

# Phase I Study using Trappsol<sup>®</sup> Cyclo<sup>™</sup>

Initial findings from a Phase I clinical trial using hydroxypropyl beta cyclodextrin intravenously in Niemann-Pick Type C patients

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Niemann-Pick Disease Type C is a rare genetic disorder characterized by cholesterol accumulation in every cell of the body. Hydroxypropyl beta cyclodextrins (HPBCDs) have been found in pre-clinical studies to release cholesterol from cells, normalize cholesterol homeostasis, delay symptom onset, and increase lifespan. We present data from the first four patients in a Phase I study using Trappsol<sup>®</sup> Cyclo<sup>™</sup>, the proprietary formulation of HPBCD of CTD Holdings. The trial is randomized, double-blinded, with no control group (NCT02939547). Patients received either 1500 mg/kg or 2500 mg/kg of the drug intravenously over 8 to 9 hours every two weeks for 7 doses total. Results presented remain blinded to dose. Individual and cumulative safety data to date show the drug to be well tolerated. In particular, no clinically significant or permanent hearing problems were observed from intravenous dosing of Trappsol<sup>®</sup> Cyclo<sup>™</sup> as measured by standard audiometric testing. Lathosterol, a validated serum biomarker reflecting whole body cholesterol synthesis, was reduced after intravenous administration of the drug, accompanied by a concomitant rise in cholesterol metabolites (24S-, 25-, 27-, and 4B- hydroxycholesterol), suggesting that trapped cholesterol is released and cleared from cells, and cells are responding by suppressing cholesterol synthesis. Cerebrospinal fluid (CSF) sampling at timed intervals following the start of intravenous administration showed increasing levels of drug in the CSF up to 12 hours, indicating that the drug crosses the blood-brain-barrier. Measurements of CSF tau taken at baseline and after the 7<sup>th</sup> dosing were reduced on average of 30% while two other biomarkers of neuroinflammation, TNF-alpha and GFAP, were below limits of detection at baseline and after the 7<sup>th</sup> dose. Results on liver ultrasound and elastography taken at baseline and after the 7<sup>th</sup> dose will be presented. Overall, initial findings and clinician impressions are encouraging.