Press Release

Pharnext reports the end of double-blind treatment in PREMIER trial, the pivotal Phase III clinical trial of PXT3003 in Charcot-Marie-Tooth disease type 1A

PARIS, France, August 24, 2023, 08:30 am CET – Pharnext SA (FR001400GUN7 - ALPHA) (the "Company"), an advanced late-clinical stage biopharmaceutical company developing novel therapeutics for neurodegenerative diseases with high unmet medical need, today reports that the last patient randomized to the double-blind period of the **PREMIER** trial, pivotal Phase III clinical trial of its lead drug candidate, PXT3003, in development in Charcot-Marie-Tooth disease type 1A (CMT1A), has finished the last visit.

The **PREMIER** trial, initiated in March 2021, is an international, randomized, double-blind, two-arm placebo-controlled, pivotal Phase III study, where the primary objective is to evaluate the efficacy and safety of PXT3003 versus placebo in mild-to-moderate CMT1A patients, over a 15-month double-blind period. The dose of PXT3003 tested in the **PREMIER** trial corresponds to the high dose (HD) tested in the prior Phase III clinical study, the **PLEO-CMT** trial, and its ongoing open-label extension Phase III study, the **PLEOCMT-FU** trial.

As agreed with regulatory agencies, the primary efficacy endpoint is the Overall Neuropathy Limitations Scale ('ONLS') which measures functional motor disability. A total of **387** patients with mild-to-moderate CMT1A, were enrolled in the **PREMIER** trial (exceeding the initial enrolment target of 350 subjects as defined in the study protocol):

- **153** in the United States,
- **183** in Europe,
- **39** in Canada,
- **12** in Israel.

After completion of the 15-month long double-blind period of the **PREMIER** trial, patients were offered continued treatment by rolling over into an open-label extension period named **PREMIER-OLE** (Open-Label Extension). Thus, CMT1A patients randomized in the **PREMIER** trial have the opportunity to receive PXT3003 HD until the treatment is commercially available, should PXT3003 be approved in the US and Europe, respectively by the FDA and the EMA. The first patient entered the **PREMIER-OLE** period in September 2022.

As of August 18th, 2023, out of the 387 patients randomized in the **PREMIER** trial:

- **42** early-terminated the double-blind period of the **PREMIER** trial,
- **315** are in the open-label extension period, **PREMIER-OLE**, and are all treated with PXT3003 HD,
- **25** did not enroll in the **PREMIER-OLE** period after completing the double-blind period of the **PREMIER** trial,
- **5** early-terminated the **PREMIER-OLE** period.

The **PREMIER** trial is progressing as initially planned and Pharnext is making a diligent effort to carry out this ambitious program. The topline results announcement of this study is planned in Q4 2023.

Gilbert Wagener, CMO of Pharnext, said: "*We are pleased to inform patients with Charcot-Marie-Tooth type 1A, all our investigators and the scientific community that we have completed the double-blind treatment period of our global Phase III PXT3003-06 study in patients with moderate CMT1A. This is an important milestone to prepare the NDA and MAA of PXT3003 for the treatment of CMT1A patients. The successful completion of this program will enable us to offer treatment to patients who are left without treatment options now.*"

Melissa Israel, VP of Clinical Operations of Pharnext, said: "*Timely completion of recruitment and treatment is particularly challenging in orphan disease clinical trials. We would like to thank all patients, patient advocacy organizations, investigators, and all clinical research staff for their contribution to the successful conduct of the study.*"

Hugo Brugière, CEO of Pharnext, said: "*We are now looking forward to the analysis of the primary and secondary endpoints by Q4 2023 that will build the basis for the NDA and the MAA and unlock the potential of value creation of the company*."

