Shareholder Letter
"Time to reveal Pharnext true value"

PARIS, France, January 11th, 2023, 8:30 am CET – Pharnext SA (FR001400BV89 - ALPHA) (the "Company"), an advanced late-clinical stage biopharmaceutical company developing novel therapeutics for rare neurodegenerative diseases with high unmet medical need, today publishes a Letter to Shareholders from its new Chairman and Chief Executive Officer, Hugo Brugière. Hugo reviews the company's latest developments and discusses his priorities.

Dear Shareholders,

Many of you may not know me yet as I was appointed Chairman of the Board of Directors and CEO of our Company on December 26, 2022. I am therefore using this letter as an opportunity to introduce myself and, above all, to tell you what my priorities are for this very promising company. The world of biotechnology companies is familiar to me as I have been the Chairman and CEO of Neovacs since 2020, and I am also an investor in promising life science companies. When we first started discussions with Pharnext, I immediately identified the considerable potential of this Company, one of the few biotechs listed in Paris, which is developing a drug candidate, PXT3003, in pivotal Phase III for a rare disease with an important unmet medical need. Therefore, I agreed to finance and then lead our Company, with 3 major objectives in 2023:

1. **Complete the ongoing clinical study of PXT3003** in Charcot-Marie-Tooth disease type 1A ("CMT1A") to potentially bring, as quickly as possible, a therapeutic solution globally to patients suffering from this disease;
2. **Optimize the operational management** of the Company to limit financial needs in a more difficult global financial environment;
3. **Optimize the valuation of the Company's assets.**

The challenge here is huge, I am fully aware, but we have this unique opportunity, with PXT3003, our lead drug candidate in development in CMT1A, to potentially bring for the first time a therapeutic solution against this rare, inherited, debilitating, peripheral neuropathy. We remain entirely commited to bringing safe and effective therapies to market for the CMT community - patients, their relatives and caregivers. This is a constant focus and a strong motivation for all the people working in our Company.

It is through our relentless work that we aim to contribute to changing the lives of hundreds of thousands of patients, and therefore millions of people globally, and thus reveal the true value of Pharnext.

I will keep you informed of our progress through 2023, while respecting our communication obligations and any confidentiality agreements signed with potential partners.

I wish you all the best for this new year.

Best regards,

2023 should be a great year for PHARNEXT!
thank you very much for your support and
now: let's go!

Hugo Brugière
Chairman of the Board of Directors and CEO

Complete the clinical development of PXT3003 in CMT1A

2023 will be a pivotal year as we are expecting to announce the topline results from the pivotal Phase III clinical study of PXT3003, also known as the PREMIER trial, in December this year. If positive, these data would form the basis of the dossier of the marketing authorization application which should be submitted to the FDA in the US between the end of S1 and the middle of S2 2024, and then to the EMA in Europe, at the end of 2024 – beginning of 2025. If following these applications, PXT3003 received a marketing authorization, it would be the first treatment specifically approved for patients with CMT1A. Therefore, it has the potential to bring hope to hundreds of thousands of patients who suffer in their everyday life from this rare and debilitating peripheral neuropathy.

To date, almost 800 patients around the world have been enrolled in clinical trials of PXT3003:

- 80 patients in the Phase II clinical study;
- 323 patients in total enrolled in the first Phase III program (double-blind Phase III clinical study, the PLEO-CMT trial, followed by an ongoing open-label extension study, the PLEO-CMT-FU trial), including around 120 patients still on treatment with PXT3003 in the PLEO-CMT-FU trial;
- 387 patients in total enrolled in the second Phase III program (ongoing double-blind pivotal Phase III clinical study, the PREMIER trial, followed by an ongoing open-label extension study, the PREMIER-OLE trial), including around 40 patients already enrolled in the PREMIER-OLE trial on January 1st, 2023.

In May 2022, we announced the long-term data of the PLEO-CMT trial after 5-year total trial time[1] which showed a sustained treatment benefit for patients with CMT1A treated with PXT3003 High Dose (same dose as the one tested in the PREMIER trial) with a good safety profile and continuous treatment effect as measured on the Overall Neuropathy Limitation Scale (ONLS) which evaluate patients' functionnal motor disability. In May 2022, we also completed the enrollment of 387 patients in our pivotal Phase III clinical study of PXT3003, the PREMIER trial, in CMT1A. Patient enrollment in the PREMIER trial took place in 52 centers across the U.S., Canada, Europe and Israel, with topline data expected to be announced in Q4 2023[2]. In September, the first patient who completed the PREMIER trial was enrolled in the PREMIER-OLE (Open Label Extension) trial[3]. The decision to conduct the PREMIER-OLE trial was triggered by encouraging data from the open-label extension study of the first Phase III program, the PLEO-CMT-FU trial.

