

From: [Jarvis, Candace](#)
To: [James L'Italien, PhD \(jlitalien@avexis.com\)](#)
Cc: [Nancy Boman](#); [Jarvis, Candace](#); [Galivo, Feorillo](#); [Byrnes, Andrew](#)
Subject: BLA 125694/0 | AveXis, Inc | Information Request 40(PLEASE RESPOND BY MARCH 18, 2019)
Date: Monday, March 11, 2019 1:59:58 PM
Attachments: [image002.png](#) **Importance:** High

Good afternoon Dr L'Italien,

Please see below for an information request from the Pharmacology-Toxicology Reviewer for your BLA125694\0 submission for ZOLGENSMA (onasemnogene abeparvovec):

1. Regarding the distribution data for Subject (b) (6) in Amendment 35 (Module 5.3.5.2, RPT-952), please address the following:
 - a. In Section 2.3 (pages 10-11), you state that the vector-derived transcripts were analyzed using (b) (4) by (b) (4) preparations with the same AVXS-101 (b) (4) used for vector genome analysis. Please clarify if these (b) (4) can discriminate between the vector-derived mRNA and the subject's endogenous SMN2 mRNA transcripts.
 - b. In Figures 3-5 (Section 3.1, pages 16-20), tissues from non-treated SMA Subject (b) (6) were used as negative control. However, the SMN2 genotype of Subject (b) (6) was not provided. Please provide this information and discuss if the differential immunostaining for SMN protein between Subjects (b) (6) may be affected by differences in the SMN2 genotype or if it is specific for the SMN transgene product encoded in AVXS-101.
 - c. We recommend inclusion of the tissue biodistribution data from Subject (b) (6) in the ZOLGENSMA drug label. Please let us know if there are any anticipated issues with including this data in the label.

Please provide your response via email by COB Monday, March 18, 2019. The information should also be submitted as an amendment to the BLA.

Regards,

Candace N. Jarvis
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