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News Release

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SPRAVATO® ▼ (Esketamine Nasal Spray) Authorised in Europe for the Rapid Reduction of Depressive Symptoms in a Psychiatric Emergency for Patients with Major Depressive Disorder

- *This milestone makes esketamine nasal spray the first N-methyl-D-aspartate (NMDA) antagonist to be approved for patients with Major Depressive Disorder (MDD) in a psychiatric emergency¹⁻³*
- *European Commission (EC) authorisation is based on results from two Phase 3 ASPIRE studies, which evaluated the efficacy and safety of esketamine nasal spray used in addition to comprehensive standard of care (SOC)⁴⁻⁶*
- *This authorisation marks the second indication for esketamine nasal spray in the European Economic Area (EEA)⁷*

BEERSE, BELGIUM, FEBRUARY 8, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the European Commission (EC) has authorised the expanded use of SPRAVATO® ▼ (esketamine nasal spray), co-administered with oral antidepressant therapy in adults with a moderate to severe episode of MDD, as acute short term treatment, for the rapid reduction of depressive symptoms, which according to clinical judgement constitute a psychiatric emergency.⁷

“Depression is more than just feeling sad, it’s a debilitating combination of symptoms that are different for each person and can progress to a point where patients may experience a psychiatric emergency,” said Professor Maurizio Pompili[†], Director, University Psychiatric Clinic, Sant’Andrea Hospital, Sapienza University of Rome, Italy.

“Many antidepressants are effective in treating depressive symptomatology but do not provide rapid relief for patients and can take weeks to achieve their full effect. The fast-acting nature of esketamine nasal spray in these patients may address a key unmet need within this population.”

The EC authorisation of esketamine nasal spray is based on data from the Phase 3 double-blind, randomised, placebo controlled, multicentre ASPIRE I & II clinical studies conducted globally. These studies compared the efficacy and safety of esketamine nasal spray in combination with comprehensive standard of care (SOC) against placebo nasal spray in combination with comprehensive SOC in adult patients with moderate to severe MDD and current/active suicidal ideation with intent.^{4,5} The comprehensive SOC included initial psychiatric hospitalisation and newly initiated or optimised oral antidepressant therapy, which was determined by the treating physician based on clinical judgement and practice guidelines, for the duration of the studies. The comprehensive SOC was enhanced by twice-weekly visits with extensive clinical contact, and concomitant use of benzodiazepines was permitted during the study.^{4,5}

Within each study, patients treated with esketamine nasal spray accompanied by comprehensive SOC had a statistically significant and clinically meaningful reduction in depressive symptoms (reduction from baseline Montgomery-Åsberg Depression Rating Scale [MADRS]* total score) at 24 hours after receiving the first dose compared to placebo nasal spray in combination with comprehensive SOC ($p=0.006$). The benefit of esketamine nasal spray plus comprehensive SOC on symptoms of MDD was apparent as early as 4 hours after the first dose.^{4,5} The effectiveness of esketamine nasal spray in preventing suicide or in reducing suicidal ideation or behaviour was not demonstrated.

The safety profile for esketamine nasal spray in this patient population was consistent with previous studies in adults with treatment-resistant major depressive disorder (TRD).^{1,8} The most common treatment-emergent adverse events ($\geq 20\%$) observed in the esketamine nasal spray plus comprehensive SOC group versus the placebo nasal spray plus comprehensive SOC group during the double-blind phase were dizziness (38.3% vs 13.8%), dissociation (33.9% vs 5.8%), nausea (26.9% vs 13.8%), somnolence (20.7% vs 10.2%), and headache (20.3% vs 20.4%), respectively.⁶

“At Janssen, we are committed to reducing the devastating burden caused by serious mental illnesses and this further authorisation of esketamine nasal spray by the European Commission is a key milestone in our ongoing work towards this goal,” said Bill Martin, Ph.D., Global Therapeutic Area Head, Neuroscience, Janssen Research &

Development, LLC. "Esketamine nasal spray offers adults with MDD who are in need of urgent relief, an effective treatment to reduce their debilitating depressive symptoms. This authorisation provides a new and innovative treatment option to this vulnerable population."

This EC authorisation is valid in all 27 member states of the European Union as well as the EEA countries (Norway, Iceland and Liechtenstein), and Northern Ireland and Great Britain following the additional step of validation and processing of the baseline submission required following the end of the transition period post-Brexit. Esketamine nasal spray is already authorised by the EC for use in combination with a selective serotonin reuptake inhibitor (SSRI) or a serotonin and norepinephrine reuptake inhibitor (SNRI), in adult patients with treatment-resistant major depressive disorder (TRD).⁷

#ENDS#

*The Montgomery-Åsberg Depression Rating Scale (MADRS): A 10-item diagnostic questionnaire, that psychiatrists use to measure the severity of depressive episodes in patients with mood disorders

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

About SPRAVATO® ▼

As an antagonist of the N-methyl-D-aspartate (NMDA) glutamate receptor, SPRAVATO® ▼ (esketamine nasal spray) offers the first new approved mechanism of action in 30 years for an antidepressant.^{1-3,9}

Esketamine nasal spray is self-administered, under the direct supervision of a healthcare professional, through a single-use nasal spray device, offering a novel mode of drug administration for the treatment of patients within the licensed indications. The decision to prescribe esketamine nasal spray should be determined by a psychiatrist.⁷

Esketamine nasal spray was authorised 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. The U.S. Food and Drug Administration (FDA) authorised esketamine nasal spray for use in conjunction with an oral antidepressant, for adults living with treatment-resistant major depressive disorder in March 2019 and for use in adults with major depressive disorder with acute suicidal ideation or behaviour in July 2020.¹⁰⁻¹²

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. Adverse events should be reported to Janssen-Cilag Limited on 01494 567447 or at dsafety@its.jnj.com and to regulatory authorities.

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.^{13,14} 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.^{15,16} At its worst, MDD can be fatal, with MDD patients demonstrating a 20-fold higher risk of suicide than the rest of the population.¹⁷ Despite treatment advances, currently available antidepressant medications can take between four to six weeks to reach their full effect, and one-third of people who suffer from MDD do not respond to these treatments.^{18,19}

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 SPRAVATO® (esketamine nasal spray). 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 health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care 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 29, 2019, 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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