Pharming Group announces start of Phase II clinical trial of leniolisib for primary immunodeficiencies (PIDs) with immune dysregulation

Proof of concept clinical trial will evaluate leniolisib in PIDs with immune dysregulation linked to altered PI3Kδ signaling in lymphocytes

PIDs to include ALPS-FAS, CTLA4 haploinsufficiency, NFKB1 haploinsufficiency and PTEN deficiency, with prevalence approximately five times that of APDS

Clinical trial being conducted at the National Institutes of Health (NIH)

Leiden, the Netherlands, October 10, 2024: Pharming Group N.V. ("Pharming" or "the Company") (EURONEXT Amsterdam: PHARM/Nasdaq: PHAR) announces the start of a Phase II, proof of concept, clinical trial evaluating leniolisib in primary immunodeficiencies (PIDs) with immune dysregulation linked to altered PI3Kδ signaling in lymphocytes.

The clinical trial is open for enrollment and will include PID patients with ALPS-FAS, CTLA4 haploinsufficiency, NFKB1 haploinsufficiency and PTEN deficiency, among others. These PID patients exhibit altered PI3Kδ signaling in lymphocytes and likewise display similar clinical phenotypes to activated phosphoinositide 3-kinase delta syndrome (APDS) patients. Epidemiology suggests a prevalence of approximately seven patients per million in this targeted PID population, compared to one to two patients per million for APDS.

The Phase II clinical trial is a single arm, open-label, dose range-finding study to be conducted in approximately 12 patients. The objectives for the trial will be to assess safety and tolerability, pharmacokinetics, pharmacodynamics, and explore clinical efficacy of leniolisib in the targeted PID population. The trial has been designed to inform a subsequent Phase III program. The Phase II clinical trial is being conducted at the National Institute of Allergy and Infectious Diseases (NIAID) – part of the National Institutes of Health (NIH) – with lead investigator Gulbu Uzel, M.D., Senior Research Physician, and co-investigator V. Koneti Rao, M.D., FRCPA, Senior Research Physician, Primary Immune Deficiency Clinic (ALPS Clinic).

Anurag Relan, MD, MPH, Chief Medical Officer of Pharming, commented:

"The initiation of this study is an important milestone for Pharming as it represents the second primary immunodeficiency (PID) clinical program for leniolisib. Based on our experience in APDS, and the significant role of PI3Kδ in regulating lymphocytes, leniolisib has the potential to address the underlying immune dysregulation and deficiency in a number of rare PID disorders with significant unmet medical needs, including ALPS-FAS, CTLA4 haploinsufficiency, NFKB1 haploinsufficiency and PTEN deficiency. We are excited to be leading this important scientific effort and to sharing the results of the study with the medical community."

The first patient is expected to be enrolled in the study in the coming weeks.

This is the first clinical trial initiated by Pharming to study leniolisib in PIDs with immune dysregulation beyond APDS. The unique genetic drivers in ALPS-FAS, CTLA4 haploinsufficiency, NFKB1 haploinsufficiency and PTEN patients lead to enhanced PI3Kδ signaling and clinical phenotypes of immune dysregulation shared with APDS. Specifically, PTEN patients with immunodeficiency are frequently described as 'APDS-like'[1], patients with ALPS-FAS display predominantly lymphoproliferative clinical manifestations with frequent cytopenic episodes[2], and CTLA4 haploinsufficiency[3] as well as NFKB1 haploinsufficiency[4] patients demonstrate lymphoproliferative, cytopenic, and/or organ-specific autoimmune/inflammatory complications of immune dysregulation.

Leniolisib is marketed in the U.S. and approved in several other countries, for the treatment of APDS in adult and pediatric patients 12 years of age and older.

About leniolisib

Leniolisib is an oral small molecule phosphoinositide 3-kinase delta (PI3Kδ) inhibitor approved in the U.S. and several other countries as the first and only targeted treatment of activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) in adult and pediatric patients 12 years of age and older. Leniolisib inhibits the production of phosphatidylinositol-3-4-5-trisphosphate, which serves as an important cellular messenger and regulates a multitude of cell functions such as proliferation, differentiation, cytokine production, cell survival, angiogenesis, and metabolism. Results from a randomized, placebo-controlled Phase III clinical trial demonstrated statistically significant improvement in the coprimary endpoints, reflecting a favorable impact on the immune dysregulation and deficiency seen in these patients, and interim open label extension data has supported the safety and tolerability of long-term leniolisib administration.[5,6] Leniolisib is currently under regulatory review in the European Economic Area, Canada and Australia for APDS, with plans to pursue further regulatory approvals in Japan and South Korea. Leniolisib is also being evaluated in two Phase III clinical trials in children with APDS and in a Phase II clinical trial in primary immunodeficiencies (PIDs) with immune dysregulation linked to altered PI3Kδ signaling in lymphocytes. The safety and efficacy of leniolisib has not been established for PIDs with immune dysregulation beyond APDS.

About Pharming Group N.V.

Pharming Group N.V. (EURONEXT Amsterdam: PHARM/Nasdaq: PHAR) is a global biopharmaceutical company dedicated to transforming the lives of patients with rare, debilitating, and life-threatening diseases. Pharming is commercializing and developing an innovative portfolio of protein replacement therapies and precision medicines, including small molecules and biologics. Pharming is headquartered in Leiden, the Netherlands, and has employees around the globe who serve patients in over 30 markets in North America, Europe, the Middle East, Africa, and Asia-Pacific.

For more information, visit www.pharming.com and find us on LinkedIn.

Forward-Looking Statements

This press release may contain forward-looking statements. Forward-looking statements are statements of future expectations that are based on management's current expectations and assumptions and involve known and unknown risks and uncertainties that could cause actual results, performance, or events to differ materially from those expressed or implied in these statements. These forward-looking statements are identified by their use of terms and phrases such as "aim", "ambition", ''anticipate'', ''believe'', ''could'', ''estimate'', ''expect'', ''goals'', ''intend'', ''may'', "milestones", ''objectives'', ''outlook'', ''plan'', ''probably'', ''project'', ''risks'', "schedule", ''seek'', ''should'', ''target'', ''will'' and similar terms and phrases. Examples of forward-looking statements may include statements with respect to timing and progress of Pharming's preclinical studies and clinical trials of its product candidates, Pharming's clinical and commercial prospects, 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, commercial, competitive and technical developments. In light of these risks and uncertainties, and other risks and uncertainties that are described in Pharming's 2023 Annual Report and the Annual Report on Form 20-F for the year ended December 31, 2023, 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. All forward-looking statements contained in this press release are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. Readers should not place undue reliance on forward-looking statements. 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. Pharming does not undertake any obligation to publicly update or revise any forward-looking statement as a result of new information, future events or other information.

References

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