Overview of Phase I/II Clinical Trial with Trappsol® Cyclo™ for Niemann-Pick Type C

Presentation to NPUK Family Conference

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CTD Holdings, Inc.

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Trappsol® Cyclo™ and NPC.

- Trappsol® Cyclo™ is CTD’s proprietary formulation of Hydroxypropyl Betacyclodextrin (HPβCD)

- The exact mechanism of how Trappsol® Cyclo™ works is not known but animal studies have shown it and other HPβCDs are able to release trapped cholesterol from NPC cells.
A Little History….

- **2007:** Dr. Benny Liu working in the lab of Dr. John Dietschy showed in a mouse model of NPC that HPβCDs could prolong life, delay the onset and progression of NPC symptoms, and normalize cholesterol in the brain, liver and other organs.

- **2007:** The Hempel family contacted Dr. Liu to inquire about the use of HPβCDs in the treatment of their twin girls affected by NPC -- which eventually led them to CTD.

- **2009:** With the Hempels, Dr. Hastings and team provided Trappsol® Cyclo™ with an approved IND to Hempel twins. Intravenous administration.

- **2010:** Other families joined in intravenous compassionate use of Trappsol® Cyclo™, first in Brazil, then other countries. In the same year, Trappsol® Cyclo™ was provided to the Hempel twins intrathecally, others soon followed.
A Little History….

• CTD collected and analyzed data from compassionate use programs with Trappsol® Cyclo™ in the US and internationally. Learned that safety profile allowed physicians to administer Trappsol® Cyclo™ intravenously for up to six years (at the point of analysis), and that NPC symptoms in some patients were either stabilized or reversed. These included neurologic symptoms. Adverse events were minor, and managed with standard care.

• 2015: CTD met with 12 families at the NNPDF meeting in Chicago, and listened to recommendations, one of which was to launch a formal intravenous trial.

• CTD chose to pursue an IV route of administration in its formal clinical trials. Met with regulatory officials in the US and EU to discuss a plan, and gained approval to launch two complementary clinical trials in the US and in the EU.

CTD has Orphan Drug Status for Trappsol® Cyclo™ in the US and EU, and has Fast Track Designation in the US.
Phase I/II EU Study in a Nutshell

- Intravenous administration of Trappsol® Cyclo™ over 8 hrs. every two weeks
- 3 dose groups (1500 mg/kg; 2000mg/kg; 2500 mg/kg), no placebo group
- 48 week treatment period
- 12 patients to fully enroll, ages 2 yrs and older
- Multi-center study: UK, Sweden, Italy, Israel (announced 18 Sept 17)
- Coordinating Investigator: Dr. Reena Sharma, SRTF
What Will We Evaluate in the Study?

• Safety and Efficacy
• Pharmacokinetics, plasma
• Pharmacodynamics, serum, cholesterol precursors and metabolites
• Will measure Trappsol® Cyclo™ in cerebrospinal fluid at timed intervals
• Will examine liver size, neurological symptoms and markers, lung changes, hearing, and overall quality of life
Principal Investigators and Co-Investigators:

- Dr. Reena Sharma (Salford Royal Trust Foundation, UK)
- Dr. Robin Lachmann (UCL, UK)
- Dr. Martin Paucer and Dr. Karin Naess, (Karolinska, Sweden)
- Dr. Bruno Bembi (Udine, Italy)
- Dr. Orna Staretz (Beersheva, Israel)
- Dr. Ronen Spiegel (Afula, Israel)

With Senior Clinical Advisor to the EU trial
- Dr. Caroline Hastings
Phase I US Study in a Nutshell

- Intravenous administration of Trappsol® Cyclo™ over 8 hrs. every two weeks
- 2 dose groups (1500 mg/kg or 2500 mg/kg), no placebo group
- 7 doses over 14 week treatment period
- 12 patients to fully enroll, 18 years and older
- 1 site --- Children’s Hospital Oakland
- Lead investigator: Dr. Caroline Hastings
- Co-Investigator: Dr. Benny Liu
What Will We Evaluate in the Study?

• Safety

• Will also look at plasma portion of blood to understand how long Trappsol® Cyclo™ remains in the blood and at what concentration

• Will look at serum portion of the blood to understand effect of Trappsol® Cyclo™ on cholesterol synthesis and metabolism

• Will measure Trappsol® Cyclo™ in cerebrospinal fluid at timed intervals

• Evaluate liver size and other features, cholesterol precursors and metabolites

• Will measure neurologic and cognitive symptoms, hearing, respiratory changes and overall quality of life
Status – US and EU Trials

EU Trial

First patient dosed – Announced on July 19, 2017
Salford, Dr. Reena Sharma

Enrollment continues

Final data from EU trial expected by end of 2018

US Trial

Recent modification of protocol to allow those on stable dosing of Miglustat to participate

First patient expected to be enrolled in the near term
Our Partners
Our Family Liaisons

- Ms. Jackie Imrie  Jackie@jicltd.co.uk
- Ms. Shannon Reedy  Shannon.Reedy@hotmail.com

Families in the US and EU are also invited to speak with Dr. Caroline Hastings: chastings@mail.cho.org  510-428-3631
Special Thanks To

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