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
EMEA: European Medicines Agency
FDA: Food and Drug Administration
HPBCD: 2-hydroxypropyl-β-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