Press Release

New Data Published in PLOS ONE Demonstrates Early Therapeutic Effects of Pharnext's PLEODRUG™ PXT3003 in a Transgenic Rat Model of Charcot-Marie-Tooth disease Type 1A

PARIS, France, 8:00 am, 17 January 2019 (CET) – Pharnext SA (FR0011191287 - ALPHA) a biopharmaceutical company pioneering a new approach to the development of innovative drug combinations based on big genomic data and artificial intelligence, today announced the publication of new preclinical results for its lead PLEODRUG™ PXT3003 in PLOS ONE showing that early treatment with PXT3003 in a transgenic rat model delays the onset of Charcot-Marie-Tooth disease Type 1A (CMT1A).

The publication, titled "Early short-term PXT3003 combinational therapy delays disease onset in a transgenic rat model of Charcot-Marie-Tooth disease 1A (CMT1A)," by Prukop *et al.*, reported that early treatment with PXT3003 prevented a set of clinical and molecular manifestations of CMT1A after short-term dosing in juvenile *PMP22* transgenic rats, a well established animal model of CMT1A. Results from the study indicated that an early postnatal, short-term treatment with PXT3003 in CMT1A rats:

- Delayed disease onset into adulthood;
- Corrected motor deficits;
- Ameliorated the disturbed axon caliber distribution with a shift towards large motor axons;
- Reduced *PMP22* mRNA overexpression;
- Improved the dysbalanced molecular pathways (AKT/ERK) involved in Schwann cell differentiation.

The paper can be accessed at https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0209752

Michael Sereda, M.D., Professor of Neurology at the Max Planck Institute of Experimental Medicine (MPI-EM) and the University Medical Center (UMG), Göttingen, Germany, said: "We were surprised that only two weeks of early, post-natal treatment with PXT3003 dramatically improved the motor phenotype in CMT1A rats reaching wildtype levels. Similar to previous preclinical studies, this underlines the importance of treating the molecular defects caused by PMP22 overexpression in CMT1A during this critical time window in myelin development."

Daniel Cohen, M.D., Ph.D., Co-Founder and Chief Executive Officer of Pharnext, said: "These results provide key insights into the disease progression of CMT1A and the potential of PXT3003 to slow the onset of the disease, particularly in children and adolescents with CMT1A. Such findings validate our preclinical data on PXT3003 in CMT1A to-date, as well as our clinical data, based on the positive top-line Phase 3 data from October 2018. From the findings in this publication, we believe that PXT3003 has the potential to change the treatment paradigm for children with CMT1A – for whom there are currently no pharmacological treatments available – and we look forward to initiating a Phase 3 trial of PXT3003 in pediatric patients by the end of 2019."

Pharnext intends to lauch a pediatric Phase 3 clinical trial in children to investigate the safety and efficacy of PXT3003. The investigation plan was agreed with the European Medicines Agency.

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 by the end 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 a loss of sensation and pain. Patients with CMT1A have reduced quality of life. The 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 products in clinical development. PXT3003 completed an international pivotal Phase 3 trial with positive topline results for the treatment of Charcot-Marie-Tooth disease type 1A and 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 www.pharnext.com

CONTACTS:

Pharnext
Rodolphe Hajj
Chief Pharmacology Officer
contact@pharnext.com
+33 (0)1 41 09 22 30

Financial Communication (France)
Actifin
Stéphane Ruiz
sruiz@actifin.fr
+33 (0)1 56 88 11 15

Investor Relations (U.S.)
Stern Investor Relations, Inc.
Kendra Packard
kendra@sternir.com
+1 212 362 1200

Investor Relations (Europe)
MC Services AG
Anne Hennecke
anne.hennecke@mc-services.eu
+49 211 529252 22

Media Relations (Europe)
Ulysse Communication
Bruno Arabian
barabian@ulysse-communication.com
+33 (0)1 81 70 96 30

Media Relations (U.S.)
RooneyPartners
Kate L. Barrette
kbarrette@rooneyco.com
+1 212 223 0561