Errata to the FDA Briefing Document

Joint Meeting of the Psychopharmacologic Drugs Advisory Committee (PDAC) &

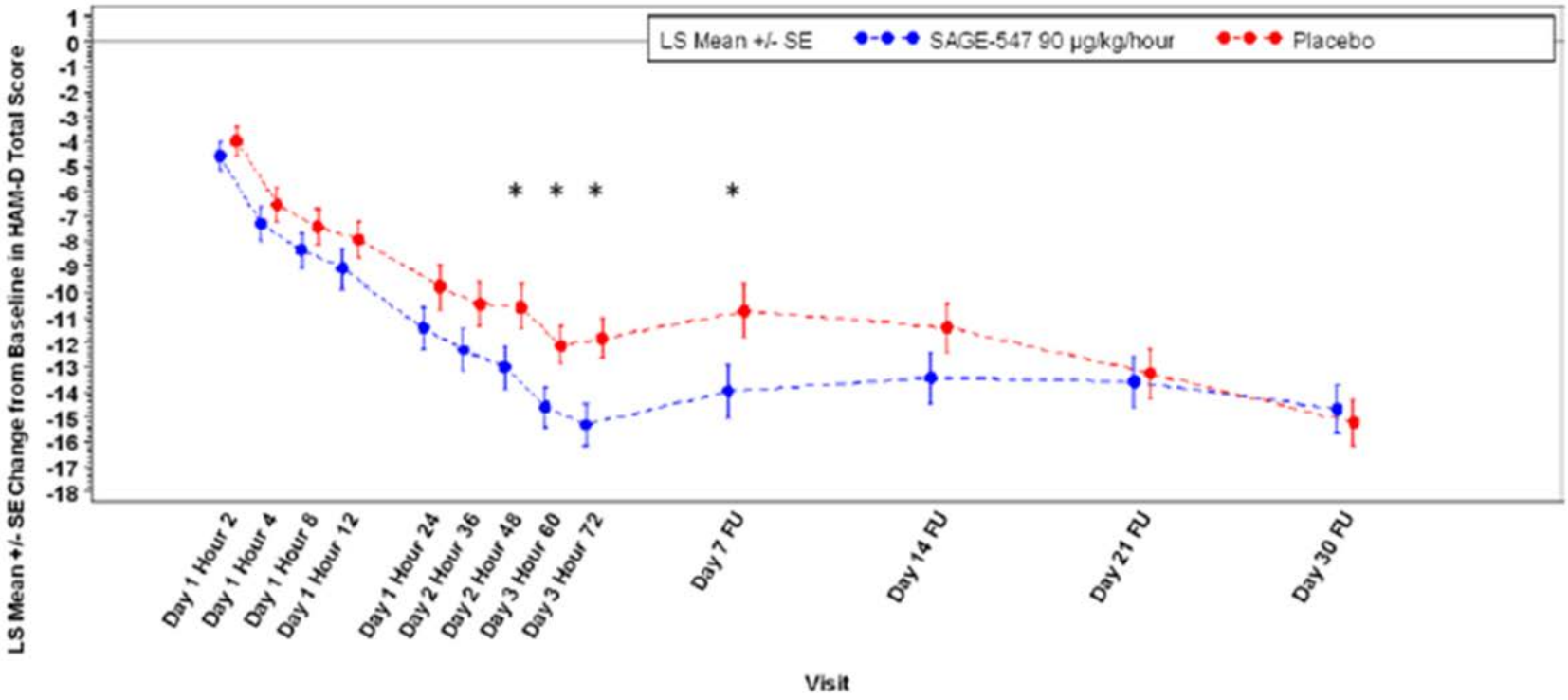
Drug Safety and Risk Management Advisory Committee (DSaRM)

November 2, 2018

Page Number, Paragraph	Current Text	Replace with
Division Director Memorandum		
Page 6, paragraph 1	Brexanolone is a proprietary analogue of the endogenous human hormone allopregnanolone.	Brexanolone is chemically identical to the endogenous human neurosteroid hormone allopregnanolone.
2.2 Postpartum Depression		
Page 9, paragraph 4	Brexanolone dosing was, therefore, based on returning women to pre-delivery levels of allopregnanolone. The initial titration was intended to allow women to develop tolerance to the associated sedation.	Brexanolone dosing was based on an expectation of tolerability at pre-delivery levels of allopregnanolone. The initial titration was intended to minimize the potential for dizziness and somnolence.
2.5.3 Study PPD-202B		
Page 13, paragraph 3	The intention-to-treat (ITT) population contains all 122 randomized subjects who received brexanolone or placebo.	The full analysis set contains all 122 randomized subjects who received brexanolone or placebo.
2.5.4 Study PPD-202C		
Page 20, Figure 4	*Figure illustrates MADRS.*	*See Appendix for correct figure (illustrating HAM-D).*
2.6.2 Deaths, Serious Adverse Events…		
Page 21, paragraph 6 bullet 3	Subject (b) (6), Study 202C, brexanolone 90 µg/kg/h arm; discontinued study drug after 8 hours of infusion due to SAEs of syncope and altered state of consciousness.	Subject (b) (6), Study 202C, brexanolone 90 µg/kg/h arm; discontinued study drug after 9 hours of infusion due to SAEs of syncope and altered state of consciousness.
2.6.5 Loss of Consciousness Events		
Page 27, paragraph 3	He developed somnolence, confusion, and dizziness while receiving brexanolone 150 µg/kg.	He developed somnolence, confusion, and dizziness while receiving brexanolone 180 µg/kg/h.

Page Number, Paragraph	Current Text	Replace with
2.6.5 Loss of Consciousness Events (continued)		
Page 29, paragraph 1	In animal studies, there was no drug-effect on respiratory parameters at brexanolone exposures 6-times clinical exposure; however, some rats and dogs experienced respiratory changes in acute 14-day general toxicology studies.	In animal studies, there was no drug-effect on respiratory parameters at brexanolone exposures 7-times clinical exposure; however, some rats and dogs experienced respiratory changes when under anesthesia or showing signs of sedation in acute and 14-day general toxicology studies.
3 Abuse Potential Assessment		
Page 30, paragraph 2 bullet 1	Receptor binding studies indicate that brexanolone has significant affinity for $GABA_A$-chloride channels, androgen, progesterone, and $GABA_A$-benzodiazepine receptors.	Receptor binding studies indicate that brexanolone has significant affinity for $GABA_A$-chloride channels, androgen, progesterone, and $GABA_A$-benzodiazepine receptors. Brexanolone is a potent positive allosteric modulator of $GABA_A$-receptors at clinically and biologically relevant concentrations. It has affinity for the androgen and progesterone receptors at supratherapeutic concentrations (approximately 180 to 4500-fold greater than clinical exposure when protein binding is taken into consideration).

Appendix. Change over Time in HAM-D Total Score, Study 202C (Applicant Figure).



Abbreviations: HAM-D = Hamilton Rating Scale for Depression; FU = follow-up; LS = least squares; SE = standard error

Note: * indicates time points when statistically significant improvement was achieved for SAGE-547 as compared with placebo. Ns for Day 14 and Day 21 are lower than surrounding time points as these visits were added with Amendment 3.

Source: Figure 14.2.1.2 and Table 14.2.1.2

Source: Clinical Study Report Figure 2.