



U.S. FOOD & DRUG
ADMINISTRATION

DATE August 17, 2022

FROM Colonious King, 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 Jakob Reiser, PhD Chair
Karl Kassamon, MD, Clinical Reviewer
Cara Pardon, MS, RPM

SUBJECT Bioresearch Monitoring Final Review Memo
SPONSOR: Bluebird bio, Inc.
PRODUCT: betibeglogene autotemcel (Zynteglo)
BLA: STN: 125717/0

FINAL SUMMARY STATEMENT:

Bioresearch Monitoring (BIMO) inspections were performed for the Sponsor and three clinical investigators participating in the conduct of Protocols HGB-207 and HGB-212 in support of this original Biologics License Application (BLA). The inspections did not reveal problems that impact the data submitted in the application.

BACKGROUND:

BIMO inspection assignments were issued for the following two protocols in support of this BLA:

Protocol HGB-207: A phase 3 single arm study evaluating the efficacy and safety of gene therapy in subjects with transfusion-dependent β -thalassemia, who do not have a β^0/β^0 genotype, by transplantation of autologous CD34+ stem cells transduced Ex Vivo with a lentiviral β^{A-T87Q} -Globin vector in subjects ≤ 50 years of age.

Protocol HGB-207 was conducted at nine centers worldwide with three sites in the United States. Thirty-two subjects were screened, and 23 subjects enrolled in Protocol 207. The inspections covered 39% of the enrolled subjects.

Protocol HGB-212: A phase 3 single arm study evaluating the efficacy and safety of gene therapy in subjects with transfusion-dependent β -thalassemia by transplantation of autologous CD34+ stem cells transduced ex vivo with a Lentiviral β^{A-T87Q} -Globin vector in subjects ≤ 50 years of age.

Protocol HGB-212 was conducted at nine centers worldwide with three sites in the United States. Nineteen subjects were screened, and 18 subjects were enrolled in Protocol 212. The inspections covered 50% of the enrolled subjects.

The BIMO inspections were performed in accordance with FDA's Compliance Program (CP) 7348.811, Inspection Program for Clinical Investigators and CP 7348.810, Inspection Program for Sponsors, Monitors and Contract Research Organizations (CRO). Information submitted in the BLA was compared to source documents at the site, and the inspection assignment included specific questions concerning the clinical study.

BIMO INSPECTION SUMMARY:

Site Number	Protocol Number	Location	FDA Form 483 Issued	Final Classification
103	207, 212	The Children's Hospital of Philadelphia	No	No Action Indicated (NAI)
104	207, 212	UCSF Benioff Children's Hospital Oakland	No	NAI
110	207, 212	Ann and Robert H. Lurie Children's Hospital of Chicago	No	NAI
Sponsor	207, 212	Bluebird bio, Inc. Cambridge, MA	No	NAI

SIGNIFICANT INSPECTIONAL FINDINGS: No significant inspectional findings were observed.

SPONSOR ISSUES: No sponsor issues were identified.

FINANCIAL DISCLOSURE:

The Clinical Investigator CP directs the FDA investigator to ask the clinical investigator if and when he/she disclosed information about his/her financial interests to the sponsor and/or interests of any sub-investigators, spouse(s) and dependent children, and if and when the information was updated. The information submitted to the BLA was verified for each of the inspected clinical sites.

ADMINISTRATIVE FOLLOW-UP:

Should you have any questions or comments about the contents of this memo or any aspect of BIMO, please contact me at 240-402-8759.

Colonious King
Consumer Safety Officer