Encouraging preliminary 6-month results in the Phase I/II trial of Batten-1 in Batten disease (CLN3)

- *Reduction of neurofilaments, a biomarker of neuronal death, after 6 months of treatment*
- *Stabilization of motor symptoms for treated patients in comparison to the decline expected with the natural disease course*

Lyon, France – Austin, Texas, United States – 14 June 2023 – 7.30am CEST – Theranexus, a biopharmaceutical company innovating in the treatment of rare neurological diseases, and the Beyond Batten Disease Foundation (BBDF), have today announced encouraging preliminary results achieved with their drug candidate, Batten-1, in juvenile Batten disease as part of the Phase I/II ongoing trial after 6 months of treatment. These preliminary results suggest an effect of Batten-1 on neuronal death and initial signs of clinical efficacy.

Theranexus and BBDF are conducting a Phase I/II trial of their drug candidate in six patients with Batten disease (CLN3) aged 17 years and over who are due to receive treatment over a 24-month period. The first results of this Phase I/II trial after 9 weeks of treatment showed a good tolerability and pharmacokinetic profile[1] for Batten-1. The new preliminary results, achieved after 6 months of treatment, show **an average 17% decline in neurofilament light chain (NfL)** levels in the blood of dosed patients. Neurofilaments are a recognized biomarker of neurodegeneration[2]. Moreover, **motor symptoms assessed by the modified physical subscale of the disease-specific UBDRS[3] did not progress over the same period** (mean score of 31.8 after 6 months of treatment as against 32.4 at baseline), whereas according to data available describing the natural course of the disease, this clinical score should have progressed[4] by around one point in these patients. Lastly, the drug candidate continues to show a good tolerability profile after six months of treatment.

For **Theranexus' CEO Mathieu Charvériat**, "*In our Phase I/II trial on Batten-1 in patients aged 17 and over and unfortunately at a rather advanced stage of the disease, we measure the levels of neurofilaments NfL and motor symptoms via the modified UBDRS, which provide data indicative of Batten-1's efficacy. Today we present our initial six-month results, which confirm the strong therapeutic potential of Batten-1 in Batten disease owing to its ability to reduce neuronal death and consequently the progression of the disease".*

In conclusion, Theranexus' Chief Medical Officer Marie Sebille added: *«These preliminary results are very promising for this devastating disease for which there is currently no treatment. They reveal a convergence of positive signals with the reduction of neurofilaments and stabilization of motor symptoms after six months of treatment. This offers a great hope for children affected by this disease and their families".*

The preliminary six-month results will be presented to the scientific and medical community at NCL2023, the 18th International Congress on Neuronal Ceroid Lipofuscinoses to be held in Hamburg, Germany from 26 to 30 September 2023.

[1] https://www.theranexus.com/images/pdf/Theranexus_PR_Batten-1_Program_VDEF.pdf
[2] Dang Do AN, et al. Neurofilament light chain levels correlate with clinical measures in CLN3 disease. Genet Med. 2021 Apr;23(4):751-757
[3] Unified Batten Disease Rating Scale
[4] An increase of this score corresponds to a worsening condition of the patient

About Batten-1

Batten-1 is a novel and exclusive proprietary drug containing the active ingredient miglustat. The mechanism of action of this substance blocks the accumulation of glycosphingolipids and neuroinflammation, thus significantly reducing neuronal death that contributes to a progressive loss of function in patients. For patients over 17 years of age in the Phase I/II trial, the product is administered in solid form. In the Phase III trial, it will be administered in a liquid form better suited to pediatric patients.

Phase I/II trial design: this is an open-label trial involving 6 patients over 17 years of age with CLN3 Batten disease, treated with miglustat up to 600 mg/day for a 2-year period. The primary endpoint is patient safety and tolerability, assessed using reports of adverse effects, biological tests and ECG, as well as the pharmacokinetics of miglustat. The secondary endpoints include efficacy monitoring: Unified Batten Disease Rating Scale, visual acuity, measurement of brain volumes by MRI and measurement of the thickness of the neuronal layer of the retina by optical coherence tomography scans. Administration of Batten-1 in escalating doses with a maximum of 600 mg/day was well tolerated, with no severe side effects observed causing treatment discontinuation. The most commonly reported adverse events are reversible gastrointestinal effects of often light to moderate severity, thus demonstrating the good tolerability profile of Batten-1 in this population. Batten-1 will continue to be assessed in these patients treated over a 24-month period. Further information about the trial is available on https://clinicaltrials.gov/ct2/show/NCT05174039.

About Batten disease

Juvenile Batten disease, also known as Spielmeyer-Vogt or CLN3 disease, is a rare, fatal, inherited disorder of the nervous system for which there is no treatment or cure. Juvenile Batten disease belongs to a group of disorders referred to as neuronal ceroid lipofuscinoses (NCLs). Over 400 different errors in 13 genes have been attributed to various forms of NCL, which differ from one another primarily by when symptoms first appear. The first symptom in the juvenile form, progressive vision loss, appears between the ages of 4 and 6 and is followed by cognitive disorders, behavioral disorders, and motor disorders. Seizures commonly appear within 2-4 years of the onset of disease. Over time, patients continue to decline mentally and physically. Eventually, those affected become wheelchair-bound, are bedridden, and die prematurely.

Juvenile Batten disease is always fatal; usually by the late teens to early 20s. In the United States and Europe, the juvenile form is the most common of the NCLs, which together, affect nearly 2,000 patients[5]. In pathophysiological terms, interactions between neurons and glial cells play key roles in the emergence and progression of all the NCLs.

About Beyond Batten Disease Foundation

Beyond Batten Disease Foundation (BBDF) is the world's largest nonprofit organization dedicated to funding research for a treatment and cure for juvenile (CLN3) Batten disease. Since its inception in 2008, over $35 million has been invested in research by leveraging donations, co-funding and strategic partnerships. BBDF is spearheading a unique, cohesive strategy, incorporating independent scientific resources and collaboration with related organizations to drive research in juvenile Batten Disease[6]. Today there is a treatment in sight. BBDF funded research has discovered a drug – Batten-1 – that slows the progression of the disease in Batten models. More information can be found at www.beyondbatten.org.

About Theranexus

Theranexus is an innovative biopharmaceutical company that emerged from the French Alternative Energies and Atomic Energy Commission (CEA). The company has a unique platform for the identification and characterization of advanced therapy drug candidates targeting rare neurological disorders and an initial drug candidate in clinical development for Batten disease. Theranexus is listed on the Euronext Growth market in Paris (FR0013286259- ALTHX).

[5] National Organization for Rare Disorders (NORD)/Orphanet

[6] Settembre et al, TFEB links autophagy to lysosomal biogenesis, Science 2011

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