June 11, 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 treatment of injectable regionally or distantly metastatic melanoma. Please submit your response to this information request by **June 18, 2015** referencing the date of this request. If you anticipate you will not be able to respond by this date, please contact FDA immediately so a new response date can be identified.

1. Ongoing Registry study protocol 20120139:

- Please provide a summary of data to date, including clinical outcomes and a listing of adverse events, and updated information on the number of enrolled subjects.
- Additionally, as clarified in previous communications, the final protocol should revise the exclusionary criteria for this study to include subjects who receive retreatment with T-VEC outside of a clinical trial.
- Please provide the anticipated date for submission of the final revised study protocol 20120139.

2. Ongoing viral shedding study protocol 20120324:

- Please provide revised study timeline.
- Please provide any additional updated information on the number of enrolled subjects.

3. Postmarketing study protocol 20130193:

- FDA has been in communication with Amgen, as well as the discussion at the April 29, 2015 Advisory Committee, regarding the practicality of the proposed process for sample collection from suspected herpetic infections in patient contacts (close contacts and healthcare providers). The original protocol had noted (b) (4), and it was not clear why Amgen subsequently excluded this from their protocol. What was the rationale for exclusion, and for not pursuing an option along the following lines?
    - (b) (4) for direct sampling by the (b) (4) reporting herpetic infection (as proposed in the original protocol and later excluded by Amgen). (b) (4) will use shipping kit to mail sample to the central laboratory.
    - Additional option of (b) (4) for sample collection by an Amgen contracted agency from the local area of the individual reporting herpetic infection, and subsequent mailing of sample to the central laboratory.
- Please clarify if you intend to include the following modifications to the postmarketing study protocol, and if not provide rationale:

- It is recognized that T-VEC administration may potentially result in recurrence of wild-type HSV-1 herpetic infection. The current protocol tests for herpetic infections (in patients or contacts) only by qPCR assay for T-VEC. For better characterization of herpetic infections, do you intend to test by qPCR for both T-VEC and (b) (4)
- All adverse reactions and serious adverse reactions are secondary endpoints of this study. There is the potential for a subject to exhibit clinical manifestations of diseases associated with (b) (4). Do you intend to include laboratory testing for (b) (4) in the study protocol when, and if, clinically indicated?
- Additionally, as clarified in previous communications, the final protocol should specify that both herpetic *lesions* (mucocutaneous) and herpetic *manifestations* (keratitis, encephalitis, disseminated infection) will undergo qPCR testing.

- Please provide anticipated date for the submission of the final revised study protocol 20130193.

4. In a previous communication from Amgen, (b) (4) assays (b) (4) were stated to be under development; please provide an update on when FDA can anticipate their submission.