



Dear members of the Huntington's community,

As we approach the upcoming 2017 HDSA Annual Convention, we want to provide an update on the status of the IONIS-HTT_{Rx} program.

Our Recent Clinical Trial Announcement

We recently announced the completion of enrollment in the Phase 1/2a randomized, placebo-controlled, dose escalation study of IONIS-HTT_{Rx} in patients with Huntington's disease. The safety and tolerability profile of IONIS-HTT_{Rx} in the completed cohorts of the Phase 1/2a study supports the continuation of its clinical development. Working with our partner Roche we are starting to prepare an open-label extension (OLE) study of IONIS-HTT_{Rx} for those patients who participated in the Phase 1/2a study.

What the Trial Was Designed to Do

The Phase 1/2a study is a randomized placebo-controlled Phase 1/2 clinical study to evaluate the safety and tolerability of IONIS-HTT_{Rx} in patients in the early stages of Huntington's disease (HD).

What is IONIS-HTT_{Rx}

IONIS-HTT_{Rx} is an investigational drug being developed for the potential treatment of HD. IONIS-HTT_{Rx} offers a unique mechanism to moderate the underlying genetic cause of HD by decreasing the production of the toxic huntingtin protein. IONIS-HTT_{Rx} is an antisense drug designed to reduce the amount of huntingtin RNA in the brain, and with less RNA "message" available, less huntingtin protein is made. IONIS-HTT_{Rx} is designed to reduce the production of all forms of the huntingtin (Htt) protein, which in its mutated variant (mHtt) is responsible for HD. As such, IONIS-HTT_{Rx} offers a unique approach to treat patients, irrespective of their individual HTT mutation.

What Is Next

The dosing in the final patient group continues, and Ionis plans to report top-line results from this study around the end of the year or early next year. Upon study completion, the next step for this program will be to conduct a study to investigate if decreasing mutant huntingtin protein with IONIS-HTT_{Rx} can slow the progression of this terrible disease.

The next studies in the clinical program will be designed with the intent of a robust evaluation of the safety and efficacy of the drug in as short a time frame as possible. Eligibility criteria for future studies have not been established at this time. We will announce plans for additional studies as this information becomes available as well as post study information on how to get involved on HDTrialFinder.org and ClinicalTrials.gov. Future studies for the program will be conducted globally and will include US study sites.

We Are Committed to Developing This Potential Therapy for HD

Ionis and Roche are working vigorously to establish an appropriate, efficient development plan to conduct the trials needed to demonstrate safety and efficacy of IONIS-HTT_{Rx}. We can assure you our number one goal remains our commitment to advancing IONIS-HTT_{Rx} development, a drug that has the potential to transform the treatment of HD.

Sincerely,
Your Ionis Team