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News Release

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New Data from the Phase IIIb ESCAPE-TRD Study Show SPRAVATO® ▼ (Esketamine Nasal Spray [NS]) Improves Rate and Time to Remission versus Quetiapine Extended-Release in Patients with Treatment-Resistant Depression and Two or Three Plus Prior Treatment Failures[1]

Findings presented at Royal College of Psychiatrists International Congress (RCPsych 2023) confirm the importance of SPRAVATO® as a therapeutic option for adults with treatment-resistant major depressive disorder in patients with 2 and ≥3 prior treatment failures[1]

High Wycombe, UK, 10 July 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced further findings from the ESCAPE-TRD study. Data shows that treatment with esketamine nasal spray (NS) increased the likelihood of remission versus treatment with quetiapine extended release (XR) in sub-groups of treatment resistant depression (TRD) patients that had 2 and ≥3 prior treatment failures in the current episode.[1] At Week 32, significantly more patients treated with esketamine NS vs quetiapine XR achieved remission in both sub-groups, 59.6% vs 41.3% in the group with 2 prior treatment failures (P≤0.001); 48.1% vs 29.8% in the group with ≥3 prior treatment failures (p<0.01).[1]

Furthermore the time to remission was shortened with esketamine NS in both sub-groups; patients with 2 and ≥3 prior treatment failures were respectively 1.5 ([1.21, 1.98]; p<0.001) and 2.0 times ([1.47, 2.91]; p<0.001) as likely to achieve remission at any timepoint versus quetiapine XR, when both were dosed as per their respective labels

and used in combination with a continuing selective serotonin reuptake inhibitor (SSRI) or serotonin and norepinephrine reuptake inhibitor (SNRI).[1] The findings were presented at the Royal College of Psychiatrists International Congress (RCPsych 2023) taking place from 10 July to 13 July in Liverpool, United Kingdom, following earlier top line data from the study presented at the German Association for Psychiatry, Psychotherapy and Psychosomatics (DGPPN) Congress last year, and further findings presented at the 31st European Congress of Psychiatry (EPA 2023) in March of this year.[1,2,3]

"We are excited that new treatments for depression are being developed, particularly for severe depression where patients have not responded to existing medications and other interventions," says Marjorie Wallace, Chief Executive of SANE. "There has been a dearth of new ideas, which is why so many patients are given repeat prescriptions of drugs made available over 30 years ago. The only way forward is to encourage those in a position to do so to develop innovative treatments that may potentially transform the future of those whose suffering may drive them to debilitation and despair."

Approximately a third of people who experience major depressive disorder (MDD) do not respond to treatment and are considered to have TRD – a term for people living with MDD who have tried two or more antidepressant treatments without experiencing any relief.[4,5] MDD and TRD can be serious and debilitating conditions and are much more common in the UK than people may think – MDD affects around one in five people in the UK at some point in their lives.[6]

"Patients who have experienced three or more prior treatment failures are typically less likely to respond to the current treatments available for TRD" said Professor Allan Young, Director, Centre for Affective Disorders, Institute of Psychiatry, Psychology and Neuroscience, King's College London. "These findings demonstrate the significant effect esketamine nasal spray has in patients living with the condition in both sub-groups, and an even greater relative effect in those with three or more prior treatment failures. This marks a major milestone in offering a potential treatment option that could improve quality of life for these individuals."

ESCAPE-TRD is a long-term, comparative, randomised, open-label, rater-blinded Phase IIIb clinical study designed to evaluate the short- and long-term efficacy, safety and tolerability of flexibly dosed esketamine NS compared with quetiapine XR, both in combination with a continuing SSRI or SNRI, in adults with TRD.[2,7] The study evaluated

676 adults aged 18-74 years with TRD, randomised to receive either esketamine NS (n=336) or quetiapine XR (n=340), both in combination with a continuing SSRI/SNRI.[2,7] TRD was defined as non-response to at least two consecutive adequately dosed treatments (including the ongoing treatment) during the current depressive episode.[1] Safety findings demonstrated that the rate of 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).[2] Treatment discontinuation due to treatment-emergent adverse events (TEAEs) was lower in esketamine NS arm (4.2%) versus the quetiapine XR arm (11.5%).[2]

