

Inside Information

Pharnext Announces Positive Topline Results from Pivotal Phase 3 Trial of PXT3003 for Treatment of Charcot-Marie-Tooth Type 1A Disease

- Higher dose met primary endpoint, the Overall Neuropathy Limitation Scale (ONLS), with statistical significance ($p = 0.008$)
- Higher dose met secondary endpoint, the 10-meter walk test, with statistical significance ($p=0.016$)
- Safe and well tolerated, no treatment related serious adverse event reported in the higher dose group
- Based on these positive results, Pharnext intends to file for market approval in the US and Europe
- Conference calls today at 11:30 am EDT / 5:30 pm CET in French and 1:00 pm EDT / 7:00 pm CET in English

PARIS, France, 7:30 am (CET), October 16, 2018 – Pharnext SA (FR0011191287 - ALPHA), a biopharmaceutical company pioneering a new approach to the development of innovative drug combinations based on big data genomics and artificial intelligence, today announced positive topline results from its pivotal Phase 3 clinical trial (PLEO-CMT) evaluating two doses of PXT3003 compared to placebo during 15 months for the treatment of Charcot-Marie-Tooth type 1A disease (CMT1A).

PLEO-CMT was a pivotal, 15-month, double-blind Phase 3 study that assessed the efficacy and safety of PXT3003 compared to placebo for the treatment of patients with mild to moderate CMT1A. The study evaluated two doses of PXT3003, and patients were randomized 1:1:1. The study enrolled 323 patients aged 16 to 65 years in 30 sites across EU, USA and Canada. The primary endpoint was the Overall Neuropathy Limitation Scale (ONLS) measuring patient disability, in agreement with FDA and EMA for this pathology. A reduction of 0.3 point on this scale was determined to be meaningful according to previously described methodology.¹

Characteristics of the three groups were comparable at baseline. For endpoint analysis, there were 87 patients in placebo, 93 patients in lower dose and 55 patients in higher dose arms at baseline. The lower number of patients in the higher dose is due to unexpected formulation/ stability issues. Nevertheless, compelling results were obtained: compared with placebo, a mean reduction of 0.4-point ONLS (95% CI [0.1,0.6], $p=0.008$) was observed in the higher dose group. A sensitivity analysis demonstrated the consistency of this result across various statistical models. The secondary endpoints confirmed the superiority of the higher dose, in particular the improvement on the 10-meter walk test with a reduction of 0.5 sec (95%CI [0.1,0.9], $p=0.016$).

A linear dose effect was observed. PXT3003 was safe, well tolerated and showed a similar safety profile as seen in the Phase 2 study.

In this study, PXT3003 provided first evidence of a meaningful improvement of CMT1A patients in showing a statistically significant amelioration on the ONLS disability scale (primary endpoint) confirmed by sensitivity analysis and secondary endpoints together with a good safety profile. Based on these results, Pharnext intends

to file for market approval in the US and EU. The statistical plan and the results have not yet been reviewed by the regulatory authorities.

Pharnext initiated a 9-month, open-label, follow-up extension study, PLEO-CMT-FU, in March 2016 that is currently ongoing with patients who completed the PLEO-CMT study. It is designed to confirm the long-term safety and tolerability of PXT3003 with results expected in H2 2019.

Pharnext also expects to initiate a Phase 3 trial of PXT3003 in pediatric CMT1A patients in the first half of 2019, based on a Pediatric Investigation Plan (PIP) agreed upon with the EMA. The results of this trial are not needed for market approval for the adult indication.

“We are thrilled with the outcome of the trial and with the clearly demonstrated efficacy of PXT3003 in addressing the debilitating disease progression of CMT1A. We look forward to working closely with regulatory agencies to bring this therapy to patients,” said Professor Daniel Cohen, MD, PhD, Pharnext’s Co-Founder and Chief Executive Officer. “These results validate the broad potential of our PLEOTHERAPY™ drug discovery platform in other neurodegenerative and other disorders and, of course, represent a tremendous milestone for Pharnext.”

