

**Lay summary.** During the past 6 months we have completed and submitted for publication (Vite et al , in review) our work on the efficacy and toxicity of 2-hydroxypropyl-beta-cyclodextrin (HPBCD) in the cat model of NPC disease. This manuscript describes our experience injecting HPBCD directly into the spinal fluid every two weeks beginning at 3 weeks of age, which is before clinical signs begin. Injections were made at the back of the head at the cerebellomedullary cistern. Cats treated in this manner did not develop neurological signs of NPC disease during the period of study. These data have been provided to the Therapeutics for Rare and Neglected Diseases (TRND) NPC group and have helped guide the clinical trial in patients. We are now focused on three studies: 1) the efficacy of treating cats presymptomatically by administering HPBCD at the lumbar cistern (the location where children are currently receiving drug), 2) the optimal treatment of NPC disease in cats that are already showing clinical signs of disease – this group of cats is most similar to children which are most commonly diagnosed with NPC disease after signs are already present, and 3) developing methods to decrease hearing loss in cats receiving HPBCD.