

18 January 2022

Dear global HD partners,

Following your request to receive timely updates about the Roche and Genentech Huntington's disease (HD) research efforts, we are pleased to inform you that the tominersen research programme will continue with a new Phase II trial, based on findings from the GENERATION HD1 study in adults with manifest HD.

As you recall, dosing of tominersen was stopped in the Phase III GENERATION HD1 study in March 2021, based on an overall benefit:risk assessment from the independent data monitoring committee. The GENERATION HD1 and GEN-EXTEND studies have since continued without dosing, and participants have been followed by their physicians for safety and clinical outcomes.

Since our last community update, new exploratory *post hoc* analyses of GENERATION HD1 suggest that low exposure (less frequent dosing) tominersen may benefit younger adult patients with lower disease burden (measured by CAP score, a research tool calculated using a person's age and CAG repeat number). These findings, together with safety data of low exposure tominersen, support the continuation of the development program with a new Phase II clinical trial in younger adult patients with lower disease burden. While the findings are encouraging, confirmation in a randomised, placebo-controlled study is important.

*Post hoc* analyses are conducted after data have been seen, therefore they are not definitive. Additionally, the findings are not statistically significant (i.e., clearly different) versus placebo, so they could represent a chance result.

We had hoped that GENERATION HD1 would meet its primary objectives for the overall patient population in the study, but we are encouraged that there is a path forward to continue tominersen research in a subset of HD patients. We recognise that this may still be disappointing news for some members of the HD community. However, GENERATION HD1 was the first-ever Phase III study testing the huntingtin-lowering theory and the vast amount of data from the study provides valuable information for all HD research.

### Next Steps

- **Tominersen programme continues with plans for a new study:** We are in the early stages of designing a new Phase II clinical trial. The trial intends to explore the safety and efficacy of different doses of tominersen in a younger adult patient population with less disease burden. Specifics about the study are still being determined, including enrolment criteria, planned start date, and study sites. We will share details after they are finalised, including who may be eligible to take part in the study.
- **Current tominersen studies (GENERATION HD1, GEN-EXTEND and GEN-PEAK) will close by the middle of the year:** Participant follow-up in GENERATION HD1 will continue as planned until the last participant completes their last clinic visit, which is expected in March/April 2022. The GEN-EXTEND study will also complete in March/April 2022. The GEN-PEAK study is now considered complete, because Part 1 of the study finished and the optional Part 2 will not be conducted. Closure activities at study sites will be completed by the middle of this year. We understand that study participants may have questions about how this information may impact them. Our team will continue to closely collaborate with study sites throughout the year to support

participants. We encourage participants or family members to reach out to their study team for more information and next steps.

- **Presentation at upcoming community webinars:** Our team has been asked to present at several scientific- and patient-community webinars in the coming days. More information about the tominersen programme and results from GENERATION HD1 will be shared at those events.

We will continue to work in partnership with the HD community as we follow the science and plan for the new clinical trial. We are very grateful for the commitment of all tominersen study participants, their families and study teams. Their contributions led to important scientific insights that unquestionably moved HD research forward.

Sincerely,



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