12th February 2024

Dear DRPLA community,

Since we established CureDRPLA in 2019, our mission has been to connect families, physicians and scientific investigators to further DRPLA research and work towards a treatment for DRPLA. We tirelessly continue to work towards our mission and there is a lot of work ahead of us. Nevertheless, we have reached an important milestone towards our mission – an upcoming experimental treatment for a pioneer individual with DRPLA in the United States (US) in what is known as an 'n-of-1'.

We are sharing with you the work of the n-Lorem Foundation, a non-profit organization that charitably provides experimental antisense oligonucleotides (ASO) to treat people with rare diseases that affect very few people in the US. This clinical trial is a collaboration between n-Lorem, Dr Jennifer Bain at Columbia University and CureDRPLA. n-Lorem has an investigational ASO specific for DRPLA and it will be tested for the first time in an individual with DRPLA. In DRPLA, there is an accumulation of an abnormal protein (called ATN1) in cells, and therefore reducing the levels of this abnormal protein is thought to be a useful therapeutic approach. ASOs have emerged as a promising strategy in various neurodegenerative disorders because they can block the ability of a certain gene to make a protein.

This n-of-1 clinical trial has progressed positively and is in the final stages of development prior to administering the first dose to the patient. CureDRPLA will provide updates on the development of this clinical trial as soon as we are able, keeping the community fully informed to the extent possible about this. n-Lorem and CureDRPLA are committed to helping as many individuals affected by DRPLA as possible. What we will learn about DRPLA from this trial and the potential treatment will help the entire community as we move forward to helping more individuals with DRPLA.

We remain committed to our mission. For more information about this trial and potential opportunities for DRPLA families, please read the following pages. If you have questions about this clinical trial, please email CureDRPLA at silvia.prades@curedrpla.org.

On behalf of the CureDRPLA team.

ADDITIONAL INFORMATION ABOUT THE DRPLA N-OF-1 CLINICAL TRIAL

This clinical trial is possible because in the US there is a path established by the Food and Drug Administration (FDA) to develop new drugs for rare diseases that affect a very small number of individuals. This path is also referred to as “n-of-1” clinical trials because they are designed for a population of one person.

US-based families

Details are available on the n-Lorem website about their work, who may be eligible to be considered for a new n-of-1 trial and how to apply. Some crucial steps are:

a. The patient must have a genetic test confirming the DRPLA diagnosis and present symptoms attributed to DRPLA.
b. The patient must be in the US for a minimum time to include the first 12 months of treatment.
c. Each family must work with a research physician who submits the application for treatment to n-Lorem on behalf of the patient through the n-Lorem application portal on www.nlorem.org.
d. The physician must be based in the US and affiliated with a US-based institution such as a hospital where the treatment can be done.

Please note that n-Lorem communicates with the physicians that submit cases on behalf of the families and they do not communicate directly to the patient or family. Families interested in exploring this further are encouraged to forward this letter to their treating neurologist or physician. Families struggling to find a physician who is willing to explore this are welcome to contact CureDRPLA and we will do our best to help you find one.

Approvals for treatment are done on a case-by-case basis through n-Lorem. If the case is approved, n-Lorem and the physician will apply to the FDA for permission to do the trial and the FDA will decide whether it can go ahead.

Please visit the following pages for more information:
https://www.nlorem.org/access-treatment/qualifications-for-treatment/
https://www.nlorem.org/access-treatment/application-for-treatment/

Non-US based families

n-Lorem and CureDRPLA are committed to helping families outside the US, but the regulatory pathway for n-of-1 trials is not defined outside the US and it may be different in each country.

The FDA, which regulates approvals for new treatments in the US, was the first regulatory agency to establish a framework to test experimental treatments in one patient at a time with ultra-rare conditions. Other countries are developing similar pathways to ensure experimental treatments can be administered on an n-of-1 basis.

Families living outside the US who are interested in exploring this further are encouraged to forward this letter to their treating neurologist or physician. The next crucial step is to identify a physician who is interested in collaborating with n-Lorem and CureDRPLA to explore what the pathway would be in your country. Once a physician has been identified, the physician should contact n-Lorem to discuss next steps.

Contact information

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