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

February 2022

Dear Global Huntington's Disease Community,

We are pleased to share with you an important update on the clinical development program for Sage'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). The U.S. Food and Drug Administration (FDA) has granted Fast Track Designation to SAGE-718 for development as a potential treatment for HD. 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.

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. 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.

The DIMENSION Study lasts for up to four months, with nine in-person clinic visits required over the course of the trial. Eligibility criteria for the DIMENSION Study include:

- 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:
  - Being ambulatory (use of assistive devices such as a walker or cane is acceptable)
  - Not participating in another clinical study within the past 180 days (observational only studies – where no treatment is administered – is allowed)

Additional information about the DIMENSION Study, including individual site status and a complete list of inclusion and exclusion criteria, is available on clinicaltrials.gov (ID: NCT05107128) as well as hdtrialfinder.org. You may also visit the DIMENSION Study website: YourDimensionStudy.com.

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 sites in the United States, Canada, Australia, and the United Kingdom are expected to begin recruiting this year. 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.

Two additional studies in the PERSPECTIVE Program are planned to begin in 2022: the SURVEYOR Study, which will examine real-world functioning in participants treated with SAGE-718, and an open-label extension study, which will provide more information about the long-term safety of SAGE-718. Individuals who take part in the DIMENSION or SURVEYOR Studies may be eligible to participate in the

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open-label extension study where all participants will receive SAGE-718. Additional details on these studies 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 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 potentially life-changing 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,

Aaron Koenig, MD
Vice President, Medical Science Early

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.

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.