From: Pracht, Leigh
Sent: Thursday, November 29, 2012 11:12 AM
To: Tung Koh
Subject: Information requests for BLA 125426 and IND 13551
Our Reference: BL 125426/0
BB IND 13551

Inspiration Biopharmaceuticals, Inc.
Attention: Ms. Tung Koh
November 29, 2012,
Sent by email

Dear Ms. Koh:

We are reviewing both your April 5, 2012 biologics license application (BLA) for Coagulation Factor IX (Recombinant) and your IND for Coagulation Factor IX (Recombinant) rFIX, IB1001. We are providing the following comments and requests for additional information to continue our review:

Pre-Clinical:

1. The design of your proposed rat pharmacokinetics study, submitted as Amendment 08 to STN BLA #125426/000 and amendment #59 to IND #13551 is acceptable to evaluate the expected exposure and kinetics of IB1001 both prior to and following the proposed process change (i.e., to incorporate (b) (4) to remove contaminating host cell proteins from the IB1001 drug substance). However, the rat pharmacokinetics study is not designed to confirm whether the immunogenic component or components, i.e. the host cell proteins from the Chinese hamster ovary cell line used to produce IB1001 which elicited the antibody responses in patients, have been sufficiently removed. To further evaluate the effectiveness of the proposed manufacturing change, we strongly recommend that you conduct an additional nonclinical study specifically to assess the development of anti-host cell protein antibodies in response to the pre- and post-process change IB1001 drug substance. We recommend that this study be conducted in rabbits rather than in a rodent species to maximize the chance of development and detection of antibodies to the Chinese hamster ovary cell proteins, and that this study include repeat dosing with both the pre- and post-process change IB1001 drug substance, so that a meaningful evaluation of the effects of removal of the host cell proteins may be performed. We also recommend that you submit your nonclinical protocol for our feedback prior to initiating the study.

Chemistry, Manufacturing, and Controls:

1. With regard to the proposed IND amendment, please include the following:

   - (b) (4)

- (b) (4)

- The data from the re-validation study of the viral filtration step using at least one model virus, such as (b) (4)

- (b) (4)

2. In your response to FDA's Information Request dated 25 July 2012, you reported an (b) (4) recognition of HCP by the (b) (4), as determined by comparison of the (b) (4) analysis. We consider this level of HCP coverage by the (b) (4) to be insufficient, and a potential cause for the under-estimation of HCP levels in the (b) (4) of IB1001. Therefore, please improve the (b) (4) for HCP by using (b) (4) and include the validation report in the BLA amendment.

The review of this submission is on-going and issues may be added, expanded upon, or modified as we continue to review this submission.

Please submit your responses to this information request as amendments both files referencing the date of this request.

The action due date for the BLA is February 4, 2013.

If you have any questions, please contact me at (301) 827-6116.

Sincerely,

Leigh A. Pracht
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