



Pharming receives agreement of Paediatric Investigation Plan and Promising Innovative Medicine designation for leniolisib from UK MHRA

April 26, 2022

An agreed Paediatric Investigation Plan (PIP) is the regulatory pathway to market authorization for leniolisib as a treatment for activated phosphoinositide 3-kinase delta syndrome (APDS) in children

A Promising Innovative Medicine (PIM) designation is an early indication that leniolisib is a candidate for the MHRA's Early Access to Medicines Scheme

LEIDEN, Netherlands, April 26, 2022 /PRNewswire/ -- Pharming Group N.V. ("Pharming" or the "Company") (EURONEXT Amsterdam: PHARM) (Nasdaq: PHAR) announces that it has received a positive decision from the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) on a Paediatric Investigation Plan (PIP) submission for leniolisib, an oral, selective phosphoinositide 3-kinase delta (PI3K δ) inhibitor, for the treatment of activated phosphoinositide 3-kinase delta syndrome (APDS) in patients from 1 year of age to less than 18 years of age. The Company also announces that the MHRA has granted Promising Innovative Medicine (PIM) designation to leniolisib for the treatment of APDS.



A PIP is a development plan aimed at ensuring that the necessary data are obtained to support the marketing authorization of a medicine in the pediatric population. All applications for [marketing authorization](#) for new medicines in children require the results of studies as described in an agreed PIP, unless the medicine is exempt due to a deferral or waiver. The leniolisib PIP includes two planned global clinical trials in pediatric patients with APDS, the first in children ages 4-11 years and the second in children ages 1-6 years. The Company expects to initiate recruitment for this pediatric program for leniolisib during the second half of 2022.

A PIM designation indicates that a medicinal product is a promising candidate for the MHRA's Early Access to Medicines Scheme (EAMS), which provides pre-market access to products that are intended for the treatment, diagnosis, or prevention of a life-threatening or seriously debilitating condition and have the potential to address an unmet medical need.

Anurag Relan MD, Pharming's Chief Medical Officer, commented:

"We are pleased to have received agreement of this PIP and the PIM designation from the MHRA, these represent important regulatory milestones as we continue to advance leniolisib for the treatment of APDS, a rare, often debilitating, and sometimes fatal condition. The agreed PIP and the PIM designation further support our confidence in the potential of leniolisib to address APDS, as they provide us with a pathway toward marketing authorization in the United Kingdom. Pharming looks forward to continuing to work with regulatory authorities globally to bring leniolisib to patients with this significant unmet medical need as expeditiously as possible."

Leniolisib, which has received Orphan Drug Designation in Europe, received the same designation from the US Food and Drug Administration on January 30, 2018.

As previously announced, Pharming plans to begin submitting global registration filings for leniolisib in the second quarter of 2022 and, subject to approval, launching the treatment in the US in the first quarter of 2023 and starting a series of European launches in the second half of 2023.

About Activated Phosphoinositide 3-Kinase δ Syndrome (APDS)

APDS is a rare primary immunodeficiency that affects approximately one to two people per million. Also known as PASLI, it 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 PI3K δ (phosphoinositide 3-kinase delta) pathway.^{1,2} Balanced signaling in the PI3K δ 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.^{1,3} APDS is characterized by 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, 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 The only way to definitively diagnose this condition is 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 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 and regulates a multitude of cell functions such as proliferation, differentiation, cytokine production, cell survival, angiogenesis, and metabolism. Unlike PI3K α and PI3K β , which are ubiquitously expressed, PI3K δ and PI3K γ are expressed primarily in cells of hematopoietic origin. The central role of PI3K δ 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 PI3K δ is a valid and potentially

effective therapeutic target for several immune diseases.

To date, leniolisib has been well tolerated during both a Phase 1 first-in-human trial in healthy subjects and a Phase II/III registration-enabling study.

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.

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 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. 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.

References:

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

For further public information, contact:

Pharming Group, Leiden, The Netherlands
Sijmen de Vries, CEO: T: +31 71 524 7400 E: investor@pharming.com

FTI Consulting, London, UK
Victoria Foster Mitchell/Alex Shaw
T: +44 203 727 1000

FTI Consulting, USA
Jim Polson
T: +1 (312) 553-6730

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

US PR:
Emily VanLare
E: Emily.VanLare@precisionvh.com
T: +1 (203) 985 5596

EU PR:
Dan Caley
E: Dan.caley@aprilsix.com
T: +44 (0) 787 546 8942

Logo - https://mma.prnewswire.com/media/1454235/Pharming_Group_NV_Logo.jpg

 View original content to download multimedia: <https://www.prnewswire.com/news-releases/pharming-receives-agreement-of-paediatric-investigation-plan-and-promising-innovative-medicine-designation-for-leniolisib-from-uk-mhra-301532428.html>

SOURCE Pharming Group N.V.