

# Panel Questions

## Device Effectiveness

### STUDY 01

1. Please discuss the results for the primary effectiveness endpoint (MADRS at Week 4), including the statistical and clinical significance of:
  - a. The results from the pre-specified per-protocol analysis; and
  - b. The sponsor's post-hoc adjustment and the results obtained.

2. The results for multiple secondary outcome measures were provided in the marketing submission. These included various analyses for several different clinician-rated and patient-rated severity scales. Please discuss:
  - a. The scientific validity of analyzing secondary outcomes as a measure of device effectiveness given that the per-protocol primary effectiveness endpoint did not achieve statistical significance and how the need to correct for multiplicity testing should be addressed;
  - b. The clinical significance and consistency among the secondary effectiveness endpoints at Week 4; and
  - c. The relative importance of clinician-rated versus patient-rated scales when assessing depression symptoms and responses to therapy.

3. Given that more than half of the evaluable population (N=156) exited Study 01 between Weeks 4 and 6, please discuss the effectiveness results from Week 6 and how, if at all, they contribute to the interpretation of the Week 4 data for the NeuroStar™ System.

4. The sponsor conducted several analyses to assess difference in application site pain among treatment groups and the integrity of the study blind. Considering the information provided, please discuss the issue of blinding and any potential impact on the clinical data and results.

# Panel Questions

**Device Effectiveness**

**STUDIES 02 and 03**

5. Given that both Study 02 and Study 03 were open label and had missing data, please discuss any conclusions that can be drawn from these studies.

# Panel Questions

## Device Safety

6. Please discuss the safety results reported in the clinical trial and whether they raise any concerns.

7. Based on the trial design treatment with this device would require that subjects be withdrawn from antidepressant medications prior to treatment with the device. Please comment on whether removing medication therapy while instituting device therapy poses any clinical safety concerns or risks.

# Panel Questions

## Patient Population And Device Use

8. The mean number of ATHF level 3 exposures for subjects enrolled into Study 01 was 1.6. Over 50% of the subjects met the criteria for ATHF group 1, i.e. had failed only one antidepressant medication during the *current* episode. Please discuss your interpretation of the severity of the depressive episode of subjects enrolled in Study 01.

9. The sponsor has submitted the following Indications for Use (IFU) statement:

“The treatment of Major Depressive Disorder (MDD).”

Considering that the IFU should reflect the population that was studied, please discuss whether the sponsor’s clinical trials support this general IFU. If not, please comment on the population which might be best considered for treatment with this device based on the specific population enrolled and evaluated in the clinical trial.

# Panel Questions

**Overall Device Risk-Benefit**

10. Taking into account your day's deliberations and your responses to the prior FDA questions please discuss your interpretation of the overall risk-to-benefit profile for the NeuroStar™ System for the proposed indication for use and population, as well as how that profile compares to that of ECT devices.