January 27, 2022

**Community update:**
**Status VIBRANT-HD, the study of branaplam/LMI070 in Huntington's Disease**

Dear Huntington's Disease Community:

We are sharing this update to make sure you have the latest information about Novartis' branaplam development program in Huntington's Disease (HD). Branaplam is being developed as a potential first in class orally administered disease modifying therapy for HD. Novartis is pleased to announce a Phase IIb study (VIBRANT-HD) in adults with early-stage manifest HD is underway and currently enrolling. You will find the latest information regarding trial sites by visiting ClinicalTrials.gov. More sites will be listed as they become active. Novartis has also received notice that the US Food and Drug Administration (FDA) has granted Fast Track designation for branaplam for the treatment of HD.

## VIBRANT-HD

VIBRANT-HD is a randomized, double-blind, placebo-controlled study which will take place in Europe and North America and will be conducted in approximately 75 early manifest HD participants. The goal of this study is to identify a safe and well-tolerated orally administered dose of branaplam that lowers mHTT sufficiently in cerebral spinal fluid to expect a clinical benefit.

After screening and baseline assessments are completed, participants will enter the Core Treatment Period (CTP) which is double-blinded and placebo-controlled. Three cohorts will be enrolled in the CTP, the study uses a staggered design to evaluate the safety of lower doses before proceeding to higher doses.

After the optimal dose(s) is determined at the end of the CTP, all participants will roll over into the Open Label Extension (OLE) and will be given branaplam for approximately 1 year while attending clinic visits every 4 weeks. At the end of the OLE, the study may be amended to provide open label branaplam beyond 1 year or a separate extension study may be initiated.

## Fast Track Designation

On December 13, 2021, the FDA granted Fast Track designation for branaplam for the treatment of HD. Fast Track designation facilitates the development and expedites the review of drugs to treat serious conditions and fill unmet medical needs (FDA Fast Track Information). Existing treatments for HD address individual

symptoms and have no effect on the course of the disease. The HD community is acutely aware of the urgent and unmet medical need for therapies that delay the onset or slow the progression of HD. Branaplam has the potential to address this unmet medical need. Branaplam is an investigational disease modifying treatment, taken orally and has the potential to alter the pathology and progression of HD by modifying HTT mRNA throughout the brain and the body, resulting in lower levels of HTT protein.

We hope to provide regular updates as additional study sites begin recruiting. To find updated information, you may wish to visit HD Trialfinder, a trusted HD community resource for information regarding trials. We would like to thank the HD community for their input, participation, and continued support of VIBRANT-HD.

Yours sincerely,

The branaplam team