We look forward to generating additional long-term data from our both ongoing extension studies, to confirm the potential safety and efficacy of PXT3003 for patients with CMT1A. For all of Pharnext's teams, it is truly an ethical commitment to allow patients with CMT1A already enrolled in our Phase III studies to continue to access to PXT3003 in open-label extension studies. These patients currently have no specific therapeutic options for CMT1A and it is important to support them in their daily lives. We want to be a company truly focused on patients' needs and support.

Optimize financial management and security

As announced on December 28th, 2022[4], Néovacs has committed to increase its funding commitment in Pharnext to cover the Company's financial needs at least until the topline results of the PREMIER trial of PXT3003 in CMT1A which should be available in Q4 2023. Specifically, Neovacs would commit to increase its financial support to up to an additional €2 million per month by the end of 2023, in addition to the €20.7 million net financing agreement signed in October[5], via the issuance of several tranches of bonds with warrants. Thus, as stated on several occasions, Néovacs is part of a long-term strategy as a reference shareholder and not simply as a funder.

We acknowdledge that convertible bond financing can put downward pressure on the share price and can be highly dilutive at low market capitalization values. This is the reason why Pharnext has decided to implement a plan to optimize its organization, operating costs and investments in 2023. The objective is simple: to limit the monthly needs of the Company as much as possible and, consequently, the need to rely on the currently available financing tools. In any case, the €30 million the Company may need before the end of 2023 is a reasonable investment considering the underlying value of the asset.

[1] New Data from the Open-Label PLEO-CMT-FU Trial Shows Sustained Benefit with PXT3003 in Patients with Charcot-Marie-Tooth Disease Type 1A After 5 Years of Total Trial
[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
[4] Pharnext strengthens its ties with Néovacs to secure the next steps in its development
[5] Pharnext executes a financing agreement with Néovacs for EUR 20.7 million net to further develop PXT3003 for Charcot-Marie-Tooth disease type 1A

Making the most of the Company's assets

We believe that potentially positive topline results from the PREMIER trial in Q4 2023 could generate significant value for our shareholders. PXT3003 could be the first drug approved specifically for CMT1A. If successful, we hope to launch PXT3003 in 2025 in the U.S. and then in other countries. Our own modeling indicates that PXT3003 could generate global sales of up to €1 billion, which today translates into a risk-adjusted net value (NPV) of several hundred million euros.

This valuation was confirmed by Edison Investment Research at almost €300 million in October 2022[6]. This gives a good hint of the value creation potential of Pharnext considering the current market capitalization on one hand and the underlying value of PXT3003 in CMT1A on the other hand, if clinical data are positive and marketing authorization (MA) is obtained.

This valuation could be done in the context of a capital transaction that could eventually lead to a takeover of the Company. Pharnext currently favors an agreement with a player in the pharmaceutical industry. In order to optimize this search, Pharnext's Board of Directors have decided to form an ad hoc committee, consisting of Joshua Schafer, Director, James Kuo, Director, Rob Quinn, CFO and Xavier Paoli, COO. Joshua has led successful M&A transactions in excess of $16 billion. James has raised several rounds of financing as Managing Director and led HealthCare Ventures, a $378 million venture capital fund. Rob has raised over €200 million in financing to date and Xavier will bring his knowledge of PXT3003 after working 9 years at the Company.

2023: a pivotal year for Pharnext

Even before the completion of the pivotal Phase III clinical study of PXT3003 in CMT1A, the PREMIER trial, this year will be rich in news showing the concrete progress of our work.

We are also looking forward, in Q2, to announcing new data from the ongoing open-label Phase III extension study of PXT3003, the PLEO-CMT-FU trial, with 6-year total trial time data cut.

New "real world" data on CMT1A disease burden from the digital lifestyle study, CMT&Me, will be available for the CMT community through various channels: a peer-reviewed publication expected during S1 2023 and several abstracts if accepted during key conferences (PNS in June in Copenhaguen and AANEM in November in Phoenix in the U.S.).

We will also pursue the manufacturing technological transfer of PXT3003 in the U.S. to prepare the potential commercial launch in this country and pursue our interactions with health regulatory agencies (FDA in the U.S. and EMA in Europe) with the objective to file the NDA dossier in the US in 2024.

We will pursue our societal commitment to the CMT community, patients, families and healthcare professionals.

[6] Funding headroom to support PXT3003 progress

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 aiming at developing novel therapeutics for rare neurodegenerative diseases that currently lack curative and/or disease-modifying treatments. 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 with currently no existing approved therapies. PXT3003 benefits from orphan drug status in both Europe and the United States. In 2018, PXT3003 completed an international Phase III clinical study, the PLEO-CMT trial, with encouraging topline results. PLEO-CMT was followed by an open-label extension study, the PLEO-CMT-FU trial, with around 120 patients still on treatment with PXT3003. Long-term data suggest a sustained benefit, safety and efficacy, of PXT3003 after 5 years of total trial time. An international pivotal Phase III study of PXT3003, the PREMIER trial, is currently ongoing in the US, Canada, Europe and Israel 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: FR001400BV89).

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