ADDITIONAL DISCLOSURE DATA FOR SWITZERLAND

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Date: *30 March 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.: ESKETINTRD3004

Title of Study: An Open-label, Long-term, Safety and Efficacy Study of Intranasal Esketamine in Treatment-resistant Depression

Study Name: SUSTAIN-2

EudraCT Number: 2014-004587-38

NCT No.: NCT02497287

2. **Protocol change history**

Protocol and Amendments:

Original Protocol, 21 April 2015

Amendment-1, 11 June 2015 – substantial

Amendment-2, 17 February 2016 – substantial

Amendment-3, 06 June 2016 – substantial

Amendment-4, 06 July 2016 – substantial

3. Clinical trial investigators and study centres

Principal Investigator*:* Gerard Sanacora M.D., Ph.D.

Study Centres: Countries and number of sites in each country in which the study was conducted: Argentina (11), Australia (5), Austria (2), Belgium (2), Brazil (4), Bulgaria (13), Finland (1), France (3), Germany (4), Italy (3), Malaysia (4), Mexico (3), Poland (2), Republic of Korea (5), South Africa (4), Spain (8), Sweden (6), Taiwan (6), Turkey (8), United Kingdom (5), and United States (15)

4. Medication used

Test Product, Dose and Mode of Administration, Batch No.: Esketamine was supplied as a solution of esketamine hydrochloride (16.14% weight/volume [w/v]; equivalent to 14% w/v esketamine base) in a nasal spray device, that delivered 16.14 mg esketamine hydrochloride (14 mg esketamine base) per 100-μL spray. Each nasal spray device contained a total of 28 mg (ie, 2 sprays). Esketamine batch numbers were: 160663, 500122, 500491, 501298, 501487, 501698, 501908, 502169, 502169, and 502228.

Reference Therapy, Dose and Mode of Administration, Batch No.: Oral antidepressant medications were obtained from commercial stock and remained in their commercial packaging: duloxetine 30 mg batch numbers: C413520, C464905, C488361, C517829; escitalopram 10 mg batch numbers: 2403193, 2417821, 2438864; sertraline 25 mg batch numbers: L14907, N30302; sertraline 50 mg batch numbers: H79697, L72845, N00893; venlafaxine XR 37.5 mg batch numbers: J13805, L42928, N92024; venlafaxine XR 75 mg batch numbers: L13316, L25831, M32758, N37062, R77597.

5. Study population

Number of participants – planned: 750

Number of participants – analysed: 802

6. Summary and conclusion

- Overall the long-term safety of intermittent esketamine administration (including subjects $\geq$65 years of age) in treatment-resistant depression was favorable with acceptable tolerability following a 4-week induction phase of twice weekly dosing and up to 48 weeks of optimization/maintenance phase with once a week or every other week dosing.
- Most clinically relevant safety findings such as adverse events in the psychiatric and nervous system disorders SOCs and blood pressure increases were transient and resolved on the same

day. There were no new adverse events associated with repeated dosing over time. Most of the adverse events during esketamine treatment were seen shortly after administration and resolved the same day.

- The results associated with up to 1 year of exposure to esketamine nasal spray in adult and elderly subjects with TRD appeared to show that depressive symptoms were improved in the induction phase and the improvement appeared to be sustained with repeated dosing over the optimization phase, although caution is needed in interpreting these results, given the absence of a control group and given subjects were unblinded.

7. Results reporting

Date of Clinical Trial Report: 14 August 2018

Prepared by: Janssen Research & Development, LLC

Publication(s) Reference(s):

- Wajs E, Aluisio L, Holder R, Daly E, Lane R, Lim P, George JE, Morrison R, Gerard Sanacora G, Young L, Kasper S, Sulaiman AH, Li CT, Paik JW, Manji M, Hough D, Grunfeld J, Hong JJ, Wilkinson ST, Drevets WC, Singh JB. Esketamine Nasal Spray Plus Oral Antidepressant in Patients with Treatment-Resistant Depression: Assessment of Long-term Safety in a Phase 3, Open-label Study (SUSTAIN-2). J. Clin. Psych. 2020; 81. Doi: 104088/JCP.19m12981 (in press)

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