“CMT1A is a chronic, severe and debilitating inherited condition affecting about 125,000 people in the USA and EU and, until now, there has been no prospect of effective pharmacological treatment,” said David Cornblath, MD, Professor of Neurology, Johns Hopkins University, Baltimore, Maryland. “In this trial, PXT3003 demonstrated a significant improvement in patients with mild-to-moderate CMT1A and provided encouraging results that indicate PXT3003 may change the treatment paradigm for the disease. As a clinician, I am excited about the therapeutic potential of PXT3003 and what it means for CMT1A patients and their families.”

“This is the first large multi-center trial that has demonstrated a positive effect in CMT,” said Richard Lewis, MD, Professor of Neurology, Cedars-Sinai Medical Center, Los Angeles, California. “I am delighted that this safe and novel approach may be available to patients with CMT1A.”

“These results are the first direct translation of a preclinical treatment developed in animal models to CMT1A patients,” said Michael Sereda, MD, Professor of Neurology at the Max-Planck Institute of Experimental Medicine, Göttingen, Germany. “I am impressed by the consistency of the therapeutic effect in both preclinical and clinical trials. Data derived from CMT rat models give us important insight regarding the effect of PXT3003 on the diseased peripheral nervous system in CMT1A.”

Pharnext would like to express its gratitude to the investigators and their teams and to the patients and their families for their commitment to this trial.

Conference Call

Pharnext will host two conference calls to discuss the study data today, Tuesday, October 16, 2018:

- Call in French at 5:30 p.m. CET (11:30 a.m. EDT). To participate in this call, please dial +1 (409) 217-8230 (French & International) or (866) 417-2001 (USA), and refer to conference ID 3092454.
- Call in English at 1:00 p.m. EDT (7:00 p.m. CET). To participate in this call, please dial (866) 417-2001 (USA) or +1 (409) 217-8230 (International) and refer to conference ID 2099809.
- To participate in either call, a local French dial-in number is available: 0170807153

A live webcast and accompanying slides of each call can be accessed on the Company's website at www.pharnext.com/en/investors/presentation and will be available beginning approximately two hours after each call until 30 days.

About Phase 3 PLEO-CMT Trial

PLEO-CMT was a pivotal, 15-month, double-blind Phase 3 study that assessed the efficacy and safety of PXT3003 compared to placebo for the treatment of patients with mild to moderate CMT1A. The study evaluated two doses of PXT3003, and patients were randomized 1:1:1. The study enrolled 323 patients aged 16 to 65 years in 30 sites across EU, the USA and Canada.

The higher daily dose consisted of 12 mg baclofen, 1.4 mg naltrexone and 420 mg sorbitol. The lower daily dose of PXT3003 consisted of 6 mg baclofen, 0.7 mg naltrexone and 210 mg sorbitol. Study treatment was administered as a liquid formulation twice a day orally.

The primary endpoint was based on the ONLS scale, which measures patient disability. This endpoint was recommended by the FDA for CMT1A and also accepted by the EMA.

About PXT3003

Pharnext's first-in-class PLEODRUG™ PXT3003, developed using Pharnext's R&D platform, PLEOTHERAPY™, is a novel oral fixed-dose combination of baclofen, naltrexone and sorbitol, with Orphan Drug Designation in EU and the USA. PXT3003, Pharnext's lead PLEODRUG™, has shown positive results both in preclinical and Phase 2 studies for the treatment of CMT1A. These results were published in the Orphanet Journal of Rare Diseases (OJRD) in December 2014^{2,3}. In preclinical studies, PXT3003 inhibited the overexpression of the PMP22 gene, improved myelination of peripheral nerves and motor / sensory impairments. In a Phase 2 clinical trial in 80 adult patients with CMT1A, PXT3003 improved multiple efficacy endpoints beyond stabilization, particularly the ONLS scale. In addition, PXT3003 was safe and well tolerated. In December 2015, Pharnext initiated the PLEO-CMT study, a pivotal 15-month, double-blind Phase 3 study that assessed the efficacy and safety of PXT3003 in 323 CMT1A patients aged 16 to 65 years. In this study, PXT3003 met the FDA and EMA pre-specified primary endpoint of ONLS with a statistically significant difference compared to placebo (p=0.008). PLEO-CMT was followed by a 9-month, open-label, follow-up extension study, PLEO-CMT-FU, initiated in March 2016 and currently ongoing. PLEO-CMT-FU, designed to assess the long-term safety and tolerability of PXT3003, enrolled patients who completed the PLEO-CMT study. Pharnext expects to initiate a Phase 3 trial of PXT3003 in pediatric CMT1A patients in the first half of 2019, based on a Pediatric Investigation Plan (PIP) agreed upon with the EMA.

