20 April 2020

Update on tominersen (RG6042)* Huntington's disease (HD) clinical programme: Recruitment into GENERATION HD1 clinical trial has been completed

Dear global HD patient community,

Today we are pleased to announce that worldwide recruitment has been completed for the Phase III GENERATION HD1 clinical trial. Following the completion of recruitment in the US that was previously announced in October 2019, a total of 791 people living with manifest HD across 18 countries have been recruited to complete global enrollment to the study. 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 this news and update you on what happens next.

This achievement is a result of the HD community's commitment from the beginning, and we are very grateful to all trial participants, their families, the clinical trial sites and staff, and the broader HD community who have supported the design, initiation and recruitment phases of the study.

What happens now that recruitment is complete? When will results be available?

Whilst recruitment completion is exciting news, the diligent work of trial participants and researchers is still just beginning. Each trial participant will undertake tests, medical evaluations, intrathecal injections of either the investigational therapy tominersen or placebo, and use digital monitoring tools over a twenty-five month period. Participants' safety and trial experience will be regularly monitored by researchers at trial sites and Roche/Genentech.

After all the study participants have completed their 25-month trial period, researchers will analyse the overall study data, which we expect sometime in 2022. Should the benefit-risk profile of tominersen appear favourable, data will be submitted to health authorities for consideration as an approved treatment for people with HD.

Is the COVID-19 pandemic affecting tominersen studies?

We would like to reassure you that tominersen studies are ongoing at clinical trial sites around the world, where local guidance allows. The GENERATION HD1 trial is continuing, in collaboration with study participants, clinical trial investigators and health authorities, while also ensuring patient safety and data integrity throughout the studies given the ongoing impact of COVID-19. If trial participants have specific questions about their situation, we encourage them to discuss with their clinical trial site.

During these exceptional times, we continue to consider how we can best support the community and welcome any suggestions. For now, we wanted to thank the community again for its support and interest in the study, which has meant this important milestone could be achieved.

If you have any questions about this update, please do not hesitate to contact us.

Sincerely,

David West
Senior Director, Global Patient Partnership, Huntington's Disease

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Senior Group Director, Global Patient Partnership, Rare Diseases

**RG6042 has a new name: tominersen*

Tominersen is the international non-proprietary name (INN), also known as the generic name, for the investigational molecule most recently known as RG6042.

The INN process is formally run by the World Health Organization and can only be started if an investigational molecule is in the clinical trial testing phase. There are many considerations when applying for an INN, such as using the required word "stem" or name ending that allows healthcare professionals to recognise a similar group of substances (-rsen), sufficient uniqueness from other approved INNs to aid safe prescribing, and if the INN can be utilised and pronounced in multiple languages.

Tominersen is an investigational medicine not approved for the treatment of HD by health authorities. If an investigational medicine is ultimately approved by health authorities, a brand name would then be assigned.

Questions and Answers

1. **What is the GENERATION HD1 study?**

   The GENERATION HD1 study is evaluating the efficacy and safety of the tominersen in people with manifest HD. The 25-month study is testing two dosing regimens compared to placebo - tominersen once every two months (eight weeks) or once every four months (16 weeks).

2. **Can people still join the GENERATION HD1 study?**

   As recruitment for the study has ended, we are unable to enrol any new participants. This allows us to progress the study and complete it as quickly as possible. We will continue to keep the HD community updated on the progress of the study, and will share data results when they are available.

3. **If enrolment has been so strong, why stop short of 801 patients?**

   With 791 people with manifest HD from around the world recruited into the Phase III GENERATION HD1 study, we have reached ~99% of the targeted 801 participants. Given the dynamic situation with COVID-19, we decided to close recruitment at 791 participants globally in order to avoid additional pressure on clinical trial sites who were screening potential participants. We are confident that this number of patients is sufficient to provide the information required to thoroughly assess the benefit-risk profile of tominersen in manifest HD.

   This decision also enables the GENERATION HD1 study to continue to progress within planned timelines.

4. **Can I access tominersen outside of clinical studies?**

   Currently, access to tominersen is only through clinical study participation because the benefits and risks of tominersen are not yet fully understood. This means that we are not able to grant any pre-approval, compassionate use or "right-to-try" requests.

5. **Your clinical studies are in manifest HD. Will you study tominersen in other HD populations (e.g., juvenile onset HD or pre-symptomatic HD)?**

   We recognise the critical medical need for a treatment for HD, especially for people living with severe forms like juvenile onset HD. Once there is sufficient scientific and safety rationale, our team will consult with HD community experts to see how we can explore potential studies of tominersen in populations beyond manifest HD.

6. **How is Roche able to continue this clinical trial during the COVID-19 pandemic?**

   We are working closely with the research teams, trial sites and local authorities to reduce any new risks posed by COVID-19 and ensure the trial can continue as long as it is safe to do so. Our primary focus is ensuring patient safety and data integrity. As such:

   - We advise those participating in clinical studies to discuss individual circumstances with their respective study sites, follow the provided advice, and abide by any guidance issued by local authorities
   - Where patients and families can no longer go into hospital to receive treatment or assessments, research teams will be in close contact over the phone to monitor their health and discuss any potential adverse events or any other issues

   We are regularly reviewing the situations of tominersen trial sites across the globe and will keep you updated as and when new developments occur.