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Janssen Seeks Expanded Use of SPRAVATO®▼ (Esketamine) Nasal Spray in Europe as a Treatment for Depressive Symptoms in Adults with Major Depressive Disorder Who Have Current Suicidal Ideation with Intent

In two pivotal Phase 3 trials, SPRAVATO®▼ combined with comprehensive standard of care achieved statistically significant rapid reduction of depressive symptoms in patients with major depressive disorder who have current suicidal ideation with intent compared to comprehensive standard of care alone

BEERSE, BELGIUM, JANUARY 15, 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the submission of a Type II Variation Application to the European Medicines Agency (EMA) for SPRAVATO®▼ (esketamine) nasal spray. The application seeks to expand the use of esketamine nasal spray, beyond its current indication, as an acute short-term treatment, co-administered with oral antidepressant therapy, for the rapid reduction of depressive symptoms in adults with a moderate-to-severe depressive episode of major depressive disorder (MDD) who have current suicidal ideation with intent.

The submission is based on results from two double-blind, randomised, placebo-controlled multicentre Phase 3 clinical studies (ASPIRE I & II), which evaluated both the efficacy and safety of esketamine nasal spray versus a placebo nasal spray when used in addition to comprehensive standard of care (SOC). In these studies, SOC included initial hospitalisation and newly initiated and/or optimised antidepressant therapy, enhanced with extensive twice-weekly visits during the double-blind phase.[1,2,3]

In both ASPIRE I & II, esketamine nasal spray combined with comprehensive SOC was associated with a reduction in depressive symptoms, and demonstrated clinically meaningful and statistically significant superiority over a placebo nasal spray plus comprehensive SOC in rapidly reducing symptoms of MDD at 24 hours after the first

dose.[1,2,3] The benefit of esketamine nasal spray plus comprehensive SOC on symptoms of MDD was apparent as early as 4 hours after the first dose.[1,2,3]

"Janssen is committed to reducing the devastating burden caused by serious mental health disorders," said Husseini K. Manji, M.D., Global Head, Neuroscience Therapeutic Area, Janssen Research & Development, LLC. "There is a need to provide treatments that can rapidly reduce depressive symptoms of individuals living with MDD who are in need of urgent relief. We therefore look forward to working with the EMA to provide a new targeted treatment that could potentially deliver meaningful results for these patients."

The safety profile was consistent with that observed in the clinical trial programme of esketamine in patients with treatment-resistant depression, with no new safety signals. In the clinical trials, the most common adverse events (≥20%) were dizziness, dissociation, nausea, somnolence and headache.[1]

"Patients with MDD who are assessed to be at imminent risk for suicide constitute a psychiatric emergency that require immediate intervention," explains Professor Maurizio Pompili, Director, University Psychiatric Clinic, Sant'Andrea Hospital, Sapienza University of Rome, Italy. "While currently available antidepressants are effective in treating depressive symptomatology, they can often take weeks to achieve their full effects. This delay is potentially dangerous, especially since suicide risk is highest early in treatment."

In ASPIRE I & II, both esketamine nasal spray plus comprehensive SOC and placebo nasal spray plus comprehensive SOC resulted in an improvement in severity of suicidality as measured by the revised Clinical Global Impression of Severity of Suicidality (CGI-SS-R) at 24 hours after the first dose. The treatment difference between the two groups on this secondary endpoint was not statistically significant. This may be due to the substantial beneficial effects of comprehensive SOC used in the clinical trial, including the impact of inpatient psychiatric hospitalisation in diffusing the acute suicidal crisis in subjects in both treatment groups.[1,2,3]

In October 2019, a supplemental New Drug Application was also submitted to the U.S. Food and Drug Administration (FDA) for esketamine nasal spray for the rapid reduction of depressive symptoms in adult patients with MDD who have active suicidal ideation with intent.[4]

#ENDS#

*Professor Maurizio Pompili is a paid consultant for Janssen. He has not been compensated for any media work.

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About SPRAVATO®▼

As an antagonist of the N-methyl-D-aspartate (NMDA) glutamate receptor. SPRAVATO®▼ (esketamine) nasal spray offers the first new mechanism of action in 30 years to treat major depressive disorder (MDD).[5,6]

Esketamine nasal spray is self-administered through a single-use nasal spray device, offering a novel mode of drug administration for the treatment of MDD. The decision to prescribe esketamine nasal spray should be determined by a psychiatrist.[7]

Esketamine nasal spray was approved by the European Commission for use in combination with a selective serotonin reuptake inhibitor (SSRI) or serotonin and norepinephrine reuptake inhibitor (SNRI), in adult patients with treatment-resistant major depressive disorder (TRD) in December 2019, and was approved for use in TRD patients by the conjunction with an oral antidepressant, for adults living with treatment-resistant depression by the U.S. Food and Drug Administration (FDA) in March 2019.[7,8,9] The FDA granted Breakthrough Therapy designation to esketamine nasal spray for major depressive disorder with imminent risk for suicide in August 2016.[10]

Adverse events should be reported. ▼This medicinal product is subject to additional monitoring and it is therefore important to report any suspected adverse events related to this medicinal product. Reporting forms and information can be found at www.yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Janssen-Cilag Limited on 01494 567447 or at dsafety@its.jnj.com.

For further safety information, please see the Summary of Product Characteristics available at https://www.ema.europa.eu/en/documents/product-information/spravato-epar-product-information_en.pdf.

About Major Depressive Disorder

Major depressive disorder (MDD) affects nearly 40 million people of all ages in Europe and is one of the leading causes of disability worldwide.[11,12] Individuals with depression, including MDD, experience continuous suffering from a serious, biologically-based disease, which has a significant negative impact on all aspects of life, including quality of life and function.[13,14] At its worst, MDD can be fatal, with MDD patients demonstrating a 20-fold higher risk of suicide than the rest of the population.[15] Despite treatment advances, currently available antidepressant medications can take between four to six

weeks to reach their full effect,[16] and one-third of people who suffer from MDD do not respond to these treatments.[17]

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.

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

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Cautions Concerning Forward-Looking Statements.

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding the product development of SPRAVATO®▼. 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-Cilag International NV, 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 December 30, 2018, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," in the company's most recently filed Quarterly Report on Form 10-Q, and in 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. Neither 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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