



April 10, 2019

Dear global HD community,

Today we are sharing an update on the timing of the topline data readout from our ongoing PRECISION-HD program, which consists of two global Phase 1b/2a clinical trials evaluating investigational therapies WVE-120101 and WVE-120102 for patients with Huntington's disease (HD).

Due to slower than anticipated trial enrollment, we now expect to report topline clinical data from the PRECISION-HD program by the end of year. The reason for the revised timeline is operational and is not due to a preclinical or clinical safety finding. Specifically, screening and scheduling of patients across global sites has been slower than anticipated. Importantly, the two clinical trials continue to enroll patients at sites globally and we are making every effort to speed recruitment into these important studies.

While we are disappointed that enrollment is not as fast as we anticipated, we remain very excited about the potential of our two investigational therapies and are pleased that there continues to be strong interest in the trials. Like many of you, we are eagerly looking forward to the first clinical results from PRECISION-HD and are grateful for the support that we have received from the entire HD community.

Those interested in participating in one of the PRECISION-HD clinical trials should speak to their physician or seek a recommendation from an HD specialist.

Thank you to all of the PRECISION-HD clinical trial participants and their families. Your commitment and involvement are critical to advancing the scientific and medical understanding required to defeat this devastating disease.

Sincerely,

A handwritten signature in black ink, appearing to read "Michael Panzara", with a long, sweeping tail extending to the right.

Michael Panzara, MD, MPH  
Chief Medical Officer

## Frequently Asked Questions

### **What are the two investigational therapies being studied in the PRECISION-HD program?**

WVE-120101 and WVE-120102 are investigational stereopure antisense oligonucleotides designed to selectively target the mutant huntingtin (HTT) mRNA transcript of SNP rs362307 (SNP1) and SNP rs362331 (SNP2), respectively. SNPs, or single nucleotide polymorphisms, are naturally occurring variations within a given genetic sequence and in certain instances can be used to distinguish between two related copies of a gene where only one is associated with the expression of a disease-causing protein. This is called an allele-selective approach. *In vitro* studies in patient-derived cell lines have shown that WVE-120101 and WVE-120102 selectively reduce levels of mutant HTT mRNA transcript and protein, while leaving wild-type, or healthy, HTT mRNA transcript and protein relatively intact. Accumulation of mutant HTT causes progressive loss of neurons in the brain and is thought to be the underlying cause of Huntington's disease. The healthy transcript is required to produce healthy HTT protein which is critical for neuronal function, as evidenced by multiple preclinical studies indicating that long-term suppression of healthy HTT protein may have detrimental consequences.

### **What is the PRECISION-HD program?**

Our PRECISION-HD program is the first clinical program to use an allele-selective approach to target the underlying cause of Huntington's disease. PRECISION-HD1 and PRECISION-HD2 are Phase 1b/2a multicenter, randomized, double-blind, placebo-controlled clinical trials evaluating the safety and tolerability of WVE-120101 and WVE-120102, respectively. Together, these compounds could provide treatment for up to 70% of patients with Huntington's disease.