FACTSheet NPC Therapies

Therapy and description:	Trappsol® Cyclo™	IB1001 (N-acetyl-L-leucine)	Arimoclomol
	• Trappsol® Cyclo™ is a proprietary form of hydroxypropyl beta cyclodextrin from Cyclo Therapeutics with a mechanism of action that releases cholesterol trapped in cells and that can normalize cholesterol metabolism. • Clinical Trials: To date Trappsol Cyclo has been studied in 3 formal clinical trials for NPC (Clinical Trials.gov NCT02939547, NCT02912793 and NCT03893071). • Expanded Access for NPC: Trappsol Cyclo is currently in use on a compassionate basis in multiple countries in Europe, Israel, and Taiwan. • Other indications: An Expanded Access program for late-onset Alzheimer's Disease (NCT03624842) was completed, paving the way for an Advice meeting with FDA on a formal program. • Regulatory Designation: Trappsol Cyclo has received Orphan Drug Designation for NPC in the US and Europe, and Fast Track designation in the US.	• IB1001 is a small-molecule (modified amino acid) N-acetyl-L-leucine. • IB1001's mechanism of action known to be multi-modal, including normalization of neuronal membrane potential, modulating glucose and antioxidant metabolism, reducing lysosomal volume, and the reduction of neuroinflammation in the brain. Due to this multi-modal MOA, IB1001 is believed to have rapid symptomatic benefit, as well as disease-modifying, neuroprotective effects. • Clinical Trials: To date IB1001 has been studied in 1 clinical trial in NPC (NCT03759639). No clinical trials are in the recruiting stage. • Other indications: IB1001 is also being studied in clinical trials for treatment of GM2 Gangliosidosis (Tay-Sachs and Sandhoff) and Ataxia-Telangiectasia. • Regulatory Designations: IB1001 has received Orphan Drug Designation for NPC in the US and Europe and Rare Pediatric Disease Designation and Fast Track Designations for NPC.	• Arimoclomol is an investigational drug being developed as an oral formulation for the treatment of NPC; currently under FDA review. The mechanism of arimoclomol is believed to be amplification of the production of heat shock proteins which rescue misfolded proteins, aid in the degradation of aggregated proteins, and promote lysosomal function. • Clinical Trials: To date, arimoclomol has been studied in several Phase I trials and one pivotal Phase II/III trial in NPC. • Other indications: Arimoclomol is currently also being studied for the treatment of Amyotropic Lateral Sclerosis, Inclusion Body Myositis and Gaucher Disease.
How is it administered?	• Intravenous infusion given every 2 weeks. Both hospital and home infusions being done depending on the clinical study.	• Sachet (mixed with water) taken orally two to three time daily depending on patient's age/weight.	• Capsule taken orally 3 times a day. Capsule contents can be dissolved in water, soft foods, or administered via feeding tube.
Clinical Trials or Expanded Access Programs available for enrollment:	• A Phase I "open-label" trial is ongoing with home infusions in adults where patients demonstrated stability or improvement as measured by the 17-point NPC-CSS at about 1 year. • A Phase I/II trial in patients age 2 and older is nearing its completion with topline results expected to be announced soon. • A Phase III trial has been approved by FDA, expected to begin enrollment soon, sites to be announced on ClinicalTrials.gov in near term. • Cyclo Therapeutics reviewing Expanded Access program in light of increasing requests.	• A Phase II clinical trial for patients ages 6 and older with NPC has been completed. Topline results demonstrate a statistically significant and clinically meaningful improvement on the primary endpoint, the Clinical Impression of Change in Severity (CI-CS), and secondary endpoints including SARA (Scale for Assessment and Rating of Ataxia) and the CGI-C (Clinical Global Impression of Change scale). IB1001 was very well-tolerated, with no serious adverse reactions. • Extension Study of Phase II Trial – a 2-year extension – ongoing to assess neuroprotective, disease-modifying effects. • No clinical trials are currently in recruiting stage, including any Expanded Access Programs. • We are awaiting to learn next steps in the clinical development program.	• A Phase II/III clinical trial (NCT02612129) has been completed in patients 2-19 yrs old with NPC. The top line results observed evidence of slowing of disease progression by an abbreviated 5-point domain. • There are no ongoing clinical trials at this stage; an expanded access program is available for eligible NPC patients. • A New Drug Application (NDA) for the treatment of NPC was accepted by the FDA under Priority Review with a target action date of June 17, 2021 under the Prescription Drug User Fee Act (PDUFA). • Market Authorization Application (MAA) for approval was submitted in November to the European Medicines Agency (EMA).

Information above was provided to NNPDF by each company for our webinar on February 18, 2021.

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