Press Release

Pharnext unveils the latest progress of the PREMIER trial, pivotal Phase III clinical trial of PXT3003 in Charcot-Marie-Tooth disease type 1A

PARIS, France, February 2nd, 2023, 08:30 am CET – Pharnext SA (FR001400BV89 - ALPHA) (the "Company"), an advanced late-clinical stage biopharmaceutical company developing novel therapeutics for neurodegenerative diseases with high unmet medical need, today provides an update on the **PREMIER** trial, pivotal Phase III clinical trial of its lead drug candidate, PXT3003, in development in Charcot-Marie-Tooth disease type 1A (CMT1A).

The **PREMIER** trial, initiated in March 2021[1], 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 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 will be the Overall Neuropathy Limitations Scale ('ONLS') which measures functional motor disability. A total of 387 patients with mild-to-moderate CMT1A, was enrolled in the **PREMIER** trial (exceeding the initial enrolment target of 350 subjects as defined in the study protocol)[2]: **153 in the United States, 183 in Europe, 39 in Canada and 12 in Israel**.

The 15-month double-blind phase of the **PREMIER** trial is followed by an open-label extension phase named **PREMIER-OLE** (Open Label Extension). All patients who completed the double-blind phase of the **PREMIER** trial are eligible to join the open-label extension phase, **PREMIER-OLE**, and 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** phase in September 2022[3].

As of January 30th, 2023, out of the 387 patients randomized in the **PREMIER** trial:

- **277** are in the 15-month double-blind phase of the **PREMIER** trial (PXT3003 HD *versus* Placebo),
- **38** early-terminated the double-blind phase of the **PREMIER** trial (no discontinuation due to serious adverse events related to study drug, and almost half of early-terminations are due to personal reasons such as far distance from the clinical site or plans to become pregnant),
- **64** are in the open-label extension phase, **PREMIER-OLE**, and are all treated with PXT3003 HD,
- **7** did not enroll in the open-label extension phase, **PREMIER-OLE**, after completing the double-blind phase of the **PREMIER** trial,
- **1** early-terminated the **PREMIER-OLE** phase.

The PREMIER trial is progressing as initially planned and confirms Pharnext's ability to carry out this ambitious program. The topline results announcement of this study is still planned in Q4 2023.

Burkhard Blank, MD, Chief Medical Officer of Pharnext, declared: "*We are pleased that the pivotal Phase III of our lead asset PXT3003 is progressing well and as planned. Notably, we are encouraged to see that almost 90% of the patients who completed the double-blind phase of the PREMIER trial decided to enroll in the open label extension phase of the trial where they will be all treated with PXT3003 High Dose. This is an additional opportunity to generate long-term safety and efficacy data of PXT3003 in CMT1A. We are very much looking forward to announcing the top-line data of the PREMIER trial in Q4 2023 which, if positive, would be a central element in the marketing authorization application in the United States and Europe*".

[1] Pharnext Announces First Patient Enrolled in the PREMIER Trial, its Pivotal Phase III Clinical Development Program of PXT3003 in Charcot-Marie-Tooth Disease Type 1A ('CMT1A')
[2] Pharnext Announces On-Schedule Completion of Patient Enrollment in its Pivotal Phase III Trial of PXT3003, the PREMIER Trial, for the Treatment of Charcot-Marie-Tooth Disease Type 1A
[3] Pharnext Announces First Patient Enrolled in Open Label Extension of the Pivotal Phase III Study of PXT3003 for the Treatment of Charcot-Marie-Tooth Disease Type 1A, the PREMIER Trial

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 therapeutics for neurodegenerative diseases that currently lack curative and/or disease-modifying treatments. Pharnext has two lead products in clinical development. PXT3003 completed an international Phase III trial with positive topline results for the treatment of Charcot-Marie-Tooth disease type 1A ('CMT1A') and benefits from orphan drug status in Europe and the United States. An international pivotal Phase III study of PXT3003 in CMT1A, the PREMIER trial, is currently ongoing. PXT864 has generated encouraging Phase II results in Alzheimer's disease and will be advanced through partnerships. Both of Pharnext's lead assets 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: FR001400BV89).

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