Brief Summary of the Neurological Devices Panel Meeting – March 21, 2019

neuroAD Therapy System

Introduction:

The Neurological Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on March 21, 2019, to discuss and make recommendations on information related to the De Novo application for the neuroAD™ Therapy System.

The sponsor has proposed the following Indications for Use:

The neuroAD™ Therapy System is intended for neuro-stimulation concurrently combined with cognitive training. neuroAD™ Therapy System is indicated for the treatment of mild to moderate dementia of the Alzheimer's type in patients with a baseline Alzheimer's Disease Assessment Scale (ADAS) Cognitive Subscale (ADAS-Cog) score up to 30. The neuroAD™ Therapy System may be used in conjunction with other pharmacological and non-pharmacological therapies.

Panel Deliberations/FDA Questions:

Question 1: Are the risks for the neuroAD adequately reported and characterized?

Overall, the Panel agreed that that the risks of the neuroAD system are adequately reported and characterized in the United States (US) pivotal study. However, there were concerns that the US pivotal study protocol did not contain specific assessments for psychiatric adverse events and cognitive worsening. The Panel also expressed some uncertainty with the reporting of adverse event data in supplemental studies reported.

Questions 2: Does the U.S. pivotal study demonstrate a clinically meaningful benefit for the neuroAD as an adjunctive therapy?

The Panel agreed broadly that the data from the US pivotal study did not demonstrate a clinically meaningful benefit, with the potential for results that may inform a future study. Panelists agreed that better, more objective outcome measures were needed to better identify meaningful changes. Other Panelists expressed the need for the development of better outcome measures that were clinically oriented as opposed to research-based. The Panel also suggested that the minimum amount of improvement in the ADAS-Cog alone that could be considered clinically meaningful would be at least 2 points, with several Panelists suggesting 3 to 5 points. On the Clinical Global Impression – Change (CGI-C) scale, Panelists suggested at least moderate improvement (1 to 2 points on the CGI-C Scale) was important.

Question 3: When the neuroAD is used as an adjunctive therapy, what minimum amount of improvement in ADAS-Cog alone is clinically meaningful, as well as what is the minimum amount of clinically meaningful improvement in the CGIC?

The panel referred FDA to the response to question 2.

Question 4: Is the ADAS-Cog≤30 population is a clinically plausible subset and can patients be screened using the ADAS-Cog for the neuroAD?

The Panel agreed that the ADAS-Cog≤30 population does not represent a clinically plausible subset of patients, and that ADAS-Cog would not be a suitable instrument for screening patients being considered for the therapy. Several Panelists indicated that consideration may be best made using categorical diagnoses and clinically relevant tools (e.g., Mini Mental State Exam (MMSE)) instead of the ADAS-Cog.

Question 5: Is the post-hoc identification of the ADAS-Cog≤30 population at a later time point when no treatment is given an adequate analysis of the US pivotal study data, in concert with the supplemental data provided, to demonstrate probable benefit?
The Panel agreed that the post-hoc identification of the ADAS-Cog≤30 population did not represent an adequate analysis of the pivotal study data to demonstrate probable benefit. Additional comments were that this analysis may be useful for designing a new study with endpoints that extend beyond 12 weeks and some suggested assessment endpoints of six months to one year to better inform physicians and patients.

Question 6: Do the probable benefits of the neuroAD system outweigh the probable risks?
The Panel was in unanimous agreement that the probable benefits to health of the neuroAD™ Therapy System do not outweigh the probable risks to health.

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