Pharming Group announces first patient dosed in Phase II clinical trial of leniolisib for common variable immunodeficiency (CVID) with immune dysregulation

Multi-center clinical trial includes sites located in the US, UK and EU

Second Phase II clinical trial studying leniolisib for additional primary immunodeficiencies (PIDs)

CVID patients demonstrate clinical phenotypes similar to APDS, with global prevalence estimated at approximately 39 per million

Leiden, the Netherlands, March 20, 2025: Pharming Group N.V. ("Pharming" or "the Company") (EURONEXT Amsterdam: PHARM/Nasdaq: PHAR) announces that the first patient has been dosed in a Phase II, proof of concept, clinical trial evaluating leniolisib in common variable immunodeficiency (CVID) patients with immune dysregulation.

The Phase II clinical trial is a single arm, open-label, dose range-finding, multi-center study to be conducted in approximately 20 patients 12 years of age and older. The trial will include patients with a CVID diagnosis, a requirement for evidence of lymphoproliferation, and at least one additional clinical manifestation of immune dysregulation, including interstitial lung disease, autoimmune cytopenias, or enteropathy. The objectives for the trial are to assess safety and tolerability, pharmacokinetics, pharmacodynamics, and explore clinical efficacy of leniolisib in the targeted CVID with immune dysregulation population. The trial has been designed to inform a subsequent Phase III program. The lead investigator for the Phase II study is Jocelyn Farmer, M.D./PhD, Director of the Clinical Immunodeficiency Program of Beth Israel Lahey Health (Lahey Hospital & Medical Center in Burlington, MA), with additional clinical sites in the US, UK and EU.

Jocelyn Farmer, MD, PhD; Allergist and Immunologist, Lahey Hospital & Medical Center, Burlington, MA; Director, Clinical Immunodeficiency Program, Beth Israel Lahey Health, MA; Associate Professor, UMass Chan-Lahey Medical School, Burlington, MA commented:
"As a physician with clinical responsibility for a large group of common variable immunodeficiency (CVID) patients, I understand the significant disease burden they face. This includes autoimmune and end-organ lympho-infiltrative clinical complications resulting from their immune dysregulation. Due to the absence of effective therapies for these CVID patients, the disease manifestations can easily progress, leading to the well-documented early mortality in this patient group. PI3Kδ is a multi-faceted regulator of lymphocytes, functioning to control their proliferation, differentiation, antibody production and migration, and hence leniolisib has significant potential to treat the immune dysregulation seen in these CVID patients. Therefore, I am very excited that we have dosed our first patient with leniolisib in this phase 2 proof of concept study in CVID patients with immune dysregulation, where leniolisib provides an opportunity to help these patients with a large, unmet medical need."

CVID represents the largest group of symptomatic primary immunodeficiency (PID) patients, where approximately 50% display autoimmune, lymphoproliferative and/or end-organ lympho-infiltrative clinical manifestations driven by immune dysregulation.[1,2,3] CVID patients with immune dysregulation have an unmet medical need with an 11-fold enhanced rate of mortality as compared to CVID patients with infectious manifestations alone, and the majority exhibit a spectrum of clinical manifestations with similarities to activated phosphoinositide 3-kinase delta syndrome (APDS) patients.[1,4]

Based on available epidemiological data, it is estimated that the global prevalence of the targeted CVID with immune dysregulation population is approximately 39 patients per million.

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

"The initiation of this second Phase II clinical study outside the APDS indication is a substantial expansion of our work in primary immunodeficiency disorders. Unlike the initial APDS indication and our ongoing Phase II study in PIDs with immune dysregulation with specific genetic drivers, CVID patients are diagnosed based on standard clinical findings, independently of genetics. CVID patients with immune dysregulation have significant clinical unmet need, with no approved therapies, and represent a significantly larger patient population. We are therefore very excited about the potential leniolisib holds for treating CVID patients with immune dysregulation and look forward to enrolling more patients over the coming months."

Leniolisib is marketed under the brand name Joenja® in the U.S. 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

1. Resnick ES, et al. Blood. 2012 119(7): 1650-1657.
2. Boileau J, et al. J Autoimmun. 2011 36(1): 25-32.
3. Ramirez NJ, et al. Curr Opin Immunol. 2021 72: 176-185.

4. Farmer JR, et al. Front Immunol. 2018;8: 1740.
5. Rao VK, et al. Blood. 2023;141(9): 971-983.
6. Rao VK, et al. J Allergy Clin Immunol. 2024;153: 265-74.

For further public information, contact:

Pharming Group, Leiden, the Netherlands
Michael Levitan, VP Investor Relations & Corporate Communications
T: +1 (908) 705 1696
E: investor@pharming.com

FTI Consulting, London, UK
Simon Conway/Alex Shaw/Amy Byrne
T: +44 203 727 1000

LifeSpring Life Sciences Communication, Amsterdam, the Netherlands
Leon Melens
T: +31 6 53 81 64 27
E: pharming@lifespring.nl

US PR
Christina Skrivan
T: +1 (636) 352-7883
E: Christina.Skrivan@precisionaq.com