We are pleased to inform the NPC community of an upcoming clinical trial at the NIH to study the safety and tolerability of vorinostat in adults with Niemann-Pick disease, type C1. We plan to begin enrolling patients in September 2014.

This clinical trial is an open label study for 12 patients. "Open label" means that every patient will get vorinostat. There is no placebo, or sugar pill, in this study. Patients will come to the NIH for a total of 3 visits - at baseline, 3 months and at 6 months for this trial. Each visit will last for about 7-10 days. Patients will start taking the study drug while they are at the NIH and will continue taking the study drug when they return home. They will also need to have blood drawn for safety labs every two weeks between visits while they are at home. After the 6 month visit, they will stop taking the study drug and they will be done with the trial.

Vorinostat is a pill that is taken by mouth. The purpose of this study is to test the safety and tolerability of vorinostat when it is given to adults with NPC1. Patients will have blood drawn and will have a lumbar puncture (spinal tap) to collect spinal fluid at each visit to measure how much of the drug is absorbed. Patients will also have tests of hearing, speech, swallowing and movement.

Who is eligible to participate?
To participate in this study, specific "inclusion" and "exclusion" must be met. Participants will be screened first over the phone, to try to establish eligibility for this trial before traveling to the NIH.

To be eligible for this study, patients:
- Must be between 18 years and 60 years of age
- Have a documented diagnosis of NPC1 either by fibroblast testing or NPC1 mutation testing
- Must have their skin fibroblasts treated with vorinostat, and the cells must exhibit a reduction in the filipin lysosomal storage
- Have at least one neurological symptom of NPC1
- Must be healthy enough to travel to the NIH and to be able to comply with the requirements of the protocol
- May be on miglustat, but may not start miglustat or change the dose of miglustat during the trial
- Must be willing to stop all non-prescription supplements, except an age-appropriate multivitamin
- May **not** be taking another drug in the HDAC inhibitor family, including valproic acid, unless stopped at least two months before starting the trial
- May **not** be taking more than two medications to control seizures
- May **not** take anticoagulants (blood thinners) or have a history/presence of a bleeding disorder
- May **not** have active lung disease, oxygen requirement or clinically significant history of decreased blood oxygen saturation, respiratory therapy, or requiring active suction.
- May **not** have a history of taking any form of cyclodextrin in an attempt to treat NPC1

Please note!
If an interested patient passes the phone screening, their fibroblasts (skin cells) will need to be tested to make sure their cells respond to the drug. This will help us predict if the person is likely to have a response to the study drug during the trial. Skin cells are taken by a skin biopsy, which many people with NPC have had before. We will help families schedule the skin biopsy to have the skin cells shipped to the lab for testing. If an individual has already had a skin biopsy at the NIH for the Natural History Study, they probably do not need to have another biopsy for this trial.

What are the risks of this study?
The use of vorinostat in NPC1 is experimental, and the purpose of this protocol is to determine the safety of the drug in this patient group. Vorinostat is approved for use in adults with certain types of cancer. It is not approved for use in children.

Based on prior clinical studies, the most common serious drug related adverse reactions are pulmonary embolism and thrombocytopenia (low platelets). Other side effects include anemia (low red blood cells), nausea, vomiting, diarrhea and high blood sugar. Patients will be monitored for signs and symptoms of these problems during the trial.

This effort is being supported by Notre Dame College of Science and the Ara Parseghian Medical Research Foundation and represents collaboration among investigators from Notre Dame, Broad Institute, Mayo Clinic, Weill Cornell Medical College, Washington University, and the National Institutes of Health.

The assistance of the whole NPC community has been essential in getting this trial started. We appreciate your continued support to work toward our goal of making safe and effective therapies accessible to all individuals with NPC1.

Please email nichdnpc1@mail.nih.gov if you would like more information about the study or if you are interested in participating.