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News Release

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European Commission Approves BYANNLI® (6-monthly Paliperidone Palmitate; PP6M) for the Maintenance Treatment of Schizophrenia in Adults

BYANNLI® (6-monthly paliperidone palmitate; PP6M) is the first long-acting injectable schizophrenia treatment to be approved with a twice-yearly dosing regimen[1]

The approval is based on results from the Route 6 Study, which showed that 92.5 percent of patients treated with PP6M were relapse-free at the end of the 12-month double-blind phase[1]

BEERSE, BELGIUM, 23 November, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the approval of the long-acting atypical antipsychotic therapy BYANNLI® (6-monthly paliperidone palmitate; PP6M) by the European Commission (EC) for the maintenance treatment of schizophrenia in adult patients who are clinically stable on 1-monthly paliperidone palmitate (PP1M) or 3-monthly paliperidone palmitate (PP3M).[1] The approval makes PP6M the first twice-

yearly treatment for adults living with schizophrenia to be approved by the EC, with the longest available dosing interval for an antipsychotic medication in the European Economic Area.[1,2]

"Nearly 75 percent of people living with schizophrenia experience a relapse in symptoms, and this is often driven by missed doses of prescribed medication,"[3] said Professor Eduard Parellada, Director of the Barcelona Clínic Schizophrenia Unit (BCSU), Institute of Neuroscience, Hospital Clínic of Barcelona, Spain. "The Route 6 Study results provide compelling evidence that 6-monthly paliperidone palmitate offers 12-month symptom control and prevents relapses with just two doses per year. Moreover, the observed safety profile was consistent with previous studies. This is a great step forward for individuals who want to focus less on taking medication and more on other aspects of their treatment plan."

The EC approval is based on the Route 6 Study, a randomised, double-blind, non-inferiority Phase 3 global study designed to demonstrate that PP6M is not less effective than PP3M for the prevention of relapse in participants previously stabilised on a shorter-acting formulation of paliperidone palmitate.[1,2] The study enrolled 702 adults living with schizophrenia from 20 countries, including Bulgaria, Czech Republic, France, Hungary, Italy, Poland, Russia, Spain and Turkey.[1,2] The results showed non-inferiority of PP6M compared with PP3M on the primary endpoint of time to first relapse at the end of the 12-month period. Results found that 92.5 percent of patients treated with PP6M and 95.1 percent treated with PP3M were relapse-free at 12 months.[1,2] Relapse was defined as psychiatric hospitalisation, increase in Positive and Negative Syndrome Scale (PANSS) total score, increase in individual PANSS item scores, violent behaviour resulting in self-injury or suicidal/homicidal ideation.

The safety profile observed for PP6M was consistent with previous studies of PP1M and PP3M, with no new safety signals emerging.[1] The most common treatment emergent adverse reactions (≥5.0 percent) in the Route 6 Study's PP6M group were weight increase (8.4 percent), injection site pain (7.7 percent), headache (6.7 percent) and upper respiratory tract infection (5.0 percent). There were no unexpected serious adverse reactions.[1,2]

"At Janssen, we are committed to reducing the devastating burden caused by mental

illnesses," said Bill Martin, Ph.D., Global Therapeutic Area Head, Neuroscience, Janssen Research & Development, LLC. "Today's approval of PP6M by the European Commission is a key milestone in our ongoing work towards this goal by offering patients and their loved ones the potential for a life less defined by schizophrenia medication."

The EC approval follows the positive CHMP opinion for PP6M[4] and the announcement of the U.S. Food and Drug Administration (FDA) approval of PP6M for the treatment of schizophrenia in adults after they have been adequately treated with PP1M for at least 4 months or PP3M for at least one 3-month cycle[5] in September 2021. EC approval is valid in all 27 member states of the European Union, and the European Economic Area countries (Norway, Iceland and Liechtenstein).

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About 6-monthly paliperidone palmitate

6-monthly paliperidone palmitate (PP6M) is a long-acting injectable (LAI) that works by dissolving and entering the bloodstream slowly, due to its extremely low water solubility, resulting in continuous absorption of paliperidone palmitate over a 6-month period.[1] This offers patients the potential for up to 6 months of symptom control and a reduction in their risk of relapse with only two doses a year.[1]

The U.S. Food and Drug Administration (FDA) approved PP6M under the trade name INVEGA HAFYERA™ in September 2021 for the treatment of schizophrenia in adults after they have been adequately treated with PP1M for at least 4 months or PP3M for at least one 3-month cycle.[5]

PP6M must be administered only by a healthcare professional giving the full dose in a single injection into the gluteal muscle.[1] For the full prescribing information, please see the Summary of Product Characteristics.

