We would like to update the NPC1 community on the work that we are doing at the NIH.

Phase I HPBCD Trial

We continue to escalate the dose of HPBCD. We are currently evaluating 900 mg and will soon investigate 1200 mg. The children and young adults in the trial have been doing well and, with the exception of hearing loss, the drug has been well tolerated. The hearing changes were expected based on the animal testing and these changes range from very minor and not noticeable by the patients or their families, to more significant hearing loss affecting the speech recognition frequencies of hearing at the higher doses. We can measure these hearing changes as soon as 24 hours after the drug is given, but in many cases, there has been at least partial recovery at the next hearing evaluation a month later. In some others, the hearing changes appear to be permanent. We have reviewed the detailed information with the FDA, NIH IRB (ethics review), the NIH Data Safety Review Board, and the families in the trial, and all are in agreement that the potential benefit of HPBCD outweighs the risk, and we will continue to pursue these higher doses in the phase I trial. The Phase I trial is providing critical information for designing the Phase II/III clinical efficacy trial.

Phase II/III HPBCD Trial

We are also extremely excited about the collaboration between Vtesse, Inc. and the NPC research community to develop HPBCD as a therapy for NPC1 disease. As stated in the recent press release, the investigational new drug (IND) application has been transferred to Vtesse and they and their partners have been working closely to design a multi-site and international Phase II/III HPBCD trial for NPC1. We are all very pleased with the progress made over the last few months. In the next few weeks Vtesse will reach out to the NPC community by webinar as promised in early January. More information can be found at http://www.vtessepharma.com/ and families can register on the site to receive updates from Vtesse.

Vorinostat Trial

Six adults have been enrolled in the vorinostat trial at the NIH, and screening and enrollment continues. Interested adults will need to have skin fibroblasts sent for screening if they have not already had a skin biopsy at the NIH. This can be coordinated at home. Thus far the drug is well tolerated and preliminary data analysis is underway.

Hepatocellular Carcinoma in NPC

As many families are aware, a young child with NPC1 was recently diagnosed with hepatocellular carcinoma (HCC, or primary liver cancer). This type of cancer is very uncommon in children and young adults, and based on our review, is not common in individuals with NPC. However, NPC is known to cause cirrhosis of the liver, which is a risk factor for developing cancerous lesions in liver tissue. There are a few case reports describing HCC in NPC patients. We are working with other physicians (liver specialists) in order to try to understand this better. However, please note that this appears to be a very rare complication of NPC.

At this point we are not recommending routine screening for HCC in individuals with NPC1. However we do recognize the fact that this is one more added stress on families and that screening may offer some peace of mind. Thus we are providing the following information.

- Screening for HCC can be done by local pediatricians or primary care providers
- Screening should include a liver ultrasound and a blood draw for an alpha-fetoprotein (AFP) level
- Abnormal results should prompt a referral to a GI or liver specialist

We do think it would be of value if this information were centrally collected. If you do decide to have screening done in your child and are willing to share this information we would be interested in obtaining these clinical results. We will plan on summarizing this information for the NPC community. This summary will not include your personal information. Please contact either Nicole or Lee Ann if you are interested.