

## **Timeline of Development of Cyclodextrin as Therapeutic for Niemann-Pick Disease Type C**

### **“DRAFT FOR DISCUSSION”**

- 1999** Erickson and colleagues report at the NIH conference of minimal efficacy of HPBCD (500 mg/kg) in NPC1 mouse model. Results published in 2001. Most researchers concluded that further experiments would not be productive, given that the very large dose of 500 mg/kg (only 16-fold below the lethal dose) showed no survival benefit and no CD was crossing the Blood Brain Barrier at that level.
- 2004** Mellon and colleagues published Allopregnanolone efficacy study that led to the later discovery of Cyclodextrin as the active therapeutic agent
- 2006** Natural history study on NPC begun at NIH (Porter)
- 2007- 2009**  
HBPCD reported to be efficacious in ameliorating brain disease in NPC mice (by Walkley & Dietschy groups) at 2007 APMRF meeting and in subsequent publications
- **2009** NCGC at NIH (TRND) develops high throughput screens for NPC disease therapy
  - **2009** FDA approved individual use IND treatment (IV) of Hempel twins
- 2010** NINDS workshop “Promising Therapies for Niemann-Pick Type C Disease” which focused on Cyclodextrin as therapy (organized by S. Walkley and D. Tagle)
- **2010** Trappsol given orphan drug status by the FDA
  - **2010** FDA approved IT-CD treatment of Hempel children
- 2011** TRND selected cyclodextrin as agent to move to clinical trial
- **2011** TRND and regulatory FDA-advisory meetings initiated
- 2012** NeuroNext application (for Phase II/III studies) initiated (Ory and Porter)
- **2012** Application by TRND to the FDA for orphan drug designation of Kleptose
  - **2012** IRB and FDA submission (and anticipated approval)
  - **2012** EMEA application to register HPBCD for orphan drug status (TRND and INPDA)
- 2013** **Phase I trial expected to begin**

## **Guide to Acronyms**

APMRF:	Ara Parseghian Medical Research Foundation
EMA:	European Medicines Agency
FDA:	Food and Drug Administration
HPBCD:	2-hydroxypropyl- $\beta$ cyclodextrin
IND:	Investigational New Drug
INPDA:	International Niemann-Pick Disease Alliance
IRB:	Institutional Review Board
IT-CD:	Intrathecal cyclodextrin
NCGC:	NIH Chemical Genomics Center
NeuroNext:	Network for Excellence in Neuroscience Clinical Trials
NIH:	National Institutes of Health
NINDS:	National Institute of Neurological Disorders and Stroke
NNPDF:	National Niemann-Pick Disease Foundation
NPC:	Niemann-Pick type C Disease
TRND:	Therapeutics for Rare and Neglected Diseases (NIH)

Prepared: December 2012