About the Route 6 Study (PSY3015)

The Route 6 Study was a randomised, double-blind, non-inferiority global Phase 3 study

of 702 adults (ages 18–70) with schizophrenia, designed to demonstrate that injection cycles consisting of a single administration of PP6M (700 or 1000 mg) are not less effective than two sequentially administered injections of PP3M (350 or 525 mg) for the prevention of relapse in subjects with schizophrenia previously stabilised on corresponding doses of PP1M (100 or 150 mg) or PP3M (350 or 525 mg).[1,2]

The study consisted of four treatment phases: a screening phase (up to 28 days); a transition phase (of 1 to 4 months), applicable to those adult patients who entered the screening phase before being stabilised on PP1M or PP3M; a maintenance phase (of 1 or 3 months), used to stabilise patients on PP1M or PP3M prior to the double-blind phase; and a double-blind phase (of 12 months). In the double-blind phase, all stabilised adult patients (N=702) were randomised in a 2:1 ratio to receive PP6M (n=478) or PP3M (n=224).[1,2]

Study evaluations included efficacy, pharmacokinetics, pharmacodynamics and safety. The study's duration varied from approximately 13 months to 19 months depending on treatment arm.[1,2]

About Long-Acting Injectables

Long-acting injectables (LAIs) allow for the slow release of a drug into the blood and have been on the market for more than 50 years.[6] LAI antipsychotics have been shown to offer a number of advantages compared with oral medication, including not having to remember to take drugs daily, improved patient outcomes, improved patient and physician satisfaction, and lower relapse rates.[7]

In 2002, a 1-monthly injectable formulation (PP1M) was approved by the European Commission as a maintenance treatment of schizophrenia in adult patients under the brand name XEPLION®.[8] In 2016, a 3-monthly LAI formulation (PP3M) was approved under the trade name TREVICTA®.[9]

On 1 October 2021, the World Health Organization recommended the inclusion of PP1M in the Model Lists of Essential Medicines for the maintenance treatment of schizophrenia in adults stabilised on oral therapy. The Committee noted the

public health need for long-acting antipsychotics in settings where close follow-up of patients with psychotic disorders is difficult.[10]

About Schizophrenia

Schizophrenia is a chronic and severe brain disorder affecting approximately 25 million people worldwide,[11] and an estimated 3.7 million people in the EU.[12] The disease is characterised by distortions in thinking, perception, emotions, language, sense of self and behaviour, leading to neurological impairment, severe disability and increased mortality.[12]

Antipsychotic medication is recognised as an essential component in the treatment of schizophrenia, and adherence to medication plays a critical role in preventing symptoms and relapses.[13] Early intervention in schizophrenia may improve patient outcomes as more than 69 percent of people with schizophrenia do not receive appropriate care.[11]

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Janssen Pharmaceutica N.V., Janssen Research & Development, LLC and Janssen-Cilag are part of the Janssen Pharmaceutical Companies of Johnson & Johnson. Learn more at www.janssen.com/emea. Follow us at https://twitter.com/JanssenEMEA.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding 6-monthly paliperidone palmitate (PP6M). The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying

assumptions prove inaccurate, or known or unknown risks or uncertainties materialise, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica N.V., Janssen Research & Development, LLC, Janssen-Cilag and any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behaviour and spending patterns of purchasers of healthcare products and services; changes to applicable laws and regulations, including global healthcare reforms; and trends toward healthcare cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors", and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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*Professor Eduard Parellada has been a paid consultant for Janssen. He has not been compensated for any media work

[1] European Medicines Agency. 6-monthly Paliperidone Palmitate Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/medicines. Accessed November 2021.

[2] Najarian D, et al. A randomised, double-blind, multicenter, noninferiority Phase 3 study. Poster 0533 presented at ECNP 2021.

[3] Weiden PJ, et al. Partial compliance and risk of rehospitalization among California medicaid patients with schizophrenia. Psychiatr Serv. 2004;55(8):886–891.

[4] Athanasopoulou C, et al. An analysis of online health information on schizophrenia or related conditions: a cross-sectional survey. BMC Med Inform Decis Mak. 2013;13:98. Johnson & Johnson Ltd. Press release on September 2021. Available at: https://www.janssen.com/emea/sites/www_janssen_com_emea/files/press_release_janssen_receives_positive_chmp_opinion_for_byannlir_for_the_maintenance_treatment_of_schizophrenia_in_adults.pdf. Accessed November 2021.

[5] Johnson & Johnson Ltd. Press release on September 2021. Available at: https://www.jnj.com/janssen-announces-u-s-fda-approval-of-invega-hafyera-6-month-paliperidone-palmitate-first-and-only-twice-yearly-treatment-for-adults-with-schizophrenia. Accessed November 2021.

[6] National Alliance on Mental Illness. Long-Acting Injectables. Available at: https://www.nami.org/Learn-More/Treatment/Mental-Health-Medications/Long-Acting-Injectables. Accessed November 2021.

[7] Brissos S, et al. The role of long-acting injectable antipsychotics in schizophrenia: a critical appraisal. Ther Adv Pyschopharmacol. 2014;4(5):198–219.

[8] European Medicines Agency. Xeplion Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/xeplion-epar-product-information_en.pdf. Accessed November 2021.

[9] European Medicines Agency. Trevicta Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/trevicta-epar-product-information_en.pdf. Accessed November 2021.

[10] Report of the 23rd WHO Expert Committee on the Selection and Use of Essential Medicines 2021.

[11] World Health Organization. Schizophrenia. Available at: https://www.who.int/news-room/fact-sheets/detail/schizophrenia. Accessed November 2021.

[12] Athanasopoulou C, et al. An analysis of online health information on schizophrenia or related conditions: a cross-sectional survey. BMC Med Inform Decis Mak. 2013;13:98.

[13] Higashi K, et al. Medication adherence in schizophrenia: factors influencing adherence and consequences of nonadherence, a systemic literature review. Ther Adv Psychopharmacol. 2013; 3(4):200–218.