About CMT1A

Charcot-Marie-Tooth (CMT) disease encompasses a heterogeneous group of inherited, progressive, chronic peripheral neuropathies. CMT type 1A (CMT1A), the most common type of CMT, is an orphan disease affecting at least 125,000 people in USA and EU. The genetic mutation responsible for CMT1A is a duplication of the PMP22 gene coding for a peripheral myelin protein. Overexpression of this gene causes degradation of the neuronal sheath (myelin) and nerve dysfunction. As a result, patients suffer from progressive muscle atrophy of the limbs causing problems with walking, running balance and hand function. At least 5% need wheelchairs. They may have loss of sensation and pain. Patients with CMT1A have reduced quality of life. First symptoms usually appear during childhood and progressively evolve throughout patients' lives. 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.

About Pharnext

Pharnext is an advanced clinical-stage biopharmaceutical company developing novel therapeutics for orphan and common neurodegenerative diseases that currently lack curative and/or disease-modifying treatments. Pharnext has two lead products in clinical development. PXT3003 successfully completed an international pivotal Phase 3 trial for the treatment of Charcot-Marie-Tooth disease type 1A. PXT3003 benefits from orphan drug status in Europe and the United States. PXT864 has generated encouraging Phase 2 results in Alzheimer's disease. Pharnext has developed a new drug discovery paradigm based on big genomic data and artificial intelligence: PLEOTHERAPY™. The Company identifies and develops synergic combinations of drugs called PLEODRUG™ offering several key advantages: efficacy, safety and robust intellectual property. The Company was founded by renowned scientists and entrepreneurs including Professor Daniel Cohen, a pioneer in modern genomics, and is supported by a world-class scientific team.

Pharnext is listed on Euronext Growth Stock Exchange in Paris (ISIN code: FR0011191287).

For more information, visit <http://www.pharnext.com/>.

Disclaimer

This press release contains certain forward-looking statements concerning Pharnext and its business. Such forward-looking statements are based on assumptions that Pharnext considers to be reasonable. However, there can be no assurance that the estimates contained in such forward-looking statements will be verified, which estimates are subject to numerous risks including the risks set forth in Pharnext's document de base filed with the AMF on June 2, 2016 under number I.016-0050 as well as in any other periodic report and in any other press release (a copy of which is available on www.pharnext.com) and to the development of economic conditions, financial markets and the markets in which Pharnext operates. The forward-looking statements contained in this press release are also subject to risks not yet known to Pharnext or not currently considered material by Pharnext. The occurrence of all or part of such risks could cause actual results, financial conditions, performance or achievements of Pharnext to be materially different from such forward-looking statements. Pharnext disclaims any intention or obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise.

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References

¹ Cohen J. Statistical Power Analysis for the Behavioral Sciences Second Edition, 1988. Lawrence Erlbaum Associates, Publishers.

² Chumakov et al., Polytherapy with a combination of three repurposed drugs (PXT3003) down-regulates *Pmp22* over-expression and improves myelination, axonal and functional parameters in models of CMT1A neuropathy. *Orphanet Journal of Rare Diseases* 2014, 9:201.

³ Attarian et al., An exploratory randomised double-blind and placebo-controlled phase 2 study of a combination of baclofen, naltrexone and sorbitol (PXT3003) in patients with Charcot-Marie-Tooth disease type 1A. *Orphanet Journal of Rare Diseases* 2014, 9:199.

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