Pharming announces completion of enrolment in Phase II/III study with leniolisib for activated PI3K delta syndrome

Leiden, The Netherlands, 23 June 2021*:* Pharming Group N.V. ("Pharming" or "the Company") (Euronext Amsterdam: PHARM/Nasdaq: PHAR) announces the successful completion of patient enrolment in the pivotal Phase II/III triple-blind, randomized, placebo-controlled study of leniolisib for the treatment of activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS).

Leniolisib is a small molecule PI3Kδ inhibitor that was developed by Novartis[1] and was licensed to Pharming in 2019.[8] The study, sponsored by Novartis, is a phase II/III potentially registration enabling study composed of two sequential parts, the first part including 6 patients was an open-label dose escalation study that was designed to assess the safety, tolerability, pharmacodynamics and pharmacokinetics of leniolisib[2]. The second part is a randomized, blinded, placebo-controlled study that includes approximately 30 additional patients and is designed to assess the efficacy of leniolisib in APDS patients. The co-primary endpoints of the second part of the study are (i) change in the size of lesions from baseline and (ii) change in baseline percentage of naive B cells out of total B cells. Pharming anticipates launch of leniolisib in Q4 2022, subject to regulatory approval.

APDS is an ultra-rare primary immunodeficiency disease caused by a genetic mutation affecting approximately 1-2 people per million. Current treatment is generally limited to supportive therapies, such as antibiotics and the use of immunoglobulin replacement therapy, as there is no approved therapy for the treatment of the disease.

Patients with APDS are often misdiagnosed with other immunodeficiencies or autoimmune disorders and often have a protracted journey to obtain a correct diagnosis. A definitive diagnosis can be made only by a genetic test. In March 2021, Pharming, in collaboration with Invitae Corporation, announced the launch of a genetic testing program, navigateAPDS, which is designed to assist clinicians in identifying patients with APDS and may lead to earlier diagnosis.

Anurag Relan, Chief Medical Officer of Pharming, commented:
"We remain excited by the profile of leniolisib, which we believe is a great example of solid science and deep disease understanding coming together to create a real and personalized option for patients with no other prospect of treatment. With completion of enrolment, we move one step closer to making this medicine available for APDS patients around the world. We thank patients with APDS and their families, clinical study staff and Novartis for getting leniolisib to this important point in clinical development."

About leniolisib

Leniolisib is a small molecule inhibitor of the delta isoform of the 110 kDa catalytic subunit of class IA PI3K with immunomodulating and potentially anti-neoplastic activities. Leniolisib inhibits the production of phosphatidylinositol-3-4-5-trisphosphate (PIP3). PIP3 serves as an important cellular messenger specifically activating AKT (via PDK1) and regulates a multitude of cell functions such as proliferation, differentiation, cytokine production, cell survival, angiogenesis, and metabolism. Unlike PI3Kα and PI3Kβ which are ubiquitously expressed, PI3Kδ and PI3Kγ are expressed primarily in cells of hematopoietic origin. The central role of PI3Kδ in regulating numerous cellular functions of the adaptive immune system (B-cells and to a lesser extent T cells) as well as the innate immune system (neutrophil, mast cells, and macrophages) strongly indicates that PI3Kδ is a valid and potentially effective therapeutic target for several immune diseases.
To date, leniolisib has proven to be safe and well tolerated in healthy subjects as well as the APDS patients during the Phase 1 first-in-human trial and an ongoing open label extension trial.

About APDS

APDS is an ultra-rare primary immunodeficiency disease that is caused by variants in either of two genes, PIK3CD or PIK3R1. Variants of these genes lead to hyperactivity of the PI3Kδ (phosphoinositide 3-kinase delta) pathway.[3,4] Balanced signaling in the PI3Kδ pathway is essential for physiological immune function. When this pathway is hyperactive, immune cells fail to mature and function properly, leading to immunodeficiency and dysregulation.[3-5] APDS is characterized by severe, recurrent sinopulmonary infections, lymphoproliferation, autoimmunity, and enteropathy.[6,7] Patients with APDS suffer a median 7-year diagnostic delay.[8] Because APDS is a progressive disease, this delay may lead to an accumulation of damage over time, including permanent lung damage and lymphoma.[6-9]

About Pharming Group N.V.

Pharming Group N.V. is a global, commercial stage biopharmaceutical company developing innovative protein replacement therapies and precision medicines for the treatment of rare diseases and unmet medical needs.

The flagship of our portfolio is our recombinant human C1 esterase inhibitor (rhC1INH) franchise. C1INH is a naturally occurring protein that down regulates the complement and contact cascades in order to control inflammation in affected tissues.

Our lead product, RUCONEST®, is the first and only plasma-free rhC1INH protein replacement therapy. It is approved for the treatment of acute hereditary angioedema (HAE) attacks. We are commercializing RUCONEST® in the United States, the European Union and the United Kingdom through our own sales and marketing organization, and the rest of the world through our distribution network.

In addition, we are investigating the clinical efficacy of rhC1INH in the treatment of further indications, including pre-eclampsia, acute kidney injury, and severe pneumonia as a result of COVID-19 infections.

Furthermore, we are leveraging our transgenic manufacturing technology to develop next-generation protein replacement therapies, most notably for Pompe disease, which is currently in preclinical development.

Forward-looking Statements

This press release contains forward-looking statements, including with respect to timing and progress of Pharming's preclinical studies and clinical trials of its product candidates, Pharming's clinical and commercial prospects, Pharming's ability to overcome the challenges posed by the COVID-19 pandemic to the conduct of its business, and Pharming's expectations regarding its projected working capital requirements and cash resources, which statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to the scope, progress and expansion of Pharming's clinical trials and ramifications for the cost thereof; and clinical, scientific, regulatory and technical developments. In light of these risks and uncertainties, and other risks and uncertainties that are described in Pharming's 2020 Annual Report and the Annual Report on Form 20-F for the year ended December 31, 2020 filed with the U.S. Securities and Exchange Commission, the events and circumstances discussed in such forward-looking statements may not occur, and Pharming's actual results could differ materially and adversely from those anticipated or implied thereby. Any forward-looking statements speak only as of the date of this press release and are based on information available to Pharming as of the date of this release.

Inside Information

This press release relates to the disclosure of information that qualifies, or may have qualified, as inside information within the meaning of Article 7(1) of the EU Market Abuse Regulation.

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