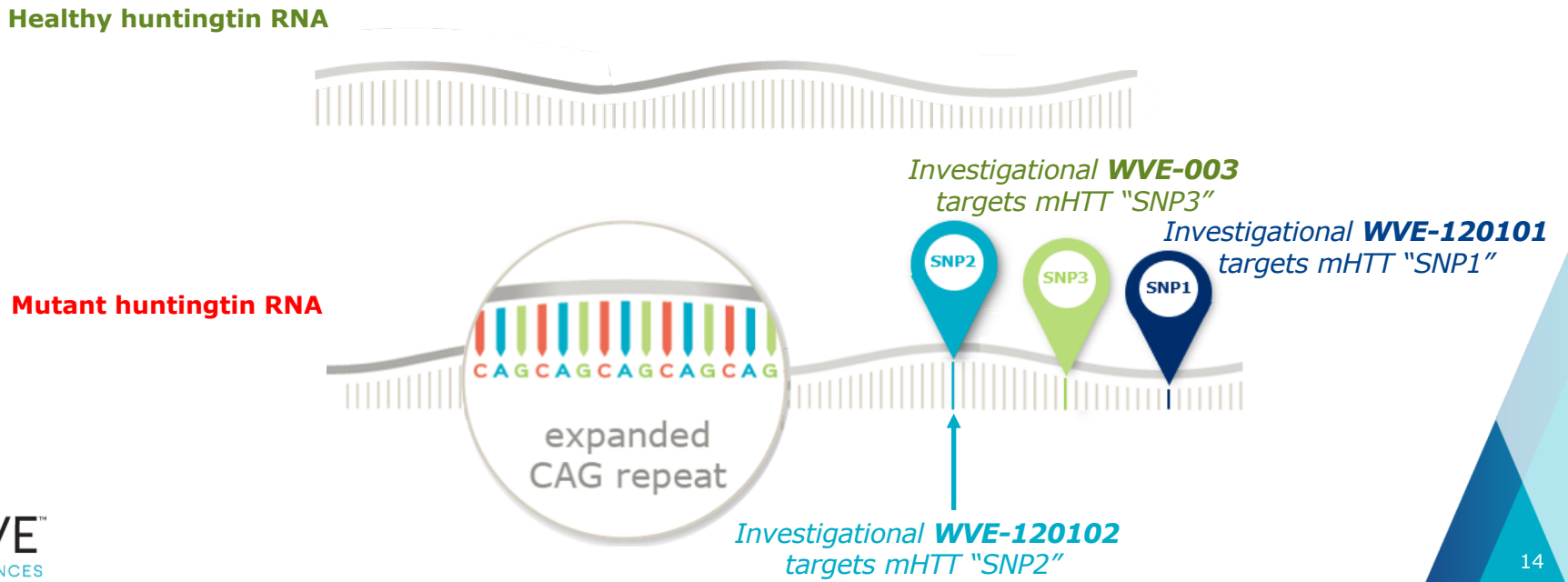
*SNP: single nucleotide polymorphism

Stereopure ASOs designed to target different SNPs on mHTT

Up to 80% of people living with HD estimated to carry SNP1, SNP2, and/or SNP3



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PRECISION HD1 & PRECISION HD2

Current Clinical Trials and Looking to the Future

PRECISION HD1 & PRECISION HD2

Study Design

- Two **Phase 1b/2a** clinical trials
- Global, randomized, double-blind, placebo-controlled

Study Objectives

- **Primary objective**: assess safety and tolerability of intrathecal doses in early manifest HD patients
- **Additional objectives**: pharmacokinetic, pharmacodynamic, clinical and MRI

Trial Locations

- Europe, North America, Australia

Dosing

- 3:1 randomization to WVE-120101/102 or placebo
- Administered intrathecally by lumbar puncture

Status and Next Steps

- The majority of patients in the PRECISION-HD clinical trials have received multiple, monthly doses of study drug, up to and including 16 mg in the Open Label Extension
- PRECISION-HD results, including complete 32 mg cohorts and available OLE data, expected

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Summary: Wave's approach to HD

Research

Wave's therapeutic approach is to **selectively lower mutant HTT protein** and leave the healthy protein relatively intact

Clinical

Clinical trials with our investigational candidates are ongoing

- Expect to share additional clinical data in the 1st quarter of 2021
- Also in 1st quarter, we expect to share data from our ongoing open-label extension (OLE) trials

Commitment

Potential to have **three HD programs in clinical development** in 2021, targeting up to 80% of the HD population

- Expect to file clinical trial application for WVE-003 in 4th quarter of 2020

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Grazie

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Robert Adam
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Kelly Bertram
Carolyn Orr

Patients and their families for their participation

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