Pharming announces first patient enrolled in pediatric clinical trial of leniolisib

The multinational Phase III study is evaluating leniolisib tablets in children aged 4 to 11 years with APDS, a rare primary immunodeficiency

Leiden, The Netherlands, February 21, 2023: Pharming Group N.V. ("Pharming" or "the Company") (EURONEXT Amsterdam: PHARM/Nasdaq: PHAR) announces that the first patient has been enrolled in its Phase III clinical trial (NCT05438407) evaluating the investigational drug leniolisib, an oral, selective phosphoinositide 3-kinase delta (PI3Kδ) inhibitor, in children with activated phosphoinositide 3-kinase delta syndrome (APDS). There is currently no approved treatment for this complex and progressive disease caused by genetic variants.

At sites in the United States, Europe, and Japan, the single-arm, open-label, multinational clinical trial will evaluate the safety, tolerability, and efficacy of leniolisib in approximately 15 children aged 4 to 11 years who have a confirmed APDS diagnosis. The study's primary efficacy endpoints are a reduction in index lymph node size and an increased proportion of naïve B cells out of total B cells from baseline at 12 weeks. Secondary endpoints include an assessment of the ability of leniolisib to modify health-related quality of life based on measures of physical, social, emotional, and school functioning using a validated patient questionnaire.

Pharming plans to initiate a similar clinical trial in the third quarter of 2023 that will include children aged 1 to 6 years, with APDS, to evaluate a new pediatric formulation of leniolisib. Eligible patients enrolled in either of the pediatric trials will continue to receive leniolisib for a year after the initial 12-week treatment period through an open-label extension trial.

Manish Butte, MD, PhD, E. Richard Stiehm Endowed Chair, Professor with tenure in the Department of Pediatrics, and Division Chief of Immunology, Allergy, and Rheumatology at UCLA, commented:

"In treating APDS, the current standard of care is to use an array of supportive therapies. While these therapies can treat some of the manifestations of APDS, they do not target the underlying cause of the disease. Pharming's studies of leniolisib in children with APDS are important for evaluating the possibility of minimizing symptoms earlier in the disease progression."

Pharming's program for the clinical development of leniolisib in pediatric APDS is supported by positive data from a Phase II/III clinical trial that investigated the drug as a treatment for patients with the disease aged 12 years and older. As announced on February 2, 2022, and recently detailed in *Blood*[1], the international medical journal of the American Society of Hematology, the trial met both its co-primary endpoints, with patients who took leniolisib versus placebo achieving significant reductions in lymphoproliferation as measured by index lymph node size and increases in immunophenotype corrections as measured by the percentage of naïve B cells in peripheral blood.

During the first half of 2022, positive opinions were received from the European Medicines Agency

(EMA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA) on the Pediatric Investigation Plan (PIP) for leniolisib as a treatment for APDS in children. The PIP(s) included the plans for both pediatric clinical trials.

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

"I am pleased we have initiated the first trial in our Phase III pediatric clinical program evaluating leniolisib in children with APDS, and I look forward to our second pediatric trial getting underway. Building on the encouraging findings from our successful Phase II/III study in patients aged 12 years and older with APDS, we are committed to bringing leniolisib to even younger patients with the goal of intervening before they develop immune-related symptoms likely to progress throughout their lives. While continuing to focus on patients of all ages with APDS, we are dedicated to collaborating with regulatory authorities with the goal of generating regulatory filings to gain approval that could support the treatment of children under 12 years of age who are living with this disease."

Based on the Phase II/III trial results and long-term open-label extension data, the U.S. Food and Drug Administration (FDA) is conducting a priority review of Pharming's New Drug Application for leniolisib as a treatment for adolescents and adults with APDS and has assigned a Prescription Drug User Fee Act (PDUFA) goal date of March 29, 2023. In addition, Pharming's Marketing Authorisation Application (MAA) for leniolisib in the same patient population is under evaluation by the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP). Pharming expects that the CHMP will issue its opinion on the leniolisib MAA in 2H 2023.

About Activated Phosphoinositide 3-Kinase δ Syndrome (APDS)

APDS is a rare primary immunodeficiency that affects approximately 1 to 2 people per million. APDS is caused by variants in either of two genes, *PIK3CD* or *PIK3R1*, that regulate maturation of white blood cells. Variants of these genes lead to hyperactivity of the PI3Kδ (phosphoinositide 3-kinase delta) pathway.[2,3] 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.[2,4] APDS is characterized by severe, recurrent sinopulmonary infections, lymphoproliferation, autoimmunity, and enteropathy.[5,6] Because these symptoms can be associated with a variety of conditions, including other primary immunodeficiencies, people with APDS are frequently misdiagnosed and suffer a median 7-year diagnostic delay.[7] As APDS is a progressive disease, this delay may lead to an accumulation of damage over time, including permanent lung damage and lymphoma.[5-8] A definitive diagnosis can be made through genetic testing.

About leniolisib

Leniolisib is a small-molecule inhibitor of the delta isoform of the 110 kDa catalytic subunit of class IA PI3K. PI3Kδ is expressed predominately in hematopoietic cells and is essential to normal immune system function through conversion of phosphatidylinositol-4-5-trisphosphate (PIP2) to

phosphatidylinositol-3-4-5-trisphosphate (PIP3). Leniolisib inhibits the production of PIP3 and PIP3 serves as an important cellular messenger 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 (neutrophils, mast cells, and macrophages) strongly indicates that PI3Kδ is a valid and potentially effective therapeutic target for immune diseases such as APDS. To date, leniolisib has been well tolerated during both the Phase 1 first-in-human trial in healthy subjects and the Phase II/III registration-enabling study in patients 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.

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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 2021 Annual Report and the Annual Report on Form 20-F for the year ended December 31, 2021, 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

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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

1. Rao VK, et al. Blood. 2022. https://doi.org/10.1182/blood.2022018546.
2. Lucas CL, et al. Nat Immunol. 2014;15:88-97.
3. Elkaim E, et al. J Allergy Clin Immunol. 2016;138(1):210-218.
4. Nunes-Santos C, Uzel G, Rosenzweig SD. J Allergy Clin Immunol. 2019;143(5):1676-1687.
5. Coulter TI, et al. J Allergy Clin Immunol. 2017;139(2):597-606.
6. Maccari ME, et al. Front Immunol. 2018;9:543.
7. Jamee M, et al. Clin Rev Allergy Immunol. 2019;May 21.
8. Condliffe AM, Chandra A. Front Immunol. 2018;9:338.

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