ADDITIONAL DISCLOSURE DATA FOR SWITZERLAND

Name of Sponsor/Company: Janssen Research & Development*

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Date: *12 May 2020*

Swiss marketing authorisation data

Swiss Marketing Authorisation number: 67103

Swiss Marketing Authorisation date: 25 February 2020

Name of the preparation: Spravato – 28 mg – nasal spray

Name of active pharmaceutical ingredient: esketamine (JNJ-54135419-AAC)

Clinical trial data

1. **Clinical trial identification**

Protocol No.: ESKETINTRD2003

Title of Study: A Double-Blind, Doubly-Randomized, Placebo-Controlled Study of Intranasal Esketamine in an Adaptive Treatment Protocol to Assess Safety and Efficacy in Treatment-Resistant Depression

Study Name: SYNAPSE

EudraCT Number: 2013-004005-11

NCT No.: NCT01998958

2. **Protocol change history**

Protocol and Amendments:

Original Protocol, 08 Oct 2013

Amendment-1, 06 December 2013 – substantial

Amendment-2, 04 March 2014 – substantial

Amendment-3, 28 April 2014 – substantial

3. Clinical trial investigators and study centres

Principal Investigator*:* Richard Shelton, MD

Study Centres: Subjects were enrolled at 13 sites in the United States, 10 sites in Japan, and 1 site in Belgium

4. Medication used

Test Product, Dose and Mode of Administration, Batch No.: Intranasal esketamine was supplied as a solution containing 16.14% weight/volume (w/v) esketamine hydrochloride (equivalent to 14% w/v esketamine base). The esketamine solution was supplied by the sponsor in a bidose nasal spray device. Each device delivered 16.14 mg esketamine hydrochloride (14 mg esketamine base) per 100 mcl spray, and contained a total of 200 mcl of solution. Intranasal esketamine batch numbers were: 13H20/G005 and 13K08/G005.

Reference Therapy, Dose and Mode of Administration, Batch No.: Intranasal placebo was supplied as a solution containing water with a bittering agent (0.001 mg/mL denatonium benzoate) added to simulate the taste of the intranasal esketamine solution. Placebo solution was supplied by the sponsor in a bidose nasal spray device. Each device delivered 0.1 µg of denatonium benzoate per 100 mcl spray, and contained a total of 200 mcl of solution. Intranasal placebo batch numbers were: 13H20/G003, 13K07/G003, and 14G07/G003.

5. Study population

Number of participants – planned: 100

Number of participants – analysed: 108

6. Summary and conclusion

- In Panel A, treatment with the 28-mg, 56-mg and 84-mg doses of intranasal esketamine significantly improved depressive symptoms in subjects with treatment-resistant depression as demonstrated by the change in MADRS total score in both periods after 1 week. The dose-response analysis demonstrated a statistically significant relationship between esketamine dose and change in MADRS total score after 1 week of treatment. While all 3 doses of intranasal esketamine (28, 56 and 84 mg) were efficacious in TRD treatment, the duration of the efficacy of the 28-mg dose was shorter, suggesting it would need to be given at a higher frequency than twice a week to sustain antidepressant response during the double-blind phase. In addition, results

from the open-label treatment phase suggest that improvements in depressive symptoms resulting from esketamine treatment could be sustained over 74 days even as the frequency of dosing was decreased from twice weekly to weekly then to every other week.

- In Panel B, although greater improvements in MADRS total score were observed in the esketamine 56-mg group compared with the placebo group and a dose response was detected in Period 1, the results from Panel B must be interpreted with caution due to a significant treatment by baseline MADRS total score interaction in Period 1, where results favored the placebo group for subjects with higher baseline MADRS total scores and the esketamine groups for subjects with lower baseline MADRS total scores.

- In general, all doses evaluated in this study (14, 28, 56 and 84 mg) appeared to be safe and tolerated in adult subjects with treatment-resistant depression. Analysis of the perceptual change symptoms (measured by the CADSS assessment) suggested that onset of these symptoms occurred shortly after the start of esketamine administration and symptoms had resolved by 2 hours after administration. The symptoms were dose dependent and attenuated over time with repeated dose administration. Overall, there were no new or unexpected safety concerns noted with the administration of intranasal esketamine during this study.

7. Results reporting

Date of Clinical Trial Report: 29 Apr 2016

Prepared by: Janssen Research & Development, LLC

Publication(s) Reference(s):

- Daly EJ, Singh JB, Fedgchin M, et. al. Efficacy and Safety of Intranasal Esketamine Adjunctive to Oral antidepressant Therapy in Treatment-Resistant Depression. JAMA Psychiatry. 2018; 75(2): 139-148.

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