"We are pleased to be presenting our latest data at RCPsych 2023 today. Our findings further inform us of the types of patients that may benefit the most from esketamine nasal spray and the potential positive effect it could have on their daily lives." said Megan Walker, Therapeutic Area Medical Director, Neuroscience, Janssen-Cilag GmbH, part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Findings presented at RCPsych 2023 showed that the percentage of patients who achieved remission increased over time with either 2 or $\geq$3 prior treatment failures in both treatment options but was consistently higher in the esketamine NS treatment arm compared with quetiapine XR treatment arm.[1]

Esketamine NS was shown to demonstrate a superior remission rate in patients with $\geq$3 prior treatment failures, with patients 2.6 times as likely to achieve remission* at Week 8 versus quetiapine XR.[1] At Week 8, 28.0% of patients treated with esketamine NS achieved remission compared to the 10.9% of patients being treated with quetiapine XR.[1]

In addition, a significantly† greater proportion of patients with $\geq$3 prior treatment failures were relapse-free through Week 32 after remission at Week 8.[1] Notably at Week 32, 18.2% of patients treated with esketamine NS were relapse-free after remission at Week 8 compared with 7.8% of patients treated with quetiapine XR.[1]

* Remission was defined as Montgomery-Åsberg Depression Rating Scale [MADRS] total score ≤10. MADRS is a clinician-rated measure of depression severity.[1]
† Tested at a two-sided 0.05 significance level without adjustment for multiple testing.[1]

Participants in the esketamine NS study arm with 2 prior treatment failures demonstrated a higher rate of remission at Week 8, compared with patients in the quetiapine XR study arm, 26.5% versus 21.8% respectively.[1] After remission at Week 8, 24.0% of patients in the esketamine NS study arm were relapse-free through Week 32 compared with the 18.0% of patients in the quetiapine XR treatment arm.[1]

-ENDS-

NOTES TO EDITORS

Professor Allan Young has been a paid consultant to Janssen; he has not been paid for contributing to this press release.

About ESCAPE-TRD

ESCAPE-TRD is a randomised, open-label, rater-blinded, active-controlled, international, multicentre Phase IIIb 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.[2]

676 adults were randomised to receive either esketamine NS (N=336) or quetiapine XR (N=340), both in combination with their current SSRI/SNRI.[2,7] The duration of the treatment period was up to a maximum of 32 weeks for all participants. Phases of the study were: 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 2-week safety follow-up following the last dose of study intervention.[2,7]

ESCAPE-TRD was conducted across 24 countries in Europe, Latin America, Africa and Asia.[7]

About treatment-resistant major depressive disorder (TRD)

Depression affects around 1 in 5 people in the United Kingdom at one point in their lifetime.[6] 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.[4] TRD is a chronic condition that places an ongoing emotional, functional, and economic burden on the individual, their loved ones, and society.[8] 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.[9,10]

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.[11,12] 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.[13] 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.[11,12] The decision to prescribe esketamine NS should be determined by a psychiatrist.[12]

Esketamine NS was first authorised by the Medicines & Healthcare Regulatory Agency (MHRA) on 18 December 2019: (i) for use in combination with a SSRI or SNRI, in adults with treatment-resistant Major Depressive Disorder, who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode, and on 30 March 2021 (ii) for co-administered use with oral antidepressant therapy in adults with a moderate to severe episode of Major Depressive Disorder, as acute short-term treatment, for the rapid reduction of depressive symptoms, which according to clinical judgement constitute a psychiatric emergency.[12]

Esketamine NS was first authorised by European Commission on 18 December 2019 (i) for use in combination with a SSRI or SNRI, in adults with treatment-resistant Major Depressive Disorder, who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode, and on 04 February 2021 (ii) for co-administered use with oral antidepressant therapy in adults with a moderate to severe episode of Major Depressive Disorder, as acute short-term treatment, for the rapid reduction of depressive symptoms, which according to clinical judgement constitute a psychiatric emergency.[14]

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/smpc#gref

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.

The marketing authorisation holder for SPRAVATO®▼ (esketamine) nasal spray in the UK is:

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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 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 1, 2023, 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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