Theranexus and BBDF win FDA approval on efficacy endpoints for the Phase III trial to evaluate Batten-1 in CLN3 Batten disease

- Phase III's primary endpoint will be visual acuity, with secondary endpoints including assessment of cognitive and motor functions,
- The FDA confirmed that this sole Phase III trial would secure Batten-1 approval for Batten CLN3 disease.

Lyon, France – Austin, Texas, United States – 9 May 2023 – 7.30am CEST – Theranexus, a biopharmaceutical company innovating in the treatment of neurological diseases, and the Beyond Batten Disease Foundation (BBDF), have today announced receipt of approval from the Food and Drug Administration (FDA) for the design and primary and secondary endpoints of the pivotal Phase III trial for Batten disease CLN3, at a meeting with the Division of Rare Diseases and Medical Genetics (DRDMG) held in mid-April.

"*We are delighted with the constructive discussions we had with the FDA on defining the endpoints of Batten-1 and the design of our pivotal Phase III trial. Its valuable guidance allows us to get fully prepared for the trial launch,*" explained **Theranexus' Chief Medical Officer Marie Sebille.**

"*We would like to thank the FDA for its support, which is fundamental to the development of our Batten-1 drug candidate, the only asset in active clinical development for Batten disease (CLN3). Our pivotal Phase III trial will enable us to gain approval for Batten-1, and also deliver rich news flow throughout the duration of the Phase III trial thanks to the parallel open-label patient cohort. More generally, we have no doubt that we can deliver a therapeutic response for patients suffering from Batten disease,*" added **Theranexus' CEO Mathieu Charvériat.**

Theranexus and BBDF worked with the FDA's DRDMG to define the following criteria for the protocol of the Phase III multicenter trial for evaluating Batten-1 in patients with juvenile Batten disease (CLN3):

- The trial will be a randomized, double-blind study conducted versus placebo in 2 parallel groups to assess the efficacy of Batten-1 at a dose of 15 mg/kg and up to 600 mg/day for a 2-year treatment period,
- The target population will be a pediatric cohort involving approximately 60 patients aged 4 to 16 years, with randomization stratified into 3 age groups of 4 to 8 years, 9 to 12 years and 13 to 16 years to achieve suitable representation for all age groups assessed,
- The primary endpoint will be visual acuity, measured using either the quantitative LogMAR[1] scale, or a qualitative scale in the most impaired patients for whom quantitative assessment is not possible,
- The secondary endpoints will include cognitive function, assessed by the Verbal Comprehension Index from the Wechsler Intelligence Scale for Children according to age, motor function assessed by a selection of motor items from the Unified Batten Disease Rating Scale (UBDRS), and visual function, assessed by OCT scan,
- An assessment of functional ability in everyday activities and a Quality-of-Life measurement will also be performed.

An additional open-label cohort of 9 patients representative of the different age groups of the target population will be enrolled in parallel. This will allow us to enrich the statistical analysis plan, in particular in comparison with natural history data, for the primary and secondary endpoints on trial completion, and produce interim results every 6 months, including measurements of biomarkers (notably, glycosphingolipids given their abnormal accumulation and role in neuronal death) and efficacy data on the same criteria as the main 60-patient cohort.

[1] LogMAR is used to express visual acuity in order to perform statistical calculations such as mean, standard deviation for visual acuity, etc.

Patient enrollment should begin by the end of 2023. The trial will run in parallel in several centers internationally, including the United States and Europe. Provided positive results are registered, the FDA confirms that a sole Phase III trial as defined above would secure approval of the Batten-1 candidate in CLN3 Batten disease. The company's goal is to use the results of this trial to win product approval in both the United States and Europe.

As a reminder, the Phase III trial follows on from Phase I/II in which initial results showed good safety and tolerability of miglustat in a population of CLN3 patients over 17 years of age, and a pharmacokinetic profile in line with expectations (see press release of 5 January 2023[2]).

In conclusion, Craig Benson, Chair of the Beyond Batten Disease Foundation, said: *"We are absolutely delighted to have had such a constructive and productive meeting with the FDA enabling us to initiate the Phase III clinical trial for Batten-1 in the near future. Patients and their families are eagerly awaiting the launch of enrollment for this trial in a disease for which there is currently no available treatment. This trial is a source of tremendous hope for them."*

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. 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, and brain MRI and 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 which is followed by personality changes, behavioral problems, and slowed learning. 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. Psychiatric symptoms or psychosis can appear at any time.

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 3,000 patients[3]. 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[4]. 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.

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[2] https://www.theranexus.com/images/pdf/Theranexus_PR_Batten-1_Program_VDEF.pdf

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

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

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).

More information at
http://www.theranexus.com
Click and follow us on Twitter and LinkedIn

Contacts

THERANEXUS
Thierry Lambert
Chief Financial Officer
contact@theranexus.com

NEWCAP
Théo Martin/Pierre Laurent
Investor Relations
+33 (0)1 44 71 94 97
theranexus@newcap.eu

FP2COM
Florence Portejoie
Media Relations
+ 33 (0)6 07 76 82 83
fportejoie@fp2com.fr