From:	Ahmed, Narin
To:	Giordano, Erica; Patel, Manisha
Cc:	Riggins, Cindy
Subject:	RE: BL 125646 Clinical Information Request
Date:	Monday, April 24, 2017 9:49:56 AM
Attachments:	image001.png response-fda-20170424 BLA 125-646.pdf
Sensitivity:	Confidential

Dear Erica,

Attached please find the response to the below request for information. This will be submitted as an amendment to BLA 125-646.

Thank you.

Best regards,
Narin

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From: Giordano, Erica [mailto:Erica.Giordano@fda.hhs.gov]
Sent: Monday, April 17, 2017 1:29 PM
To: Patel, Manisha <manisha.patel@novartis.com>
Cc: Riggins, Cindy <cindy.riggins@novartis.com>; Ahmed, Narin <narin.ahmed@novartis.com>
Subject: BL 125646 Clinical Information Request
Sensitivity: Confidential

Good afternoon,

Please see the information request below and provide a response by COB on April 20, 2017. As usual please respond directly to this e-mail and provide the information as an amendment to the BLA.

Patent Information:
In our review of your product materials, we did not note any patents for CTL019 or any of its components. In addition, we do not see patent information for any of the manufacturing products.
Please provide us with any patent data that Novartis may hold with respect to your product.

CRFs:

Please provide UPNs for the 51 subjects who were included in the IEAS analysis as well as the unique patient numbers (UPNs) for the subjects who were pheresed but failed to receive the CTL109 infusion. In addition, please provide UPNs for subjects who were consented but did not get apheresis or treatment.

CRF Review:

(b) (6)
This subject did not have a 6 month evaluation. Per the CRF, the subject received salvage therapy with cyclophosphamide, fludarabine, and a humanized CTL019 in October 2015 for acute lymphoblastic leukemia. Please provide your evidence for recurrent disease, for example: bone marrow biopsy, bone marrow aspirate, spinal tap, and/or complete blood count. We do note that MRD was measured at 0% at month 3 (8/10/2015) but flow of the marrow had 90% + CD19 cells. Please clarify the reason for censoring the subject as well as the date of the censoring.

(b) (6)
This subject appears to have been taken off therapy without a documented relapse at month 12. There is a MRD of 0.8% on 5/23/16. The subject was then treated with huCTL019 after lymphodepletion with cyclophosphamide and fludarabine. Please provide additional details as requested for the subject above (b) (6)

(b) (6)
This subject appears to have been in remission (MRD neg.) through month 9 (April 2016); the month 12 (July 2016) assessment did not include an MRD per the CRF forms. The subject received huCTL019 in October 2016 after lymphodepletion for a relapse in 9/2016. Please provide more information to justify the decision to seek additional therapy and the timing of the decision. Please confirm your date of censuring. Please provide relapse data for the subject.

(b) (6)
This subject was in remission with a negative MRD status at month 6 (March 2016). However, again taken off follow-up and received additional therapy (huCTL019 in May 2016). Please provide more information to justify the decision to seek additional therapy and the timing of the decision. Please confirm your date of censuring. Please provide relapse data for the subject.

(b) (6)
Please confirm that the subject was censored when the Ponatinib was started in 11/2016. Please provide justification for the start of Ponatinib. The chromosomal report in the CRFs does not indicate Ph+ chromosome disease. In addition, after the day 28 LP were any other LPs performed to confirm lack
of CNS disease post CTL019. In addition, the medical history states that she had asymptomatic cystic fibrosis at age 18. Please clarify.

Please confirm receipt of this request.
Thank you,
Erica Giordano

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U.S. Food and Drug Administration
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