# Pharming Group announces development plans for leniolisib for additional primary immunodeficiencies (PIDs)

***Initial development in PIDs with immune dysregulation linked to PI3Kδ signaling***

***Phase 2 clinical trial initiation planned for 2Q 2024***

**Leiden, The Netherlands, December 13, 2023:** Pharming Group N.V. ("Pharming" or "the Company") (EURONEXT Amsterdam: PHARM/Nasdaq: PHAR) announces today the expansion of its rare disease pipeline with plans to develop leniolisib for additional primary immunodeficiencies (PIDs) beyond activated phosphoinositide 3-kinase delta syndrome (APDS).

Pharming has engaged with the US Food and Drug Administration (FDA) and has received feedback on its plans to develop leniolisib for PID disorders with immune dysregulation. This includes the recent FDA review of a Phase 2, proof of concept, clinical trial protocol in PIDs with immune dysregulation linked to PI3Kδ signaling submitted under the existing leniolisib IND.

The Phase 2 clinical trial will evaluate leniolisib in PIDs with immune dysregulation linked to PI3Kδ signaling in lymphocytes, with similar clinical phenotypes to APDS. These PID disorders are defined by loss-of-function variants in the following genes: cytotoxic T-lymphocyte associated protein 4 (*CTLA4*), *FAS* (causing autoimmune lymphoproliferative syndrome or ALPS), and phosphatase and tensin homolog (*PTEN*), among others. The epidemiology of these targeted PID genetic disorders suggests a prevalence of approximately 5 patients per million.

The Phase 2 clinical trial is a single arm, open-label, dose range-finding study, to be conducted in approximately 12 patients and is planned to start in 2Q 2024. The objectives for the trial will be to assess safety and tolerability, pharmacokinetics, pharmacodynamics, and explore clinical efficacy of leniolisib in this new PID population. The trial has been designed to inform a subsequent Phase 3 program. The Phase 2 clinical trial will be 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).

***Dr. Jocelyn Farmer, MD/PhD, Director, Clinical Immunodeficiency Program, Beth Israel Lahey Health, commented:***

*"As a physician who manages a care program for primary immunodeficiency (PID) patients, I understand the large disease burden they face, with no approved therapies to target their underlying immune dysregulation. PI3Kδ is an important regulator of lymphocytes, and unbalanced PI3Kδ signaling in lymphocytes is a key signature of immune dysregulation among PID patients who develop lymphoproliferative and autoimmune disease. Therefore, I am very excited to see Pharming progressing the evaluation of the PI3Kδ inhibitor leniolisib into PIDs beyond the FDA-approved APDS indication, where it promises an opportunity to provide critical benefit to patients with a large, currently unmet, clinical need."*

***Anurag Relan, Chief Medical Officer, commented:***

*"Today's announcement is an exciting first step towards expanding our clinical pipeline into additional primary immunodeficiencies beyond APDS. Building upon the success of leniolisib for APDS, we believe that leniolisib will continue to have efficient uses in rebalancing immune dysregulation in PIDs. Our priority is the preparation and start of a Phase 2 clinical trial with leniolisib for targeted PID genetic disorders with immune dysregulation including CTLA4, ALPS-FAS and PTEN in the second quarter of 2024."*

## About Activated Phosphoinositide 3-Kinase δ Syndrome (APDS)

APDS is a rare primary immunodeficiency that was first characterized in 2013. APDS is caused by variants in either one of two identified genes known as *PIK3CD* or *PIK3R1*, which are vital to the development and function of immune cells in the body. Variants of these genes lead to hyperactivity of the PI3Kδ (phosphoinositide 3-kinase delta) pathway, which causes immune cells to fail to mature and function properly, leading to immunodeficiency and dysregulation[1,2,3] APDS is characterized by a variety of symptoms, including severe, recurrent sinopulmonary infections, lymphoproliferation, autoimmunity, and enteropathy.[4,5] Because these symptoms can be associated with a variety of conditions, including other primary immunodeficiencies, it has been reported that people with APDS are frequently misdiagnosed and suffer a median 7-year diagnostic delay.[6] As APDS is a progressive disease, this delay may lead to an accumulation of damage over time, including permanent lung damage and lymphoma.[4-7] A definitive diagnosis can be made through genetic testing. APDS affects approximately 1 to 2 people per million worldwide.

## About leniolisib

Leniolisib is an oral small molecule phosphoinositide 3-kinase delta (PI3Kδ) inhibitor approved in the US 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 II/III clinical trial demonstrated clinical efficacy of leniolisib in the coprimary endpoints; demonstrating statistically significant impact on immune dysregulation and normalization of immunophenotype within these patients, and interim open label extension data has supported the safety and tolerability of long-term leniolisib administration.[8,9] Leniolisib is currently under regulatory review by the European Medicines Agency, with plans to pursue further regulatory approvals in the UK, Canada, Australia and Japan. Leniolisib is also being evaluated in two Phase III clinical trials in children with 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, biologics, and gene therapies that are in early to late-stage development. Pharming is headquartered in Leiden, 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 and technical developments. In light of these risks and uncertainties, and other risks and uncertainties that are described in Pharming's 2022 Annual Report and the Annual Report on Form 20-F for the year ended December 31, 2022, 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.*

## 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.

## References


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