About Charcot-Marie-Tooth Disease Type 1A ('CMT1A')

Charcot-Marie-Tooth ('CMT') disease encompasses a heterogeneous group of inherited, severe, debilitating, progressive and chronic peripheral neuropathies. CMT1A, the most common type of CMT, is an orphan disease with a prevalence of 1/5000 people affecting about 150,000 people in Europe and the U.S. and about 1,500,000 people worldwide. The genetic mutation responsible for CMT1A is a duplication of the PMP22 gene coding for a peripheral myelin protein. The duplication of this gene results in overexpression of the PMP22 protein and failure of Schwann cells to produce normal myelin (neuronal sheath). The lack of a normal myelin structure and function leads to abnormal peripheral nerve conduction and axonal loss. As a result of peripheral nerve degradation, patients suffer from progressive muscle atrophy in both the legs and arms causing problems with walking, running and balance as well as abnormal hand functioning. They might also suffer from mild to moderate sensory disorders. First symptoms usually appear during adolescence and will progressively evolve throughout life. Patients with the most severe form of CMT1A end up in wheelchairs, representing at least 5% of cases. To date, no curative or symptomatic medications have been approved and treatment consists of supportive care such as orthotics, leg braces, physical and occupational therapy or surgery. More information can be found at https://pharnext.com/en/disease/charcot-marie-tooth.

About PXT3003

PXT3003 is a novel fixed-dose synergistic combination of baclofen, naltrexone and sorbitol formulated as an oral solution given twice a day. The three individual components of PXT3003 were selected to downregulate the overexpression of PMP22 protein, leading to improvement of neuronal signaling in dysfunctional peripheral nerves that are an essential part of the pathophysiology of this disease. PXT3003 could also have a positive effect on other cellular types of the motor unit such as the axon (direct protection), neuromuscular junctions or muscle cells. PXT3003 has shown promising and consistent results across preclinical and clinical studies in Phase II and Phase III (PLEO-CMT and PLEO-CMT-FU). More information can be found at https://pharnext.com/en/pipeline/pxt3003.

About the PREMIER Trial

The PREMIER trial is an international, randomized, double-blind, two-arm placebo-controlled, pivotal Phase III study, evaluating the efficacy and safety of PXT3003 versus placebo in mild-to-moderate CMT1A patients, over a 15-month period. The dose of PXT3003 tested in the PREMIER trial corresponds to the high dose ('HD') tested in the prior Phase III trial ('PLEO-CMT'). As agreed with regulatory agencies, the primary efficacy endpoint will be the Overall Neuropathy Limitations Scale ('ONLS') which measures functional motor disability. The secondary endpoints include the following outcome measures: 1) 10-Meter Walk Test ('10mWT'), 2) Quantified Muscular Testing (bilateral foot dorsiflexion dynamometry), 3) Patient Global Impression of Severity ('PGI-S'), 4) Patient Global Impression of Change ('PGI-C'), 5) Charcot-Marie-Tooth Neuropathy Score, version 2 ('CMTNS-v2'), and 6) Quantified Muscular Testing (hand grip). Safety and tolerability will be monitored throughout the study. Further information on the PREMIER trial can be found on the ClinicalTrials.gov website (study identification number: NCT04762758) here.

About Pharnext

Pharnext is an advanced clinical-stage biopharmaceutical company developing novel therapies for neurodegenerative diseases currently without satisfactory therapeutic solutions. Pharnext has a first-in-class drug candidate, PXT3003, in development for Charcot-Marie-Tooth disease type 1A (CMT1A), a rare, debilitating, inherited peripheral neuropathy. PXT3003 benefits from orphan drug status in Europe and the United States. In 2018, PXT3003 completed a Phase III clinical trial, the PLEO-CMT trial, with encouraging topline results. This trial was followed by an open-label extension study, the PLEO-CMT-FU trial, with 120 patients continuing treatment with PXT3003. Long-term data suggest a sustained benefit, safety, and efficacy, after 5 years of total trial time. An international pivotal Phase III study of PXT3003, the PREMIER trial, is currently ongoing with 387 CMT1A patients enrolled. PREMIER topline results are expected in Q4 2023. PXT3003 originated from the Pleotherapy™ R&D approach. Pharnext draws the attention of investors to the financial and other risk factors detailed in its financial reports. More information can be found at www.pharnext.com.
Pharnext is listed on the Euronext Growth Stock Exchange in Paris (ISIN code: FR001400GUN7).

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