From: Maruna, Thomas
Sent: Wednesday, May 04, 2016 2:59 PM
To: 'Janice Castillo'
Cc: Ovanesov, Mikhail V.; Tobin, Grainne A.
Subject: 04-May-2016 Information Request - BLA 125586.0 - Response Required
by 18-May-2016

Importance: High

Portola Pharmaceuticals Inc.
Attention: Ms. Janice Castillo
May 4, 2016
Sent by email

Dear Ms. Castillo:

We are reviewing your December 17, 2015 biologics license application (BLA) for the
following:

STN   Name of Biological Products

125586/0   Coagulation Factor Xa (Recombinant),
Inactivated

We have determined that the following information is necessary to
continue our review:

Direct Inhibitor Potency Assay
1.   Analytical Method Validation Report, VAL-60580-02
a.   You have stated in section 2.3.S.5.2 that Andexanet alfa (b) (4)
     (b) (4)   lot #
(b) (4)   (Portola Lot#   (b) (4)   was developed as the reference standard for
this
assay. Please explain how this Reference Standard was qualified and
provide a
representative set of qualification data.
b.   Please describe how the ░░░░░░░░░(b) (4)░░░░░░░░░ is prepared.
c.   You have measured linearity by plotting the calculated % relative
potency against
the target % relative potency. This is a measure of accuracy. Please
clarify what
sample was measured in the linearity study presented in Figure 3. Please
provide
response curves plotted against log nominal potency for your reference
standard
and drug product, including results of the parametric fit analyses and
regression
coefficients for the curves.
Indirect Inhibitor Potency Assay
2.   Analytical Method Validation Report, VAL-60583-02
a.   In your validation report, VAL-60583-02, in Table 2: Sample
Descriptions, it is

listed that sample TS1 is (b) (4) Drug Product, Lot number (b) (4) and sample TS2

is [(b) (4)], Lot number (b) (4) However, in your validation

report for the Direct Inhibitor Potency assay, VAL-60580-02, sample TS1

is (b) (4)

Drug Product, (b) (4) while sample TS2 is [(b) (4)], Lot (b) (4)

(b) (4) Please explain this discrepancy.

b.   You have measured linearity by plotting the calculated % relative potency against

the target % relative potency. This is a measure of accuracy. Please clarify what

sample was measured in the linearity study presented in Figure 3. Please provide

response curves plotted against log nominal potency for your reference standard

and drug product, including results of the parametric fit analyses and regression

coefficients for the curves.

The review of this submission is on-going and issues may be added, expanded upon, or modified

as we continue to review this submission.

You are required to submit your responses as an amendment to this file by May 18, 2016.

The action due date for these files is August 17, 2016.

If you have any questions, please contact me.

Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP), CPH
Lieutenant, U.S. Public Health Service
Senior Regulatory Management Officer
FDA/CBER/OBRR/IO
thomas.maruna@fda.hhs.gov
Office: (240) 402-8454