



Genentech  
A Member of the Roche Group

Dear global HD partners,

As part of our ongoing partnership and following your request to receive important and timely updates about Roche's HD clinical programme, we wanted to share an important update with you. We have tough news to share, and we recognise that it will be even more difficult to receive.

Throughout the Phase III GENERATION HD1 study of tominersen in manifest Huntington's disease (HD), an independent data monitoring committee (iDMC) has been in place. This committee is separate from Roche and Genentech and regularly reviews incoming clinical study data (that Roche and Genentech do not have access to) to review patient safety and assess the balance of potential risk versus potential benefit for study participants.

The committee recently met for a pre-planned review of the latest safety and efficacy data from GENERATION HD1 and made a recommendation about the investigational therapy's potential benefit/risk profile. Based on the committee's recommendation, we will permanently stop dosing with tominersen and placebo in the GENERATION HD1 study. It is important to note that the recommendation is not based on any new emergent safety concern, but on a broad assessment of the benefit/risk of the treatment arms compared to the placebo arm over time.

Unfortunately, whilst this will raise questions in the community, we do not yet have access to the data from this study. What we can share with you at this time is provided in this letter and in our press release. Please find our press release [here](#).

Beyond the GENERATION HD1 study, we have also made the decision to pause dosing in the open-label extension study (GEN-EXTEND) so we can carefully analyse data before deciding how best to proceed. We will continue the Phase I study (GEN-PEAK) because it is a short-term study where participants receive a total of two treatment doses (unlike GENERATION HD1 and GEN-EXTEND). The Roche Natural History Study does not involve any drug treatment and will continue to completion to contribute to building the understanding of HD progression.

In terms of next steps:

- We have notified all of the clinical trial sites and investigators and are now in the process of informing study participants and families. Because our clinical trials are global with sites in several countries, spanning many time zones, this may take some time and we acknowledge

that members of the community might find out at different times and in different ways.

- The studies will remain ongoing (without further dosing in GENERATION HD1 and GEN-EXTEND) and it is intended that study participants will be followed by their physicians for safety and clinical outcomes. We are very grateful for participants continuing in the studies as the additional data generated in this follow-up period will provide valuable information for tominersen and future research.
- It is our intention to provide as much information as we can to the community, which at this time is limited until we have accessed and analysed full data. As data continue to come in across the programme, we will be able to learn about tominersen and what that means in terms of next steps for the programme. We appreciate that there is a strong desire to learn from these data, and we are working with urgency to make this information available.
- In addition to the clinical studies, Roche and Genentech will continue to partner with the global HD community on other ongoing projects.

Most importantly, we would like to acknowledge the tremendous contribution of the families who are participating in these studies, as well as the broader Huntington's community for their collaboration. Without such dedication to research, unraveling the mysteries of HD would be impossible. There are so many valiant efforts ongoing - within our own Roche Group and at other companies - and it remains a tremendously hopeful time for the community.

If you have any further questions:

- For study participants or family members, we encourage them to reach out to their study physician for more information and detailed next steps.
- For members of the broader HD community who have questions about the impact of this news on their personal situation, or need someone to talk to, please reach out to your local HD or care centre, or your local patient organisation.

Sincerely,



David West, on behalf of the Roche/Genentech HD team  
Senior Director, Global Patient Partnership

*Tominersen is an investigational medicine not approved for the treatment of HD by health authorities.*

## Q&A

### **What was the recommendation from the committee?**

- The committee made the recommendation to permanently stop dosing participants in both tominersen and placebo arms in the GENERATION HD1 study
- The decision was based on the results of a pre-planned review of the data from the Phase III study conducted by an unblinded independent data monitoring committee (iDMC). The iDMC made its recommendation based on the investigational therapy's potential benefit/risk profile for study participants.
- It is important to note that the recommendation is not based on any new emergent safety concern, but on a broad assessment of the benefit/risk of the treatment arms compared to the placebo arm over time.

### **When will Roche share information from the study that led to this decision?**

- As these data were reviewed by an independent data monitoring committee, Roche does not yet have access to the full data. After data from the study is available and analysed, we will share learnings with the community. We appreciate that there is a strong desire to learn from these data, and we are working with urgency to make this information available.
- We intend to provide as much information as we can to the community. We will provide updates on significant developments related to the clinical development programme.
- Additionally, as data comes in across the programme, we will be able to learn about tominersen and what that means in terms of next steps for research. We will also share learnings with the community as we are able, so that all can learn and continue to explore potential new treatment options.

### **Does this mean that Roche is leaving the HD space?**

- Roche remains committed to the HD space and our studies are continuing.
- Data from GENERATION HD1 will advance our understanding of tominersen and inform research for other disease modifying treatments.
- In addition to tominersen, the Roche family of companies is investigating gene therapy approaches to treating Huntington's disease.

### **Who can I reach out to for help if I have questions?**

- For participants:
  - If you have any questions about the study and your involvement, we recommend you reach out directly to your study site team
  - If you have any questions on how to access additional support please do reach out to your local HD or care centre (which may be the same as your study centre), or your local patient organisation
- For members of the community:
  - If you have any questions on how to access support please do reach out to your local HD or care centre, or your local patient organisation