

Pharming announces US FDA approval of Joenja® (leniolisib) as the first and only treatment indicated for APDS

APDS (activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome) is a rare and progressive primary immunodeficiency

Joenja® is a targeted treatment of APDS for adult and pediatric patients 12 years of age and older

Joenja® is expected to launch in the US in early April

Pharming will host a conference call for investors and analysts on March 27 at 14:00 CEST/08:00 EST

Leiden, The Netherlands, March 24, 2023: Pharming Group N.V. (“Pharming” or “the Company”) (EURONEXT Amsterdam: PHARM/Nasdaq: PHAR) announces that the US Food and Drug Administration (FDA) has approved Joenja® (leniolisib) for the treatment of activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) in adult and pediatric patients 12 years of age and older. Joenja®, an oral, selective PI3Kδ inhibitor, is the first and only treatment approved in the US for APDS, a rare and progressive primary immunodeficiency. The FDA evaluated the Joenja® application for APDS under Priority Review, which is granted to therapies that have the potential to provide significant improvements in the treatment, diagnosis or prevention of serious conditions. Joenja® is expected to launch in the US in early April and will be available for shipment in mid-April.

Dr. Eveline Wu, MD, MSCR, Division Chief, Paediatric Rheumatology & Associate Professor of Paediatric Rheumatology and Allergy/Immunology at The University of North Carolina School of Medicine, said:

“The FDA approval of Joenja® is an exciting moment for the APDS community and offers to transform the treatment pathway for patients and families affected by this rare disease. This approval means that they will, for the first time, have access to an approved treatment, which has the potential to change the standard of care for the patient population suffering from APDS.”

Vicki Modell, co-founder of the Jeffrey Modell Foundation, an international, non-profit, organization dedicated to helping individuals and family members affected by primary immunodeficiency disorders, commented:

“The approval of Pharming’s Joenja® is an important step toward making a difference in the lives of individuals living with APDS who experience severe, life-altering and progressive symptoms. The FDA approval of a treatment option for one of the more than 450 primary immunodeficiencies is also a key moment for the broader primary immunodeficiency community. The Jeffrey Modell Foundation’s mission of hope, advocacy and action is dedicated to early diagnosis, genetic sequencing, treatments and ultimately, future cures for primary immunodeficiencies.”

Sijmen de Vries, Chief Executive Officer of Pharming, commented:

"This FDA approval of Joenja® is an important milestone for people living with APDS who will now have access to the first approved treatment option specifically for this debilitating disease. Until now, management of APDS has relied on the treatment of the diverse symptoms associated with APDS. We are grateful to the patients, caregivers, and physicians who participated in the clinical trials who have made today's approval a reality. I would also like to thank the Pharming and the Novartis teams who have supported the development of Joenja® and can, therefore, be justifiably proud of this FDA approval. Today also marks a landmark event for Pharming and demonstrates our commitment to transforming the lives of patients who suffer from rare diseases. The approval and near-term launch of Joenja®, our second commercial product, brings us closer to our goal of becoming a leading global rare disease company dedicated to patient communities with unmet medical needs."

APDS is a rare primary immunodeficiency that was first characterized in 2013 and is currently estimated to affect 1 to 2 people per million. It is caused by genetic variants in either one of two identified genes, known as *PIK3CD* or *PIK3R1*, which are vital to the normal development and function of immune cells in the body. While people with APDS may suffer from a wide variety of symptoms, the most common are frequent and severe infections of the ears, sinuses, and upper and lower respiratory tracts. Infections usually begin in infancy. People with APDS are susceptible to swollen lymph nodes or an enlarged spleen (splenomegaly), as well as autoimmunity and inflammatory symptoms. People with APDS may also be at higher risk for cancers like lymphoma.

The FDA evaluated the New Drug Application (NDA) for Joenja® under priority review and has approved the drug based on findings from a multinational, triple-blind, placebo-controlled, randomized Phase II/III clinical trial, which evaluated efficacy and safety in 31 patients diagnosed with APDS aged 12 years and older. Also submitted as part of the application were data from a long-term, open-label extension clinical trial in which 38 patients received Joenja® for a median of two years.

