FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Medical Imaging Drugs Advisory Committee Meeting
FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
May 10, 2017

QUESTIONS

1. **DISCUSSION: Discuss the efficacy outcomes used in this drug development program and their acceptability for substantiating the proposed claim. In your discussion, please consider each of the following points:**

    a. The Applicant presented data demonstrating the intraoperative visualization of malignant tissue with the calculation of the percentage of visualized tissue fluorescence verified by histopathology (positive predictive value, or PPV). Please discuss the clinical significance of the provided PPV measurement of malignant tissue visualization with the use of 5-ALA and whether the provided data on malignant tissue visualization are sufficient for establishing efficacy of 5-ALA.

    b. Please discuss the potential clinical importance of the finding of non-fluorescent tissue samples being also positive for malignancy on histopathology.

    c. One of the efficacy outcomes used by the Applicant is an improved completeness of resection defined on post-operative MRI enhancement. Please discuss the clinical importance of a "complete resection" in the setting of glioma surgery and comment on the clinical meaningfulness of using post-operative MRI to measure the completeness of resection.

    d. In assessing the totality of evidence of the potential benefit of 5-ALA, please comment on the clinical significance, if any, of the observed improvement in progression free survival and of the lack of improvement in overall survival. In your discussion please comment on the following:

        i. Whether either should be mentioned in the prescribing information if 5-ALA is approved for marketing in the U.S.

        ii. How the outcome of progression free survival could relate to potential assessment of patient reported outcomes (PROs) and what type of PROs would be relevant to this setting.

2. **DISCUSSION:** Please discuss possible risks associated with increased resection, e.g. the potential for increased neurological deficits

    a. Please discuss any other safety concerns you might have about this drug.

QUESTIONS (cont.)

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3. **VOTE:** Do you recommend the approval of 5-ALA for the proposed indication as an imaging agent to facilitate the real time detection and visualization of malignant tissue during glioma surgery?