



U.S. FOOD & DRUG
ADMINISTRATION

Memorandum

DATE: April 2, 2019

FROM: Erin McDowell, Bioresearch Monitoring Branch
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality

THROUGH: Dennis Cato, Branch Chief, Bioresearch Monitoring Branch

Carrie M. Mampilly, M.P.H., Director, Division of Inspections and Surveillance

TO: Andrew Byrnes, Ph.D., Chair/Primary Reviewer
Mike Singer, M.D., Clinical Reviewer
Xei Lu, M.D., Clinical Reviewer
Candice Jarvis, RPM

SUBJECT: Bioresearch Monitoring Review Memo
APPLICANT: AveXis, Inc.
PRODUCT: ZOLGENSMA (AVXS-101 gene replacement therapy)
BLA: **STN:** 125694/0

Review Summary

Bioresearch Monitoring (BIMO) inspections were conducted at four clinical investigator (CI) sites that participated in the conduct of Studies AVXS-101-CL-101, AVXS-101-CL-303, or AVXS-101-LT-001. The inspections did not reveal significant problems that impact the data submitted in the Biologics License Application (BLA).

Background

AveXis, Inc. submitted this BLA to obtain marketing approval for AVXS-101 (gene replacement therapy) for treatment of Spinal Muscular Atrophy. The following studies were conducted to support this BLA:

AVXS-101-CL-101: *Phase I gene transfer clinical trial for spinal muscular atrophy type 1 delivering AVXS-101 (survival motor neuron gene by self-complementary AAV9)*

AVXS-101-LT-001: *A Long Term Follow-up Safety Study of Patients in the AVXS0101-CL0101 Gene Replacement Therapy Clinical Trial for Spinal Muscular Atrophy Type 1 Delivering AVXS-101*

AVXS-101-CL-303: Phase 3, Open-Label, Single-Arm, Single-Dose Gene Replacement Therapy Clinical Trial for Patients with Spinal Muscular Atrophy Type 1 with One or Two SMN2 Copies Delivering AVXS-101 by Intravenous Infusion.

Studies AVXS-101-CL-101 and AVXS-101-LT-001 were conducted at a single site. Ongoing Study AVXS-101-CL-303 was conducted at 10 sites. Four CI sites were inspected in support of this BLA representing 100% of the subjects enrolled in AVXS-101-CL-101 and AVXS-101-LT-001 and 52% of the subjects enrolled in study AVXS-101-CL-303 at the time of the data cut-off date. The sites were selected based on previous inspectional history and geographic location. The inspections were performed in accordance with FDA's Compliance Program Guidance Manual (CPGM) 7348.811, Inspection Program for Clinical Investigators. The inspection assignments included specific questions concerning the study protocol and information submitted in the BLA was compared to source documents at the site.

Inspectional Findings

The table below summarizes the BIMO inspection.

Site ID	Study Inspected	Study Site	Location	483 Issued	Final Inspection Classification
001	AVXS-101-CL-101 AVXS-101-CL-303 AVXS-101-LT-001	Nationwide Children's Hospital	Columbus, Ohio	No	No Action Indicated
005	AVXS-101-CL-303	Boston Children's Hospital	Boston, Massachusetts	No	No Action Indicated
008	AVXS-101-CL-303	Stanford Neuroscience Health Center	Palo Alto, California	No	No Action Indicated
010	AVXS-101-CL-303	Nemours Children's Hospital	Orlando, Florida	No	No Action Indicated

The inspections did not reveal significant findings related to the conduct of the study.

Sponsor/Monitoring Issues

No sponsor or monitoring issues were identified during the clinical site inspections.

Financial Disclosure

The CI Compliance Program directs the FDA investigator 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, spouse(s) and dependent children, including 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:

Information letters were issued to the CI at each of the inspected sites. Should you have any questions or comments about the contents of this memo or any aspect of BIMO, please contact me at 240-402-9014.

Erin McDowell
Consumer Safety Officer

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EDR 125694/0 Application Folder
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