

## T846.02 Reference Product Exclusivity Period Determination Review

Application Information	
BLA STN#	125694
Proprietary Name:	onasemnogene abeparvovec (suffix to be determined)
Established/Proper Name:	Zolgensma
Applicant:	AveXis Inc.
Date of CBER Receipt:	10/1/18
Target Review Date (90 days from receipt of complete information):	3/15/19

### I. Intake Eligibility Screening

1. Is the product approved or pending approval under a 351(a) application?

☐ No: Stop. Product is not eligible to be categorized as a Reference Product

☒ Yes:

a. If pending approval under a 351(a) application, proceed to section II.

b. If an approved product, what is the date of original licensure (date the product was first licensed) from the Purple Book \_\_\_\_\_

<http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/biosimilars/ucm411418.htm>

b. If an approved product, is the original approval date less than 12 years from date of request?

\_\_\_ No: Stop. Outside of Exclusivity Period

\_\_\_ Yes: Continue to Section II Product Description and History Summary.

## **II. Product Description and History Summary**

The product onasemnogene abeparvovec is a non-replicating adeno-associated virus (AAV) gene therapy vector that encodes the SMN cDNA. When injected i.v., the vector transduces cells and directs expression of the SMN protein. The SMN protein is deficient in patients who have spinal muscular atrophy (SMA).

BLA 125694 was submitted on 10/1/18 and filed on 11/28/18. The applicant, AveXis, is a Novartis company. We are conducting a priority review with an action due date of 5/31/19, although action may be taken 2-4 weeks earlier than this due date.

## **III. Reference Product Exclusivity Request Information**

The applicant provided the following statement in section 1.3.5.3 of the BLA: *AveXis claims 12-year reference product exclusivity for AVXS-101 under 42 USC 262(k)(7)(A) and 7-year orphan drug exclusivity for the treatment of spinal muscular atrophy, for which AVXS-101 was designated on September 30, 2014.* Note that AVXS-101 is the applicant's internal name for onasemnogene abeparvovec. The name AVXS-101 was used during clinical development of the product under IND 15699. OOPD used the name "adeno-associated virus serotype 9 expressing the human Survival Motor Neuron gene" when granting orphan product designation. All of the names refer to the same product: onasemnogene abeparvovec.

No additional justification for the reference product request was explicitly provided by the applicant. However, the BLA contains sufficient information to conclude that onasemnogene abeparvovec qualifies for designation as a reference product.

There are no licensed biologics that are structurally related to onasemnogene abeparvovec. There are no licensed gene therapy vectors that express the SMN cDNA. There is one licensed AAV vector (voretigene neparvovec-rzyl), but it encodes a different cDNA and is therefore structurally dissimilar from onasemnogene abeparvovec.

## **IV. FDA's Analysis of Applicant's Request for Reference Product Designation Determination**

1. In the applicant's request (and as summarized in Section III), has the applicant identified any licensed biological products for which they or one of their

affiliates, including any licensors, predecessors in interest, successors in interest, or related entities are the current or previous license holder?

☒ No

☐ Yes, Consult the Associate Director for Review Management (ADRM)

2. Are you aware of any CBER records which indicate any licensed biological products that are structurally related to the biological product that is the subject of the 351(a) application being considered for which the license holder or one of its affiliates, including any licensors, predecessors in interest, successors in interest, or related entities are the current or previous license holder?

☒ No

☐ Yes, Consult ADRM

3. If no to both 1 and 2, the product is eligible to be designated as a Reference Product. Continue to V. Reference Product Exclusivity Dating Periods

**V. Reference Product Exclusivity Dating Periods**

1. Indicate the “date of first approval”: ☐ no action taken yet \_\_\_\_\_
2. Determine the date when a 351(k) product may be submitted for review (4 years after date of first approval of reference product): to be determined, if approved
3. Determine the reference product expiry date:

- a. Has pediatric exclusivity been granted? The list of products with pediatric exclusivity may be accessed on:

<http://www.fda.gov/drugs/developmentapprovalprocess/developmentresources/ucm050005.htm>

☒ No, date of expiry is date of First Approval plus 12 years

☐ Yes, extend the reference product exclusivity expiry date by six months

**REFERENCE PRODUCT DATE OF FIRST APPROVAL: \_\_\_\_\_**

**REFERENCE PRODUCT EXCLUSIVITY PERIOD EXPIRY DATES:**

**4 years (time period during which a 351(k) application may not be submitted): \_\_\_\_\_**

**12 years (time period after which a 351(k) application may be approved): \_\_\_\_\_**

**Pediatric extension** (if applicable, these will be the dates reported in the purple book):

**4 years plus 6 months:**\_\_\_\_\_

**12 years plus 6 months:**\_\_\_\_\_

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**REVIEW SIGNATORY PAGE**

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**REVIEWER**

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Reviewer

Date

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**SUPERVISORY REVIEW**

I concur with the reviewer(s) recommendation? \_\_\_\_ Yes / \_\_\_\_ No If no, provide a justification.

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Branch/Lab Chief

Date

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**REFERENCE PRODUCT EXCLUSIVITY DETERMINATION BOARD REVIEW (RPEDB)**

Date Reviewed \_\_\_\_\_

Board concurs with the reviewer recommendation? \_\_\_\_ Yes / \_\_\_\_ No If no, provide a justification.

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Chair of RPEDB, ADRM

Date