



Memorandum

DATE February 23, 2024

FROM Jennifer Chan, PharmD, Consumer Safety Officer
Haecin Chun, MS, Consumer Safety Officer
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 Tiffany Lucas, PhD, Chair, BLA STN 125758/0
Avanti Golikeri, MD, Clinical Reviewer
Monique Cortez, MS, RPM

SUBJECT Bioresearch Monitoring Final Review Memo
SPONSOR Orchard Therapeutics (Europe), Limited
PRODUCT atidarsagene autotemcel (LENMELDY)
BLA STN 125758/0

FINAL SUMMARY STATEMENT

Bioresearch Monitoring (BIMO) inspections were issued for one (1) foreign sponsor and one (1) foreign clinical investigator (CI) site participating in the conduct of study Protocol OTL-200-201222. This CI site was the only study site participating in this study. 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 one foreign sponsor and one foreign CI site that participated in the conduct of study Protocol OTL-200-201222. These inspections were conducted in accordance with FDA's Compliance Program (CP) 7348.810, Inspection Program for Sponsors and Contract Research Organizations and CP 7348.811, Inspection Program for Clinical Investigators. The inspection assignments were issued for the following study protocol:

Protocol OTL-200-201222: *A Phase I/II clinical trial of hematopoietic stem cell gene therapy for the treatment of Metachromatic Leukodystrophy (TIGET-MLD)*

The sites were selected based on previous inspectional history and geographic location. The BLA review committee concurred with the sites selected for inspection. Study OTL-

200-201222 was conducted at only one study site in Milan, Italy, enrolling a total of 20 subjects, which represented 100% of the study population. Information submitted in the BLA was compared to source documents at the inspected entities. The inspection assignments also included specific questions concerning the clinical study.

INSPECTION SUMMARY AND OUTCOME

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

Establishment Type	Site ID	Location	483 Issued	Final Inspection Classification
Sponsor	N/A	Orchard Therapeutics (Europe), Limited London, United Kingdom	No	No Action Indicated (NAI)
Clinical Investigator	212141	Ospedale San Raffaele - Telethon Institute for Gene Therapy (SR-TIGET) Milan, Italy	No	NAI

INSPECTION FINDINGS

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

Sponsor Issues

No significant sponsor issues were observed during the inspection. However, it was noted and discussed with the sponsor that some lab results were initially missing or had incorrect timepoints listed. The sponsor proactively corrected the discrepancy before the closure of the inspection, and a corrective and preventive action (CAPA) was put into place to prevent recurrence.

Clinical Investigator Issues

No significant CI issues were observed during the inspection. However, observations noted during the inspection and discussed with the CI included underreporting of adverse events and concomitant medications for two study subjects. Additionally, several recordkeeping items were also discussed for several subjects.

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 entities noted above.

Should you have any questions about the contents of this memo or any aspect of BIMO, please contact Jennifer Chan at (301) 348-1897 or by email at Jennifer.chan@fda.hhs.gov.

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Chron file

History:

Draft: Chan: 1/16/2024

Review: Chun: 1/17/2024

Review: Cato: