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**News Release**

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# SPRAVATO® ▼ (esketamine) nasal spray data from the phase 3b ESCAPE-TRD study demonstrate superior efficacy compared to quetiapine extended-release in treatment-resistant major depressive disorder[1]

*First findings from the study support the short- and long-term use of SPRAVATO® (esketamine) nasal spray in adults living with treatment-resistant major depressive disorder in achieving remission and remaining relapse free*

**High Wycombe, UK, 23 November 2022** – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced results from ESCAPE-TRD, a long-term, comparative, randomised, open-label phase 3b clinical trial designed to evaluate the short- and long-term efficacy, safety and tolerability of flexibly dosed SPRAVATO® (esketamine nasal spray [NS]) compared with quetiapine extended-release (XR), both in combination with a continuing selective serotonin reuptake inhibitor (SSRI) or serotonin and norepinephrine reuptake inhibitor (SNRI), in adults with treatment-resistant major depressive disorder (TRD).[1] The findings, presented today at the German Association for Psychiatry, Psychotherapy and Psychosomatics (DGPPN) Congress, showed that esketamine NS met its primary endpoint, demonstrating superior efficacy in achieving remission at Week 8 compared to quetiapine XR.[1] The study also met its key secondary endpoint, demonstrating that not only did significantly more participants treated with esketamine NS compared to quetiapine XR achieve remission while on study treatment at Week 8, they also remained relapse free up to Week 32.[1]

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“Achieving remission and remaining relapse free are major milestones in the treatment of depression and are especially challenging in TRD, where patients have not responded to previous therapies,” said Professor Andreas Reif, Principal Investigator for the ESCAPE-TRD trial and Head of Department, Department of Psychiatry, Psychosomatic Medicine and Psychotherapy at University Hospital Frankfurt, Germany.* “The ESCAPE-TRD findings showed that esketamine nasal spray enabled a significantly greater percentage of patients to achieve remission at Week 8 and remain relapse free in the longer term up to Week 32 compared to quetiapine extended-release. This provides further evidence for the use of esketamine nasal spray in this difficult-to-treat population and offers hope for the millions of people affected by TRD.[2,3]”

The trial evaluated 676 adults with TRD, randomised to receive either esketamine NS (n=336) or quetiapine XR (n=340), both in combination with a continuing SSRI/SNRI.[4] TRD was defined as non-response to at least two consecutive adequately dosed treatments (including the ongoing treatment) during the current depressive episode.[1,5]

The primary endpoint assessed rates of remission† while on study treatment at Week 8 between the two trial arms and demonstrated that significantly more participants achieved remission in the esketamine NS arm compared to the quetiapine XR arm (27.1% vs. 17.6%, respectively; p=0.003).[1]

The key secondary endpoint of the trial was remaining relapse free while on study treatment at Week 32, after achieving remission at Week 8.[1] Significantly more participants achieved remission at Week 8 with no relapse at Week 32 in the esketamine NS arm compared to the quetiapine XR arm (21.7% vs. 14.1%, respectively; p=0.008).[1]

In addition, remission rates continued to increase in both arms after the primary endpoint at Week 8 with a significantly greater proportion of patients in remission at Week 32 in the esketamine NS arm versus the quetiapine XR arm (55% vs 37% ; p<0.001).[1]

“People living with TRD experience significant disruption and impairment to their lives, and there is an urgent and ongoing need to identify therapies to effectively address what

* Professor Andreas Reif has been a paid consultant to Janssen; he has not been paid for contributing to this press release.
† Remission was defined as Montgomery-Asberg Depression Rating Scale [MADRS] total score ≤10[1].

can be a devastating condition," said Dr. Tamara Werner-Kiechle, EMEA Therapeutic Area Lead, Neuroscience and Pulmonary Hypertension, Janssen-Cilag GmbH, part of the Janssen Pharmaceutical Companies of Johnson & Johnson. "We are pleased to see that esketamine nasal spray has been demonstrated to be effective and well-tolerated versus a strong augmentation comparator treatment in enabling people to achieve the goals of achieving remission and remaining relapse free up to 32 weeks – important and meaningful milestones in treating TRD. Today's findings from the ESCAPE-TRD trial are an important step towards helping people who have not responded to multiple previous treatment cycles, being able to get the respite they need."

The most common (≥10%) treatment-emergent adverse events (TEAEs) observed in the esketamine NS arm were dizziness (46.7%), nausea (29.3%), dissociation (28.1%), headache (24.6%), vertigo (18.9%), somnolence (15.0%), dysgeusia (12.0%), paresthesia (11.1%) and vomiting (10.8%).[1] These results are consistent with safety data collected in previous studies.[1,6] In the quetiapine XR arm the most common TEAEs were somnolence (23.2%), weight increase (12.5%) and headache (12.8%).[1] Serious TEAEs were observed in 5.1% of participants in the quetiapine XR arm and 5.7% in the esketamine NS arm.[1] Treatment discontinuation occurred in 23.2% of participants in the esketamine NS arm compared to 40.3% in the quetiapine XR arm, and was mainly due to a lack of treatment efficacy (8.3% for esketamine NS vs. 15.0% for quetiapine XR), adverse events (4.2% for esketamine NS vs. 11.5% for quetiapine XR) or participant refusal of further treatment (8.3% for esketamine NS vs. 8.5% for quetiapine XR).[1]

**-ENDS-**

**NOTES TO EDITORS**

**About ESCAPE-TRD**

ESCAPE-TRD is a randomised, open-label, rater-blinded, active-controlled, international, multicenter phase 3b clinical trial designed to evaluate the efficacy, safety and tolerability of flexibly dosed esketamine NS compared with quetiapine XR, both in combination with a continuing SSRI or SNRI in subjects with TRD.[1]

676 adults were randomised to receive either esketamine NS (N=336) or quetiapine XR (N=340), both in combination with their current SSRI/SNRI.[1,4] The total duration of the study was up to a maximum of 36 weeks for all participants, consisting of an up-to-14-day screening phase, a treatment phase which included an 8-week acute phase and a

24-week maintenance phase, and a two-week safety follow-up following the last dose of study intervention.[4,7]

ESCAPE-TRD was conducted across 24 countries in Europe, Latin America, Africa and Asia.[4]

**About treatment-resistant major depressive disorder (TRD)**

Depression affects nearly 40 million people of all ages in Europe and is one of the leading causes of disability worldwide.[2,8] Treatment-resistant depression (TRD) is a term for people living with MDD who have cycled through two or more antidepressant treatments within the current depressive episode without experiencing symptomatic relief.[5] Approximately a third of people who suffer from MDD do not respond to treatment and are considered to have TRD.[3] TRD is a chronic condition that places an ongoing emotional, functional, and economic burden on the individual, their loved ones, and society.[9] The long-term nature of TRD means the condition has a greater patient and societal burden when compared to non-treatment-resistant MDD, including lower Health-Related Quality of Life (HRQoL), higher comorbidity, reduced functionality and increased use of health resources.[5,9,10,11]

**About esketamine nasal spray**

As an antagonist of the N-methyl-D-aspartate (NMDA) glutamate receptor, esketamine nasal spray has a different mechanism of drug administration compared to other approved depression treatments.[12,13] Esketamine is derived from part of the ketamine molecule but is appraised by health authorities as a distinct medication, due to differences in the efficacy and safety profile.[14] As such, it is important these terms are not used interchangeably.

Esketamine NS is self-administered, under the direct supervision of a healthcare professional, through a single-use nasal spray device, for the treatment of patients within the licensed indications.[12,13] The decision to prescribe esketamine NS should be determined by a psychiatrist.[13]

Esketamine NS was authorised by the European Commission for use in combination with a SSRI or SNRI in adult patients with TRD in December 2019 and for co-administered use 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 in February 2021.[13]

**Important safety information**

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 https://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.medicines.org.uk/emc/product/10977.

**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 & Retinal Diseases; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

Learn more at www.janssen.com/UK. Follow us at www.twitter.com/JanssenUK. Janssen-Cilag Limited is one of the Pharmaceutical Companies of Johnson & Johnson.

Janssen-Cilag International NV, the marketing authorisation holder for SPRAVATO®▼ (esketamine) nasal spray in the EU, Janssen-Cilag Limited and Janssen-Cilag GmbH, are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

**Cautions Concerning Forward-Looking Statements**

*This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development. 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, Janssen-Cilag Limited, Janssen-Cilag GmbH, 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 January 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other 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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