

October 2022

Dear Global Huntington's Disease Community,

We are pleased to share with you an important update on the clinical development program for Sage Therapeutics, Inc.'s investigational drug, SAGE-718. We are happy to announce that the SURVEYOR Study, a Phase 2 real-world functioning study, is now open for enrollment. The SURVEYOR Study is a randomized, placebo-controlled, double-blind study designed to evaluate the cognitive performance differences between participants with Huntington's disease (HD) and non-HD participants. The study will also evaluate the potential effects of SAGE-718 on cognition and functioning, and its safety and tolerability, in participants with pre-manifest or early manifest HD.

WHAT IS THE SURVEYOR STUDY?

As you may recall from our previous statement in February, the SURVEYOR Study is part of the PERSPECTIVE Program. This program is a set of clinical studies designed to evaluate the safety and effect of SAGE-718 on cognitive symptoms in people with HD. The DIMENSION Study, a Phase 2 clinical research study and our first study in the PERSPECTIVE Program, is also open and recruiting in select regions of North America.

The SURVEYOR Study is intended to evaluate real-world functioning via a series of assessments. These may include an optional driving simulation assessment (available at select site locations) and a virtual reality assessment that simulates key activities of daily living in a realistic and interactive virtual environment. The SURVEYOR study design is unique from the DIMENSION Study and is intended to help to better understand the potential impact of SAGE-718 on the day to day functioning of HD participants.

WHO CAN PARTICIPATE?

The SURVEYOR Study lasts for up to 70 days versus DIMENSION, which lasts up to 136 days. The SURVEYOR study requires six in-person clinic visits over the course of the trial. Eligibility criteria for the SURVEYOR Study is similar to the DIMENSION Study, including:

- Aged 25 to 65 years old at time of screening
- Have genetically confirmed HD with pre-manifest to early-manifest disease presentation, including:
 - CAG expansion ≥ 36
 - UHDRS-TFC score >6 and <13
 - No features of juvenile HD
- Experience cognitive / thinking difficulties
- Meet a list of other health requirements, including but not limited to:
 - o Being ambulatory (use of assistive devices such as a walker or cane is acceptable)
 - o Not participating in another clinical study within the past 90 days (observational only studies – where no treatment is administered – is allowed, ie., ENROLL-HD)

Other eligibility criteria apply.

Participation in any clinical research study is completely voluntary, and participants may choose to leave the study at any time for any reason.

WHERE CAN I LEARN MORE?

Additional information about the DIMENSION and SURVEYOR Studies, including individual site status and a complete list of inclusion and exclusion criteria is available on clinicaltrials.gov (IDs: NCT05107128 and NCT05358821). You may also find more information via hdtrialfinder.org or you can visit the PERSPECTIVE Program website to see if you may qualify.

We respect the role of healthcare providers in the treatment of brain health disorders, and a healthcare provider is the best resource for information and to understand eligibility for clinical trials.

Additional SURVEYOR sites in the United States and Canada are expected to begin recruiting this year. Please note that not all sites are fully activated and recruiting at this time. Additional sites will be added to the study website mentioned above as they are activated.

WHAT'S NEXT?

In addition to the DIMENSION and SURVEYOR studies, a third study in the PERSPECTIVE Program, an open-label safety study, is planned to begin by the end of 2022. Individuals who take part in the DIMENSION or SURVEYOR Studies may be eligible to participate in the open-label extension study where all participants will receive SAGE-718. Additional details on this study will be shared once available.

Please note, SAGE-718 is an investigational compound. The safety and efficacy of this investigational compound has not been established. There is no guarantee that the outcome of these studies will result in approval by a Health Authority. For more information about Sage Therapeutics, SAGE-718, and our neuropsychiatry program please visit www.sagerx.com.

We would like to again extend our immense gratitude to the patients and families who volunteer to participate, allowing us the opportunity to discover and deliver potentially life-changing medicines to support brain health. The entire Sage team is looking forward to working with the HD community and will continue to share important information about the PERSPECTIVE Program as it becomes available.

Sincerely,



Emily Gusse
Director, Pipeline Patient Advocacy