



Memorandum

DATE February 23, 2024

FROM Jennifer Chan, PharmD, Consumer Safety Officer
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Bioresearch Monitoring Branch (BMB)
Division of Inspections and Surveillance (DIS)
Office of Compliance and Biologics Quality (OCBQ)

THROUGH Dennis T. Cato, Chief BMB

THROUGH Carrie M. Mampilly, MPH, Director DIS

TO Ronit Mazor, PhD, Chair, BLA STN 125786/0
Kavita Natrajan, MD, Clinical Reviewer
Cecilia Crowley, RPM

SUBJECT Bioresearch Monitoring Final Review Memo
SPONSOR Pfizer, Inc.
PRODUCT fidanacogene elaparvovec (BEQVEZ)
BLA STN 125786/0

FINAL SUMMARY STATEMENT

Bioresearch Monitoring (BIMO) inspections were issued for three (3) foreign and one (1) domestic clinical investigator (CI) sites participating in the conduct of study Protocol C0371004 and C0371002. The inspections did not reveal significant problems impacting the data submitted in support of this original Biologics License Application (BLA).

BACKGROUND

BIMO inspection assignments were issued for three (3) foreign and one (1) domestic CI sites that participated in the study conduct of the following two protocols

Protocol C0371004: *An Open-Label, Non-Investigational Product, Multi-Center, Lead-in Study to Evaluate Prospective Efficacy and Selected Safety Data of Current Factor IX (FIX) or Factor VIII (FVIII) Prophylaxis Replacement Therapy in the Usual Care Setting of Moderately Severe to Severe Adult Hemophilia B Participants (FIX:C≤2%) Who are Negative for Neutralizing Antibodies to Adeno-Associated Virus Vector Spark100 (Benegene-1) and Moderately Severe to Severe Hemophilia A Adult Participants (FVIII:C≤1%) Who are Negative for Neutralizing Antibodies to Adeno-Associated Virus Vector 6 (AAV6), Prior to the Respective Therapeutic Phase 3 Gene Therapy Studies*

Protocol C0371002: *Phase 3, Open Label, Single Arm Study to Evaluate Efficacy and Safety of FIX Gene Transfer With PF-06838435 (rAAV-Spark100-hFIX-Padua) in Adult Male Participants With Moderately Severe to Severe Hemophilia B (FIX:C≤2%) (BeneGene-2)*

The sites were selected based on previous inspectional history, geographic location, and the data submitted in the BLA. The BLA review committee concurred with the sites selected for inspection. These inspections were conducted in accordance with FDA's Compliance Program (CP) 7348.811, Inspection Program for Clinical Investigators. The inspection assignment included specific questions related to the study protocol and the information submitted in the BLA was compared to source documents at each inspected site.

INSPECTION SUMMARY AND OUTCOME

No significant objectionable inspectional findings were observed during the inspection. The table below summarizes the BIMO inspections:

Site ID	Number of Subjects Enrolled	Location	483 Issued	Final Inspection Classification
1004	<u>C371004:</u> 3 <u>C0371002:</u> 1	Acibadem Adana Hospital Pediatric Hematology Seyhan, Adana, Turkey	No	No Action Indicated (NAI)
1046	<u>C371004:</u> 5 <u>C0371002:</u> 4	Hopital Necker Service d'Hematologie Adulte Paris, France	No	NAI
1047	<u>C371004:</u> 2 <u>C0371002:</u> 2	McMaster University Medical Centre - Hamilton Health Sciences Hamilton, Ontario, Canada	No	NAI
1059	<u>C371004:</u> 4 <u>C0371002:</u> 4	Penn Blood Disorder Center Philadelphia, PA	No	NAI

INSPECTION FINDINGS

The inspections did not reveal substantive issues that impact the data submitted in the BLA.

Sponsor Issues

No significant sponsor issues were observed during the inspection.

Clinical Investigator Issues

No significant CI issues were observed during the inspection. However, some late entries into the Electronic Medical Record (EMR) by the CI were noted during the inspection for Site #1046. After further review and discussion with CI, it was clarified that in these cases, related labs and findings were completed on the visit day and the deviation was reported as late entry in the monitoring notes.

FINANCIAL DISCLOSURE

The Clinical Investigator Compliance Program directs the FDA investigators to ask the CI if and when he/she disclosed information about his/her financial interests to the sponsor and/or interests of any sub-investigators, spouses and dependent children, and if and when the information was last updated. The information submitted to the BLA was verified at the inspected sites. No deviations were found in the submitted data.

ADMINISTRATIVE FOLLOW-UP

Field Management Directive-145 (FMD-145): Release of Establishment Inspection Report (EIR) to the inspected parties was completed for the foreign entities noted above. No administrative follow-up is warranted at this time.

Should you have any questions about the contents of this memo or any aspect of BIMO, please contact Jennifer Chan at (301) 348-1897.

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