

14 October 2019

Update on the Phase III GENERATION HD1 study

Dear global HD patient community,

Today we are pleased to announce that we are increasing the total enrolment in the GENERATION HD1 study (NCT03761849) from 660 to 801 participants worldwide. We believe that increasing enrolment now - before study recruitment closes - keeps the study on track to complete within expected timelines. This study change does not impact participants already enrolled in the study, but it allows for additional patients to enrol in each of the three study groups.

The GENERATION HD1 study is evaluating the efficacy and safety of the investigational molecule RG6042 in people with manifest HD. The 25-month study is testing two dosing regimens compared to placebo - RG6042 once every two months (eight weeks) or RG6042 every four months (16 weeks). The open-label extension of the Phase I/IIa study is ongoing and supports the exploration of the two dosing groups in the GENERATION HD1 study.

Why are we making this change?

- **More data:** The additional number of participants will provide more data to equally evaluate both dosing groups, as well as increase the statistical power of the study. This is a technical study design term that refers to the study's ability to detect a treatment effect. In interactions with the HD community, we have learned the importance of testing both doses - while acknowledging that less-frequent dosing would be less demanding for patients, families and the overall healthcare system in the real-world setting.
- **More confidence:** Prior to GENERATION HD1, a study of this size involving an intrathecally administered investigational medicine has never been conducted in HD. Since the study started recruiting this summer, enrolment has been remarkably rapid worldwide. Based on the interest from the HD community, we are confident that a larger study can fully recruit.
- **More diversity:** Expanding recruitment allows for enrolment of more patients in different parts of the world. US recruitment in particular has exceeded expectations and is now complete. Therefore the additional participants will be enrolled from our network of existing trial sites in nearly 20 countries outside of the US to diversify the study population. Achieving broader global representation in clinical trials is important to our company, as well as health authorities around the world.

We are also pleased to announce that the GENERATION HD1 study is being extended to China. This will be the first time a study testing a Huntingtin-lowering therapy will be brought to the country. Information about Chinese study sites will soon be posted on ClinicalTrials.gov.

The community has been a critical partner throughout the development and progress of the GENERATION HD1 study. The speed of recruitment is thanks to the clinical-trial readiness and commitment of the HD medical and patient community to researching treatment options. We appreciate the partnership with the community and we look forward to providing future study updates.

Sincerely,



Mai-Lise Nguyen, on behalf of the Roche & Genentech HD team
Global Patient Partnership, Rare Diseases