Press Release

Pharnext progresses in analyzing data from pivotal Phase III study of PXT3003 in Charcot-Marie-Tooth disease type 1A

PARIS, France, February 28, 2024, 08:30 am CET – Pharnext SA (FR001400N1P4 - ALPHA) (the "Company"), an advanced late-clinical stage biopharmaceutical company developing novel therapeutics for neurodegenerative diseases with high unmet medical need, provides an update on the ongoing analysis of data from pivotal Phase III study (PREMIER trial) of PXT3003, its drug candidate in Charcot-Marie-Tooth disease type 1A (CMT1A).

As a reminder, on December 11, 2023[1], Pharnext announced that, on the primary efficacy endpoint of the PREMIER trial, the Overall Neuropathy Limitation Scale (ONLS) which measures functional motor disability, patients with mild-to-moderate CMT1A experienced improvement on both treatment and placebo, rather than the slow deterioration typical of CMT1A's natural progression. This unexpected improvement in the placebo group complicated the interpretation of the results based on this endpoint. However, other data from the trial suggested no deterioration in the condition of patients under treatment, which is a positive sign in the context of a degenerative disease such as CMT1A.
In the meantime, the trial reaffirmed the high safety profile of the treatment already established in all previous studies. This safety profile is crucial for the treatment of a chronic disease such as CMT1A.

On December 19, 2023[2], Pharnext announced that pre-specified subgroup analyses of the PREMIER trial suggested an efficacy signal, including a better response in treated patients with a BMI<25, or in patients under 45 years of age.
Analysis of the data also revealed that, while the study as a whole was indeed randomized into two arms (PXT3003 and placebo), the distribution of the two treatments within each clinical investigation center was not balanced. As a result, in some centers, patients received only placebo, and in others only treatment. However, a post-hoc analysis showed that by removing data from centers with fewer than two patients per arm, i.e. 50 patients (13%), there was a statistically significant difference between the treated and placebo groups on the CMTNS score.

To advance these encouraging results, several additional studies enabled to refine our conclusions at this stage, with the analysis continuing and extending through Q1 2024.

- Considering all patients in the PREMIER trial, the CMTNS score, secondary efficacy endpoint, showed in both subgroups of patients with BMI<25 and age<45, a statistically significant improvement with PXT3003 treatment versus placebo.
- Considering only centers with at least two patients per arm, i.e. 87% of patients included in the PREMIER trial, a statistically significant improvement in CMTNS score was observed with PXT3003 versus placebo whatever the patient's weight.
- A simple comparison of adverse events collected during the PREMIER trial showed that patients in the PXT3003 group reported approximately 30% fewer CMT1A-related symptoms than patients in the placebo group (overall worsening, increased falls, weakness, pain, muscle stiffness, spasms, twitches). This observation suggests a potential positive impact of PXT3003 in alleviating typical CMT1A symptoms, potentially contributing to patients' quality of life beyond the detection capabilities of the ONLS scale.

Now, as committed on January 17, 2024[3], the Company stopped all operating expenses while completing the additional analyses for the PREMIER trial. It confirms having reduced its current consumption as announced and waiting for the results (by Summer 2024) of the Phase III trial currently being conducted in China by its partner Tasly, which acquired the licensing rights for PXT3003 in China in 2017, with 2 options:

- If the results of the study in China are negative, Pharnext will analyze these results and draw the necessary conclusions in conjunction with the Company's shareholders.

[1] Pharnext reports topline results from the pivotal Phase III clinical trial (PREMIER trial) of PXT3003 in Charcot-Marie-Tooth disease type 1A
[2] Pharnext intends to prepare registration and marketing authorization dossiers for PXT3003, its drug candidate in Charcot-Marie-Tooth disease type 1A
[3] Pharnext commits to a drastic cost-cutting plan and receives support from its financial partners to further enhance the value of its drug candidate for Charcot-Marie-Tooth disease type 1A

- If the results of the study in China are positive, showing a statistically significant benefit of PXT3003 on the primary endpoint, the ONLS score, Pharnext will continue its dialogue with the FDA and EMA to agree on a registration process for PXT3003 in CMT1A.

Hugo Brugière, Manager of Pharnext, said: "*I'm pleased to be gaining confidence as our analysis progresses, and look forward to the results of the parallel Phase III study to be completed soon in China.*
We are continuing our own analyses and will need to discuss with the FDA and EMA to agree on a registration pathway, as once again we remain hopeful of finally being able to bring a medical solution to CMT1A patients. If the results of the Phase III trial in China are positive, and even without FDA or EMA approval, the company will then be able to finance itself over the coming years solely through revenues from the Chinese license. More than ever, and thanks to many additional analyses, our teams are confident in the future".

Disclaimer
Pharnext arranged (I) financing in the form of convertible bonds financing (OCEAN-BSA) with Global Tech Opportunities 13 which, after receiving the shares resulting from the conversion or exercise of these instruments, will not remain shareholder of the Company, and (II) financing in OS bonds which were subsequently transferred to a trust, which is now responsible for their equitization.
The shares resulting from the conversion or exercise of the above-mentioned securities will generally be sold on the market at very short notice, which may create strong downward pressure on the share price. In the specific case of the trust, the shares are sold on the market in accordance with the terms set out in the trust agreement.
Shareholders may suffer a loss of their invested capital due to a significant fall in the Company's share price, as well as significant dilution due to the large number of securities issued to Global Tech Opportunities 13 and/or the trust.
Investors are advised to exercise extreme caution before deciding to invest in the securities of a listed company that carries out such dilutive financing transactions, particularly when they are carried out in succession. The Company wishes to point out that this is not the first dilutive financing transaction it has undertaken.

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. More information at www.pharnext.com.
Pharnext is listed on the Euronext Growth Stock Exchange in Paris (ISIN code: FR001400N1P4).

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