



U.S. FOOD & DRUG
ADMINISTRATION

Memorandum

DATE November 20, 2023

FROM Triet M. Tran, PharmD, BCSCP Regulatory Officer
Bioresearch Monitoring Branch (BMB)
Division of Inspections and Surveillance (DIS)
Office of Compliance and Biologics Quality (OCBQ)
Telephone: 240-425-3201

THROUGH Dennis T. Cato, Chief BMB

THROUGH Carrie M. Mampilly, MPH, Director DIS

TO Anna Kwilas, PhD, Chair
Karl Kasamon, MD, Clinical Reviewer
Hosna Keyvan, RPM

SUBJECT Bioresearch Monitoring Final Review Memo
SPONSOR Vertex Pharmaceuticals inc.
PRODUCT Exa-cel (Exagamglogene autotemcel)
BLA STN 125787/0

Final Summary Statement

Bioresearch Monitoring (BIMO) inspections were issued for two domestic Clinical Investigator (CI) sites participating in the conduct of study Protocol CTX001-121. 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 two CI sites that participated in the conduct of study Protocol CTX001-121. The BLA review committee concurred with the sites selected for inspection. The sites were selected based upon geographic location, reported adverse events, protocol deviations, number of subjects enrolled, and previous BIMO inspection histories. The inspection assignments were issued for the following study protocol:

Protocol CTX001-121- *A Phase 1/2/3 Study to Evaluate the Safety and Efficacy of a Single Dose of Autologous CRISPR-Cas9 Modified CD34+ Human Hematopoietic Stem and Progenitor Cells (CTX001) in Subjects With Severe Sickle Cell Disease.*

BIMO CI inspections are conducted in accordance with FDA's Compliance Program (CP) 7348.811, Inspection Program for CI. Two CI sites were inspected in support of this BLA.

A total of 22 subjects were enrolled at these selected sites, which represents 35% of the study population. The inspection assignment included specific questions related to the study protocol, and information submitted in the BLA was compared to source documents at each inspected site.

The inspections verified the data reported in the BLA, including but not limited to subject eligibility, protocol deviations, study drug administration, primary efficacy endpoint, and adverse events for all subjects enrolled at the inspected clinical sites.

Inspection 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
06	20	Haydar A. Frangoul, MD Nashville, TN	No	No Action Indicated (NAI)
08	2	Ami Shah, MD Palo Alto, CA	No	NAI

Noteworthy inspectional findings

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

Sponsor Issues

No significant sponsor issues were noted.

Clinical Investigator Issues

No significant CI issues were observed during the inspection.

Financial Disclosure

The CI CP 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

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 me at 240-425-3201.

Triet M. Tran, PharmD, BCSCP
Regulatory Officer

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EDR BLA STN 125787/0

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