Lay summary. The only colony of Niemann-Pick type 1 disease (NPC) cats in the world exists at the School of Veterinary Medicine of the University of Pennsylvania. The disease in cats is very similar to the disease in humans with similar clinical, biochemical, and microscopic abnormalities; it is thought to be a more accurate model of the disease than is the mouse model. We have been treating affected cats with various doses of Cyclodextrin into the spinal fluid and have determined that 30 mg (7.5 mg/ml CSF) intrathecally given every two weeks is sufficient to result in substantial amelioration of neurological disease with only mild-moderate negative effects on hearing. Treated cats are normal at 1 year of age (untreated cats die by 6 months of age).

Also, in collaboration with Dr. Dan Ory, we are evaluating the accuracy of plasma and CSF biomarkers to judge whether the dose we are giving is adequately treating disease or whether the dose should be increased. Current support of the cat colony allows for the production of approximately 15-20 affected cats per year that are enrolled in efficacy, pharmacokinetic, biomarker, and toxicity studies. We are applying to the NNPDF to secure funding in order to expand our breeding colony (six more female heterozygotes) to allow for the production of additional affected cats (n=20 over two years). These cats would then be used in two specific experiments: 1) to evaluate a new delivery method of cyclodextrin into the nervous system through an injection in the lower spine (which is necessary for the phase I and II trials), and 2) to evaluate the efficacy of the histone deacetylase inhibitor (HDAC inhibitor) Vorinostat to treat NPC disease.