## Joenja® (leniolisib) – New orphan drug approval

- On March 24, 2023, Pharming announced the FDA approval of 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.

- APDS is a rare primary immunodeficiency that was first characterized in 2013. APDS is characterized by a variety of symptoms, including severe, recurrent sinopulmonary infections, lymphoproliferation, autoimmunity, and enteropathy. A definitive diagnosis can be made through genetic testing.

    — APDS affects approximately 1 to 2 people per million worldwide.

- Joenja is a PI3Kδ inhibitor, and the first targeted treatment approved for APDS. 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.

- The efficacy of Joenja was established in a Study 2201, a blinded, randomized, placebo-controlled study in 31 adult and pediatric patients 12 years of age and older with confirmed APDS-associated genetic PI3Kδ mutation with a documented variant in either PIK3CD or PIK3R1. Patients received Joenja or placebo for 12 weeks. The co-primary endpoints were improvement in lymphoproliferation as measured by a change from baseline in lymphadenopathy (measured by the log10-transformed sum of product diameters) and the normalization of immunophenotype as measured by the percentage of naïve B cells out of total B cells.

    — The adjusted mean change between Joenja vs. placebo for lymph node size was -0.25 (95% CI: -0.38, -0.12; p = 0.0006).
    — The adjusted mean change between Joenja vs. placebo for the percentage of naïve B cells was 37.30 (95% CI: 24.06, 50.54; p= 0.0002).

- Warnings and precautions for Joenja include embryo-fetal toxicity and vaccinations.

- The most common adverse reactions (> 10%) with Joenja use were headache, sinusitis, and atopic dermatitis

- The recommended dosage of Joenja in adult and pediatric patients 12 years of age and older weighing 45 kg or greater is 70 mg administered orally twice daily approximately 12 hours apart, with or without food.

    — There is no recommended dosage for patients weighing less than 45 kg.

- Pharming plans to launch Joenja in early April 2023. Joenja will be available as a 70 mg tablet.