Results from the 12-week randomized, placebo-controlled study in 31 patients with APDS aged 12 years and older demonstrated clinical efficacy of Joenja® 70mg twice daily over placebo, and was significant in the co-primary endpoints which evaluated improvement in lymphoproliferation as measured by the reduction in lymph node size and increase in naïve B cells, reflecting the impact on immune dysregulation and normalization of immunophenotype in these patients, respectively. The adjusted mean change (95% CI) between Joenja® and placebo for lymph node size was -0.25 (-0.38,-0.12; P=0.0006; N=26) and for percentage of naïve B cells was 37.30 (24.06, 50.54; P=0.0002; N=13). The most common adverse reactions in the clinical trial (incidence >10%) were headache, sinusitis, and atopic dermatitis.

With the approval of Joenja®, as a treatment for a rare pediatric disease, the FDA granted Pharming a priority review voucher ("PRV"). Pursuant to the terms of Pharming's 2019 exclusive license agreement with Novartis for leniolisib, Novartis has the right to purchase the PRV from Pharming for a small minority share of the value of the PRV. Pursuant to the agreement, Pharming will make milestone payments to Novartis and another party for the approval and first commercial sale for

APDS totaling \$10.5 million and we agreed to make certain additional milestone payments to Novartis in an aggregate amount of up to \$190 million upon the achievement of certain leniolisib sales milestones. We also agreed to make tiered royalty payments to Novartis, calculated as low double-digit to high-teen double-digit percentage of net sales of leniolisib.

For more information regarding APDS, please visit AllAboutAPDS.com. Pharming, in collaboration with Invitae Corporation, facilitates access to no charge genetic testing and counseling in the US and Canada through NavigateAPDS.com. For more information regarding Pharming and their dedication to the rare disease community, please visit www.Pharming.com.

The Marketing Authorisation Application (MAA) for leniolisib with the European Medicines Agency's (EMA) Committee for Human Medicinal Products (CHMP) is currently under review. Pharming expects that CHMP will issue its opinion on the MAA in the second half of 2023.

US Important Safety Information for Joenja® (leniolisib)

INDICATIONS AND USAGE

Joenja® (leniolisib) is a kinase inhibitor indicated for the treatment of activated phosphoinositide 3-kinase delta (PI3K δ) syndrome (APDS) in adult and pediatric patients 12 years of age and older.

IMPORTANT SAFETY INFORMATION

Verify pregnancy status in females of reproductive potential prior to initiating treatment with Joenja®.

Joenja® may cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to a fetus and to use highly effective methods of contraception during treatment with Joenja® and for 1 week after the last dose of Joenja®.

Live, attenuated vaccinations may be less effective if administered during Joenja® treatment.

Use of Joenja® in patients with moderate to severe hepatic impairment is not recommended. There is no recommended dosage for patients weighing less than 45 kg.

The most common adverse reactions (incidence >10%) seen in clinical trials were headache, sinusitis, and atopic dermatitis.

Seven (33%) patients receiving Joenja® developed an absolute neutrophil count (ANC) between 500 and 1500 cells/microL. No patients developed an ANC <500 cells/microL and there were no reports of infection associated with neutropenia.

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 PI3K δ (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 Joenja® (leniolisib)

Joenja® (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. Joenja® 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 Joenja® in the co-primary 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 Joenja® administration.⁸ 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 a Phase III clinical trial in children aged 4 to 11 with APDS, with a further trial planned in children aged 1 to 6 years with APDS. For information about Joenja®, visit: Joenja.com

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 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 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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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.
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Investors and Analysts conference call dial-in information

March 27, 2023: 14:00CEST/08:00EST

Please note, the Company will only take questions from dial-in attendees.

Dial-in details:

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[Global Dial-In Numbers](#)

Access code: **040991**

Webcast link: <https://webcast.openbriefing.com/pharming-mar23/>

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