March 27, 2015

Information Request for BLA 125518 (original application) Imlygic™ (talimogene laherparepvec; OncoVEX^{GM-CSF}) genetically-modified herpes simplex virus type 1 (HSV-1) encoded with hGM-CSF, as oncolytic immunotherapy for the treatment of injectable regionally or distantly metastatic melanoma.

Regarding Amgen submission of registry study protocol 20120139 to BLA 125518 on March 5, 2015:

- Please provide the study timeline and clarify its current status.
- Your protocol states that an interim analysis is *not* planned; and primary analysis will be available at the end of the study. Your protocol states that the "registry study will end when the sponsor (in consultation with the regulatory authorities) has determined that the collection of long-term safety and survival data are no longer necessary." However, such a determination cannot be made without interim analyses. Please consider including interim analyses at periodic intervals.
- Please provide rationale for exclusion criteria that excludes subjects receiving talimogene treatment even though subject is allowed to be on standard-of-care treatment. If talimogene is chosen as the standard-of-care in the post-licensure period, why should subject be excluded from registry for retreatment with talimogene? Additionally, excluding those subjects going back on a second round of treatment with talimogene may eliminate subjects with poorer overall survival. A secondary descriptive analysis of subjects receiving talimogene retreatment can be performed if needed.