15 December 2025

New Phase 1 POINT-HD study starts for selective huntingtin-lowering approach

Dear Huntington's community leaders,

Following your request to receive updates about our research efforts, we are pleased to share that the planned **Phase 1 clinical study for the new investigational medicine RG6496** has started (POINT-HD; NCT07246941).

Our HD research is exploring multiple scientific approaches at the same time. You are most familiar with our ongoing clinical trials, the Phase 2 GENERATION HD2 study of tominersen that will have results in 2026 (NCT05686551) and our Phase 1 gene therapy study (NCT06826612). The POINT-HD study is a **new study** for a **different** investigational medicine.

About the research

RG6496 is a **selective ASO** (antisense oligonucleotide) developed in partnership with Ionis Pharmaceuticals. To make sure it reaches the brain, RG6496 is delivered directly into the fluid that surrounds the spinal cord and brain through an intrathecal injection (commonly called a lumbar puncture).

The goal is to lower levels of the faulty mutant huntingtin protein with minimal impact to the healthy protein. RG6496 is designed to pinpoint a genetic variation on the faulty huntingtin gene copy called a single nucleotide polymorphism (SNP), a tiny spelling difference in the DNA. Because of the worldwide participation in our ongoing HD epidemiology study (NCT06667414), early data suggest approximately 40% of the HD population carries the “Target SNP” in their mutant huntingtin gene copy.

What is the POINT-HD study and where will it run?

This is a Phase 1 study, which means it is the first time RG6496 is being tested in people. The main goal is to study safety and tolerability in people who have **early or mild HD symptoms.** The study has opened in **New Zealand** and **Australia**, and will soon open in **Argentina**. More countries/sites will be activated after we obtain approvals from health and ethics authorities. Further study and site details will be posted on clinical trial registries, such as ClinicalTrials.gov, and on ForPatients.Roche.com.

We are grateful to the HD patient organisations and advisors who shared their expertise to help shape this study. We deeply appreciate the HD community for its continued partnership to enable new research. We look forward to keeping you updated on this study and our broader HD research efforts.

Sincerely on behalf of the Roche HD team,

Mai-Lise Nguyen

Mai-Lise Nguyen
Global Patient Partnership Leader

Additional study information

Who can participate in the POINT-HD study?

The study plans to enroll 40 adults aged **25 to 65** who have **early or mild HD symptoms** and meet additional inclusion criteria. Potential participants will have a screening test for the Target SNP. The trial is only suitable for people who carry the Target SNP in their mutant huntingtin gene copy, because the drug uses the genetic marker to selectively lower mutant huntingtin protein.

How to know if a person carries the Target SNP used by RG6496?

At this time, screening for the Target SNP is only available via our clinical trial enrollment process. Data suggest that approximately 40% of the HD population carries the Target SNP in their mutant huntingtin gene copy.

What does the study involve?

The study has two parts and lasts about two years in total.

- **Part 1** lasts about 7 months and is "placebo-controlled," meaning participants will be randomly assigned to receive a single dose of either RG6496 or a placebo. More participants will receive the study drug than the placebo (specifically, three-out-of-four participants).
- **Part 2** lasts about 13 months and is an "open-label extension" where all participants will receive a dose of the study drug (no placebo will be given in Part 2).

The study involves monthly clinic visits (or clinic visits every other month in Part 2) and periodically completing digital tasks on a study-provided smartphone.

People are encouraged to have someone who can act as their ‘study companion,’ but it is not required.

How can someone participate in the POINT-HD study?

Individuals interested in learning more about the POINT-HD study should speak with their HD specialist or contact Roche Medical Information at MedInfo.Roche.com.