Genentech
A Member of the Roche Group

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June update: Getting to know Roche & Genentech, RG6042 (formerly known as IONIS-HTT$_{Rx}$) Huntington's disease development programme

Dear global Huntington's community,

As many of you are still getting to know us (and vice versa), we would like to take this opportunity to tell you more about our company, philosophy on working with the HD patient community, commitment to collaborate to advance science, and the investigational molecule RG6042 development programme.

Roche & Genentech: one company, two names
Roche is a global biotech company focused on advancing science to improve people's lives. We were founded 122 years ago in Basel, Switzerland and now have a network of more than 94,000 employees working in 100+ countries. We believe in:

- *Investing in and following the science.* We invest more on research and development than any other healthcare company – last year alone over 10 billion Swiss Francs (~$10.5 billion US dollars) – and we've translated that science into approved therapies that have fundamentally changed the way numerous conditions such as cancer, haemophilia, and multiple sclerosis are treated.
- *Innovation and focusing on areas of unmet need.* We aim to transform how diseases can be treated, and we've earned various Health Authorities designations – including 21 breakthrough therapy designations from the US Food and Drug Administration. We certainly hope to transform the way in which HD impacts your families.

Given all the communications about Roche in HD, we want to clarify our company name. Globally and in most parts of the world, you know us as Roche, but in the United States our pharmaceutical division is called Genentech. This is due to the 2009 company integration of Roche and Genentech, a US-based company and the world's first biotech company. What's important for you to know is that Genentech = Roche pharmaceuticals in the US, and we are one company working seamlessly together.

Partnering with the Huntington's disease community
At Roche and Genentech, we are proud of our history of working with patient groups. Our goal is to be a trustworthy partner and for all partnerships to reflect common values of integrity, maintenance of independence, respect, equity, transparency and mutual benefit.

We have dedicated people and teams at both the global- and country-level focused on developing sustainable collaborations with patient communities. Open and constructive dialogue is crucial. This helps you know what can be expected from us, and it helps us better understand how to serve patients, carers and physicians, and to focus our activities on areas that are most beneficial to the communities we serve.

Collaborations in HD to advance scientific progress
Since our partnership with Ionis Pharmaceuticals started five years ago, we have had the privilege of working with leading experts and HD groups to advance the scientific understanding of HD and mutant huntingtin lowering. Collaborations have led to:

- Design of the first-in-human huntingtin lowering clinical study and follow-on open label extension study,
- Optimisation of a mutant huntingtin protein (mHTT) assay or measurement test, and

- Development of clinical and digital endpoints to better understand and measure the impact of HD and disease progression.

Since taking over development of RG6042 from Ionis at the end of 2017, we have and will continue to engage with the community (e.g., patient groups, medical professionals, health authorities, payors, etc.). We commit to incorporating diverse perspectives in the design of the RG6042 development programme, as well as contributing to the advancement of the broader scientific understanding of HD. This is a commitment and journey we share with the HD community.

RG6042 development programme update
The Phase I/IIa study evaluating RG6042 in people with early HD has completed. This is an exciting time for HD, but there is still much work to be done before it can be determined if RG6042 can slow the relentless progression of HD. Big questions exist such as:

- What are the effects on lowering mHTT over a period of time longer than the 13-week Phase I/IIa study?
- Do any unexpected safety concerns emerge when we treat a larger group of people for a longer time?
- Does sustained treatment slow or stop the progression of HD?

We recognise the medical urgency that exists in HD and our team is committed to answering these big questions with other studies in early HD, collaborations with the HD community, and engaging global Health Authorities on the design of a global clinical development programme.

What's happening next?
We are planning studies that can provide Health Authorities with enough data to assess the benefits and risks of the investigational molecule RG6042, while also balancing speed and efficiency.

- A longer, larger global study. As previously announced, we are in the planning stages of a global study designed to detect clinical benefit and evaluate longer-term safety in early stage HD. Details about the study, including eligibility criteria, planned start date, and study sites around the world, will be announced as soon as these aspects are finalised.
- Additional studies. We are also committed to conducting smaller, targeted studies including:
    - The ongoing open-label extension study of RG6042 for those who participated in the Phase I/IIa study. This study looks at the safety and tolerability of longer-term dosing of RG6042, among other measures.
    - A "natural history" study to further understand the role of mHTT and disease progression in the absence of any active treatment. This small study is also in the planning stages and not yet open or enrolling.

We understand that families may wish to seek access to investigational medicines as soon as possible. However, access to RG6042 can only be through clinical trial participation at this time. Because the benefits and risks of RG6042 are not fully understood, we are not able to grant pre-approval, compassionate use or "right-to-try" requests.

With the support of the HD community we are working with urgency and care to develop an appropriate clinical development programme that answers important questions around RG6042. We look forward to providing you with additional updates in September.

Sincerely,

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