215 First Street, Cambridge, MA 02142
www.sagerx.com

November 2022

Dear Global Huntington's Disease Community,

We are pleased to share an important update on the clinical development program for Sage Therapeutics Inc.'s investigational drug, SAGE-718. The PERSPECTIVE Program, a set of clinical studies, will evaluate the safety and effect of SAGE-718 on cognitive symptoms in people with Huntington's disease (HD) at clinical trial sites opening up around the globe. The U.S. Food and Drug Administration (FDA) granted Fast Track Designation to SAGE-718 for development as a potential treatment for HD in September 2021. Fast Track is a process designed to facilitate the development and review of new treatments for serious conditions with unmet medical need such as HD.

WHAT IS THE DIMENSION STUDY?

The DIMENSION Study, a Phase 2 clinical research study and our first study in the PERSPECTIVE Program, is now open and recruiting in select regions of the United States, Canada, Australia, and the United Kingdom. The DIMENSION Study is a randomized, placebo-controlled, double-blind study evaluating the safety and effect of SAGE-718 on cognitive symptoms in adults with premanifest or early manifest HD. Cognitive symptoms may include impaired judgment, forgetfulness, difficulty paying attention, and trouble thinking through steps of an activity or complex problems.

WHO CAN PARTICIPATE?

The DIMENSION Study lasts for up to four months, with nine in-person clinic visits required over the course of the trial. Subjects will self-administer either the investigational compound or placebo once daily every morning for 12 weeks. Eligibility criteria for the DIMENSION Study include:

- Aged 25 to 65 years old at time of screening
- Meet all the following criteria for HD:
  - 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:
  - Being ambulatory (use of assistive devices such as a walker or cane is acceptable)
  - Not participating in another clinical study within the past 30 days (observational only studies – where no treatment is administered – is allowed)

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?

You may visit the DIMENSION Study website to learn more: **FocusOnCognition.com**. Additional information including individual site status in each country and a complete list of inclusion and exclusion

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criteria, is available on clinicaltrials.gov (ID: NCT05107128), ISRCTN.com (ISRCTN17896603), as well as hdtrialfinder.org.

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.

Please note that not all sites are fully activated and recruiting at this time, but we are working to have all sites up and running as quickly as possible.

WHAT'S NEXT?

An open-label safety study, which will provide more information about the long-term safety of SAGE-718, is planned to begin recruiting towards 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 the open-label safety study will be shared once available.

Please note, SAGE-718 is an investigational compound. The safety and efficacy of investigational compounds have 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 are committed to developing novel medicines to potentially treat patients with brain health disorders. Participation in a clinical study of any kind is a significant commitment, and we want to extend our immense gratitude to the patients and families who volunteer to participate. Without you, we would not be able to conduct new research to discover and deliver new potential medicines to support brain health. The entire Sage team is looking forward to continued work with the HD community and is committed to sharing important information about the SAGE-718 program as it becomes available.

Sincerely,

Emily Gusse
Director, Patient Advocacy

Fast Track is a process designed by the FDA to facilitate the development, and expedite the review, of drugs to treat serious conditions and fill an unmet medical need. Drugs that receive Fast Track designation may be eligible to be the subject of more frequent communications and meetings with FDA to review the drug's development plan including the design of the proposed clinical trials, use of biomarkers and the extent of data needed for approval. Drugs with Fast Track Designation may also qualify for priority review to expedite the FDA review process if relevant criteria are met.

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The purpose is to get important new drugs to patients who need them earlier. Fast Track addresses a broad range of serious conditions. For more information about Fast Track, please visit: https://www.fda.gov/ForPatients/Approvals/Fast/ucm405399.htm.