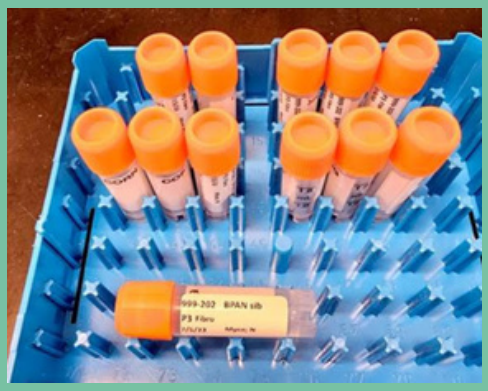
NBIAcure NEWSLETTER

-Fall 2023-

In this issue:

NBIA Disorders Association 2023 Family Conference

This past May, our NBIAcure team attended the NBIA Disorders Association's 2023 Family Conference in Houston. It was wonderful to reconnect with so many families for the first time since the pandemic.



201 blood samples

34 skin biopsies

We were touched and pleasantly overwhelmed by how many families participated in blood and skin biopsy sampling, including so many of the play area volunteers! Everyone's samples arrived safely at OHSU, where they were incorporated into our repository and will promote NBIA research all over the world for years to come.

Our team also had the honor of being designated as a Clinical & Research NBIA Center of Excellence by the NBIA Disorders Association, a distinction that we hold very dear.

Left to right: Kira Anderson, Allison Gregory, Susan Hayflick, Penny Hogarth, Alison Freed, Puneet Rai, Laken Behrndt

At home in Portland, our lab research assistant Helena received the samples and began processing and storage.

CoA-Z Clinical Trial Update

Over the past several of months, we have shared the first trial results with all of the CoA-Z study participants and their families, as well as with the wider NBIA community of families, friends, clinical providers, and supporters.

We had evidence (from earlier research in PKAN mice and human samples) that 4'-phosphopantetheine ("CoA-Z") bypasses the genetic 'roadblock' in vitamin B5 metabolism in PKAN. This leads us to believe that CoA-Z will change the progression of the disease over time. But measuring a real change in the progression of PKAN (or any neurologic disease) usually takes many years, and so the overall goals of the clinical trial were limited to figuring out whether CoA-Z causes any health problems or side effects; and whether it changes a particular measure in blood that we think is a good biomarker of disease. It's important to remember that the clinical trial was not designed to measure a change in the symptoms of PKAN, at least not in a way we could measure in the trial.

Our work so far has been focused on analyzing the data from each participant's first 6 months in the trial. This was the "double-blind" phase of the study during which participants were randomly assigned to take either placebo or one of 3 different doses of CoA-Z, when none of us knew which group a participant was in. Doing a study this way is the best way to know whether any differences we see are due to the CoA-Z itself, or are occurring just by chance. We have been very encouraged by some of the 'big picture' results of the project:

So far, we have found no major health problems or side effects from CoA-Z during the trial.

Perhaps most encouraging, we see a pattern in the biomarker results strongly suggesting that CoA-Z does change a key biological measure of disease, just as we predicted. And we found that this response was dose-dependent, meaning that higher doses tended to produce a bigger response in the biomarker.

In some ways, the biomarker results are the most important because they confirm that CoA-Z is acting on the central vitamin B5 processing problem in PKAN, just as we predicted it would. These results give us real hope that the compound will slow the progression of PKAN, though we still need to figure out the best dose and how early in life it should be started.

At the NBIA Family Meeting in May and in our follow-up communication to CoA-Z study participants, we mentioned the possibility of our doing one or more short follow-up studies of CoA-Z to supplement our clinical trial data. After further data analysis and reflection, we have decided that our current data is strong enough to submit to the FDA without doing any additional clinical studies. If the FDA agrees, then this will be the fastest path to receiving the approvals we need to make the compound more widely available to the PKAN community.

So we are setting aside any plans for follow-up studies for now, instead directing all our efforts to compiling our data to present to FDA. It is a big task, because it not only involves data from the CoA-Z clinical trial, but also from all the related background work going back to 2015: more than 500 pages in length! We don't have the resources to offer further access to CoA-Z before FDA approval, and so we feel this is the best path to make it broadly available to the PKAN community.

We know everyone feels urgency to make CoA-Z available. We feel that too. We also know the community is deeply interested in our progress, and we will continue to update you. We are excited to be at this point, and so grateful to the PKAN community and all our supporters for all your contributions to the CoA-Z study to date.

CoA-Z
PHASE II TRIAL

Penny Hogarth and the OHSU CoA-Z trial team
IRB study 18782

PKAN Gene Therapy Updates and Information Session

Our team at Oregon Health & Science University is in the early stages of a groundbreaking gene therapy project in collaboration with the University of Massachusetts (UMass). We are excited to invite members of the PKAN community to attend an upcoming information session discussing this exciting project. This session will provide a comprehensive overview of the project's potential and its implications for individuals and their families affected by PKAN, including the process of how gene therapy trials work and the steps taken for FDA approval.

During this session, you will have the opportunity to:

- Learn about the latest developments in gene therapy for PKAN
- Hear directly from leading researchers at OHSU and UMass about their work
- Ask questions and engage in discussions regarding the project's potential impact
- Learn how you can support this work

Monday

December 4th, 2023

11:00am (PST)

To ensure a secure and interactive experience, we kindly request that you register in advance. Registered participants will receive the meeting details. However, we understand that some individuals may prefer to remain anonymous. To accommodate this, we will also provide a call-in option.

To register for the information session, please register here or email Sasha Steiner, Senior Director of Development at OHSU Foundation at steinsas@ohsu.edu. Upon registration, you will receive a confirmation email with the session details and login information.

NBIAcure Registry & Repository

Blood samples	550+ samples
Skin biopsies	150+ samples
Brain imaging	500+ MRIs
Brain tissue	40+ samples

Our team at OHSU operates the largest and longest-established repository for NBIA in the world. What does this mean?

The registry and repository consists of clinical data and biosamples from people with NBIA, as well as their family members. It is a standing resource for data and samples for researchers all over the world investigating an NBIA disorder.

Data and samples from our registry have been used by our team and others around the world to make crucial advancements in NBIA research.

Right now, the registry consists of more than 1800 people from over 1000 families affected with an NBIA disorder.