



August 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).

WVE-003 is an investigational antisense oligonucleotide (ASO) designed to selectively reduce mutant huntingtin (mHTT) protein while sparing healthy, 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 Initial Update

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 cohorts, we observed 35% lower mutant huntingtin protein in their CSF with single doses of WVE-003 as compared to placebo. An assessment of wtHTT protein also suggested that, as intended, WVE-003 is not impacting wtHTT protein levels. At the time of analysis, none of the patients in the 90 mg cohort had reached day 85 so this cohort was not included in the analysis. Following this announcement and in agreement with the independent committee, Wave adapted the SELECT-HD clinical trial to expand the single dose cohorts and extend the follow-up period after each dose to enable further assessments beyond 85 days.

It should be noted that we cannot conclude that WVE-003 is efficacious at this current stage of development, and benefit/risk must still be established through continuation of SELECT-HD and other studies.

Current Status

We are happy to report that we continue to make progress with this study. In the second quarter of 2023, we initiated the multi-dose portion of our ongoing Phase 1b/2a SELECT-HD clinical trial and dosing is currently underway. We are enrolling existing participants from the single-dose portion of the study as well as screening new participants. We look forward to continuing this study and sharing additional single dose data and any available multidose data in the second half of this year.

The SELECT-HD trial is currently recruiting in Australia, Canada, Denmark, France, Germany, Italy, Poland, Spain, and the United Kingdom (England, Scotland, Wales). More details about the SELECT-HD trial can also be found on [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT05032196) ([NCT05032196](https://clinicaltrials.gov/ct2/show/study/NCT05032196)) and should be discussed with your physician.

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
On behalf of the team at Wave Life Sciences