



November 2023

Dear Huntington's disease community members,

At Wave, we are committed to keeping you informed on the continued progress of our SELECT-HD clinical trial investigating WVE-003 for people living with Huntington's disease (HD). We are happy to share that enrollment in the 30 mg every eight-week multiple-dose group of SELECT-HD is complete. This means we are another step closer to data to inform how multiple doses of WVE-003 may impact biomarkers of the disease, as well as safety and tolerability.

What is WVE-003 and SELECT-HD?

WVE-003 is an investigational antisense oligonucleotide (ASO) designed to selectively reduce mutant huntingtin (mHTT) protein considered to be the cause of HD, while sparing the fully functional, or wild-type, huntingtin (wtHTT) protein.

SELECT-HD is a Phase 1b/2a clinical trial studying WVE-003 for people with Huntington's disease. It is an adaptive trial, which means there is an independent committee that reviews the data at specific points during the trial and decides what the next dose will be and how often the drug should be administered.

Recap of Previous Data Updates

In September 2022, we announced data from the SELECT-HD clinical trial which demonstrated that WVE-003 appeared generally safe and well-tolerated for study participants who received single doses up to 90 mg. Additionally, for study participants in the 30 and 60 mg groups, a mean of 35% mutant huntingtin protein lowering was observed in their cerebrospinal fluid (CSF) with single doses of WVE-003 as compared to placebo. An assessment of wtHTT protein also suggested that, as intended, WVE-003 was not impacting wtHTT protein levels. At the time of analysis, none of the patients in the 90 mg group had reached day 85, so this group was not included in the initial analysis. Following our announcement, and in agreement with the independent safety monitoring committee, we adapted the SELECT-HD clinical trial to expand the single-dose groups and extend the follow-up period after each dose to enable further assessments beyond 85 days. Additionally, in August 2023, we announced that the multiple-dose group in SELECT-HD was underway.

Current Status

We completed enrollment in the 30 mg multiple-dose group of the SELECT-HD clinical trial, which is evaluating doses administered every eight weeks. Participants from the single-dose groups rolled over to participate in the 30 mg multiple-dose group.

We will now evaluate the completed single-dose and multiple-dose groups together and we expect to report data from the 30 mg multiple-dose group with extended follow-up, along with all single-dose data, in the second quarter of 2024.

It should be noted that we cannot conclude that WVE-003 is efficacious and benefit/risk must still be established through continuation of SELECT-HD.

Our Gratitude

We are grateful to the HD community, in particular the SELECT-HD participants and their families, study sites, and clinicians, for their continued partnership and support of this program.

Sincerely,

Chelley Casey, VP, Head of Patient Advocacy