

RECORD OF TELEPHONE CONVERSATION

Submission ID:

BLA 125694

Office:

OTAT

Product AVXS-101-onasemnogene abeparvovec;**Sponsor:** AveXis, Inc.

Telecon Date/Time: 13- May-2019; 12:00 AM **Initiated by FDA?:** No**Telephone Number:** () -**Author:**

Candace Jarvis

Purpose: The sponsor requested this call to discuss the requested PMR that was sent to AveXis on May 7, 2019**FDA Participants:**

Lei Xu

Andrew Byrnes

Mike Singer

Candace Jarvis

Larissa Lapteva

Deborah Thompson

Meghna Alimchandani

Sponsor Participants:

James L'Italien, PhD , SVP and Chief Regulatory Officer

Olga Santiago, MD, Chief Medical Officer

Nancy Boman, MD, PhD, SVP Regulatory Affairs

Doug Feltner, MD, VP Clinical Development

Petra Kaufman, MD, VP Translational Medicine

Sitra Tauscher-Wisniewski, MD, Executive Medical Director, Clinical Development

Frank Ogrinc, Francis Ogrinc, PhD, Senior Director, Head of Biostatistics

Summary of Discussion:**Requested PMR**

“Based on the uncertainty of what dose was administered in Study CL-101, we are considering a requirement for a post-marketing study. The study should be designed to assess both safety and efficacy with a sufficient follow-up duration and which evaluates 2 or more dose levels of onasemnogene abeparvovec-xioi in subjects with infantile-onset spinal muscular atrophy (SMA) with confirmed biallelic mutations in the *survival of motor neuron 1 (SMN1)* gene. Efficacy assessments should include survival; achievement of major developmental motor milestones such as independent sitting for at least 30 seconds, standing and walking; and ventilator use. Safety parameters should include hepatic abnormalities, platelet counts, and cardiac abnormalities, among others.”

RECORD OF TELEPHONE CONVERSATION

The applicant was open to putting together a PMR study. They generally agreed with the main design features of the study and the need to evaluate at least 2 doses. They proposed that the highest dose should not exceed (b) (4) vg/kg, because of the safety findings in the animal studies. FDA reiterated that the study should evaluate both efficacy and safety. The applicant agreed but stated that it would be difficult to demonstrate the statistical superiority in efficacy or safety between the dosing arms, given the relatively small difference between the doses and the limitation of numbers of patients that would be potentially enrolled. FDA acknowledged the concern and asked the applicant to draft and submit the study synopsis as soon as possible. In the synopsis, the applicant should provide the rationale for the selected doses and the sample size. They agreed.

Following the conversation above, the following issues were discussed:

- (1) The applicant asked whether they could submit some more stability data for additional lots which, in their view, would reduce FDA's uncertainty about the dosages used in study CL-101. They stated that they recently performed (b) (4) testing on (b) (4) AveXis lots (using material (b) (4)), and found that the vector concentration was unchanged from the originally-determined concentration. The applicant stated that it appeared that the product might remain stable when in the original container, but not when in the (b) (4) that they use for stability studies. The applicant asked to submit the new data from these (b) (4) lots. They also stated that they planned to test (b) (4) lots using samples obtained from the (b) (4). FDA noted that the applicant had already provided vector concentration data in April for (b) (4) other lots using material from (b) (4) had shown declines in vector concentration during storage, including a (b) (4) decrease for the NCH lot that was used in the phase I study. However, FDA agreed to look at the new data from the additional lots if the applicant submits the new data quickly.
- (2) The applicant stated that they remain in disagreement with our labeling in a) indication for the (b) (4) SMA – they would like to make it broader to infants with SMA to “enable access” to those who may benefit from the treatment in the pre-symptomatic stage, particularly because newborn screening is becoming more common; and b) no upper limit for weight. They asked for a face-to-face meeting for this as soon as we can meet. FDA responded by reminding the applicant that the BLA is approaching the action due date and asking them to submit their rationale in writing. FDA stated that the agency would review their rationale and get back to them with the decision whether additional communication is warranted. FDA also stated clearly that FDA would not be able review any additional clinical data during this review cycle within the current clock.