

From: Paul Gil To: Morris, Nevitt Subject: Re: BLA 125610 Information Request CMC 10.18.17 Date: Wednesday, October 18, 2017 4:26:51 PM Attachments: image001.png Thanks, Nevitt. I acknowledge receipt of this IR. Regards, Paul

----- Original Message -----From: "Morris, Nevitt" <Nevitt.Morris@fda.hhs.gov> Date: Wed, October 18, 2017 4:21 PM -0400 To: Jim Wang <jim.wang@sparktx.com>, Paul Gil <Paul.gil@sparktx.com>

CC: "Morris, Nevitt" <Nevitt.Morris@fda.hhs.gov> Subject: BLA 125610 Information Request CMC 10.18.17

Hi Jim and Paul:

Below is an Information Request from CMC with a response requested back by October 25, 2017 Close of business. Please acknowledge receipt of this email information request.

1.

In you BLA submission under the 3.2.S.2.5.5 Continued Process Verification and 3.2.P.3.5.8 Continued Process Verification, you stated that "Continued Process Verification (CPV) was initiated after the completion of the PPQ. The process will continue to be evaluated using the parameters and their acceptance criteria as outlined in the PPQ for a minimum of (b) (4) additional manufacturing runs. A CPV protocol is being drafted to incorporate the final control strategy criteria and will apply to all lots manufactured subsequent to the PPQ. The CPV program applies to all full-scale Drug Product production lots of voretigene neparvovec executed after the completion of PPQ." Please provide the protocols of the Continued Process Verifications for your Drug Substance and Drug Product to your BLA for review. If you don't have these protocols ready, please discuss your plans in detail to include these studies as a part of your Post-Marketing Commitment.

2.

You stated in BLA Section 3.2.S.2.2.2.10 that "following (b) (4) (b) (4) P188 (b) (4) ) is added to the (b) (4) to achieve a final concentration of 0.001%". In order to reach more accurate final P188 concentration in the Drug Substance, we recommend that you (b) (4) the P188 (b) (4) .

3. Please provide the qualification studies for (b) (4) by 9CFR (as agreed upon in the Response to IR dated September 15, 2017, under 2.2.1 and 2.3.1) to the BLA.

4.

Please submit the annotated sequence of the PPQ lot ((b) (4) ) accompanied by the sequencing report and summary of the findings to the BLA.

5.

In your Response to the IR dated September 19, 2017, under 1.3.1 of the BLA, you have informed us that an approved validation report for the (b) (4) potency assay will be ready for submission on November 10, 2017. If you have data available before that date, please submit this report to the BLA..

6.

Please provide the verification report for the Particulate Matter testing of the Drug Product and Diluent by (b) (4), to show suitability of the method. We note that environment testing as defined in (b) (4) is the basis for instrument operating as expected each time of use. Yet, as stated in (b) (4)

[REDACTED]

[REDACTED] This would apply to vortigene neparvovec product, considering the matrix (formulation with Pluronic) of the Drug Product. Verification of the assay should be performed by the CRO (b) (4) [REDACTED] ) under the conditions of use.

Thanks,

Nevitt

Nevitt Morris

Nevitt Morris, RN, BSN, BS Consumer Safety Officer Office of Tissues and Advanced Therapies Center for Biologics Evaluation and Research (CBER) U.S. Food and Drug Administration Building 71, Room 4207 10903 New Hampshire Avenue Silver Spring, MD 20993 Phone: (240) 402-8269 Fax: (301) 595-1303

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