Date: **August 13, 2018**

To: BLA 125661/0 File

Subject: Draft Labeling Discussion

FDA Attendees:
Candace Jarvis
Kay Owosela
Bindu George
Megha Kaushal
Danielle Lagasse
Zuben Sauna

Sponsor Attendees:
Michelle Meng
Maria Wang
Lisa Michaels
Anita Shah
Monika Mass Enriquez
Joel Krasnow
Olubunimi Afonja
Todd Paporello
Audrey Anderson
Silvana Schumacher
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Chi Li

Meeting Summary:

Bayer Healthcare requested a teleconference with the agency to discuss the draft labeling document with FDA edits. In particular, the applicant wanted to discuss the dose and administration section of the PI.

Bayer inquired about the (b)(4)-day dosing regimen being removed from the PI. They acknowledged that the regimen was not effective for all patients but sought agreement upon (1) description of those patients who were dosed with the (b)(4) day regimen and (2) to describe the (b)(4) day regimen in the PI .
FDA noted that he dosing recommendation should be based on the findings from the study. Upon the FDA's review, the (b)(4)-day regimen was not effective based on the high ABR rates. Moreover, 26% of the subjects required more frequent dosing due to bleeding events. FDA also stated that with the Applicant's study design, it would be

difficult for provider to identify the subset of patients where this dosing regimen could be used.
FDA recommended that the applicant starts at a higher dosing frequency at 30-40 IU/kg twice weekly, and then can titrate down to 45 (b) (4) IU/kg for 5 days, with the option of individualized prophylaxis. This would allow the provider to decrease the frequency of the dosing regimen, based on bleeding events.

The sponsor agreed to discuss internally and make their revisions to the label based on today's conversation.

Drafted: Edward Thompson/ July 18, 2017
Reviewed: Patrick Riggins/ July 18, 2017