



October 18, 2018

Dear SMA Community,

AveXis, a Novartis company, is pleased to let you know that we have submitted regulatory applications for AVXS-101 in the U.S., Europe and Japan for use in infants with SMA Type 1. This is an important and exciting initial step toward the potential approval of AVXS-101, a gene replacement therapy candidate for the treatment of the underlying root cause of SMA.

Data from our pivotal Phase 1 study conducted in SMA Type 1 formed the primary basis for these submissions. Based on the data included in the applications, our expectation is that the initial label will be for intravenous (IV) use of AVXS-101 for infants with SMA Type 1, as IV dosing has only been studied in clinical trials in infants. Our clinical development program is designed to help us understand the safety and how well AVXS-101 works in a broad set of pediatric patients with SMA. For example, our study of AVXS-101 in SMA Type 2 (STRONG) is ongoing, and data from that study will help determine the final study design for the planned study in children up to 18 years of age (REACH). Please see the table below for more information and updates on our planned and ongoing studies.

Next steps for AVXS-101 regulatory applications:

- U.S. – The U.S. Food and Drug Administration (FDA) will make the decision of whether to accept our Biologics License Application (BLA) for AVXS-101 within the next 60 days. If accepted, we anticipate the FDA will take six months to review the BLA and make a decision on whether or not to approve AVXS-101. This enables a potential approval for AVXS-101 in the U.S. in the first half of 2019. We will provide an update on anticipated approval timing if and when the BLA has been accepted for review.
- Europe – Similarly, the European Medicines Agency is evaluating our Marketing Authorization Application (MAA) for AVXS-101 and will determine its acceptability within the next couple of weeks. If accepted, the European Medicines Agency will have seven months to review the MAA and make a decision on whether or not to approve AVXS-101. This enables a potential approval for AVXS-101 in Europe in mid-2019.
- Japan – In mid-September we initiated the pre-application review period of the Japanese New Drug Application (J-NDA) for AVXS-101 with the Ministry of Health, Labour and Welfare (MHLW). Upon completion of the pre-review, we anticipate the application submission of the J-NDA to MHLW will be completed by the end of this year and will have a six-month review period once accepted. This enables a potential approval for AVXS-101 in Japan in the first half of 2019.

AveXis is excited by this progress, and we want to thank everyone in the community for your ongoing interest in AVXS-101. We especially want to thank the patients and families who have participated in our clinical trials – it is because of you that we are where we are today, and we are incredibly grateful.

We look forward to continuing to keep you updated. In the meantime, if you have any questions please contact us at medinfo@avexis.com.

Sincerely,

The AveXis Team

Frequently Asked Questions

1. When will AVXS-101 be approved by the FDA?

- We are pleased to have submitted a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA). The FDA will make the decision of whether to accept the BLA for review within the next 60 days. If accepted, we anticipate the FDA will take six months to review the BLA and make a decision on whether or not to approve AVXS-101.
- This enables a potential approval of AVXS-101 in the U.S. in the first half of 2019. We will provide an update on anticipated timing if and when the BLA has been accepted for review.

2. What is a BLA? What does it mean for a BLA to be “accepted”?

- A Biologics License Application (BLA) is a request to the FDA for permission to market a biologic product in the U.S. The application includes specific information about the product, including pre-clinical and clinical data and manufacturing information.
- The FDA first does a cursory review to ensure the BLA submission package is complete and contains all of the appropriate information. At that time, they “accept” the file and the review period begins.

3. If AVXS-101 is approved by the FDA, who will be eligible to receive it?

- The pivotal Phase 1 study in SMA Type 1 formed the primary basis for the BLA submission. Based on the data included in the application, our expectation is that the initial label will be for intravenous use of AVXS-101 for infants with SMA Type 1.
- Our clinical development program is designed to help us understand the safety and how well AVXS-101 works in a broad set of pediatric patients with SMA. See table below from more information and updates on those studies.

4. What is the latest update from the clinical development program?

- AveXis is pleased with the advances we have made in our clinical development program for AVXS-101. Recently both the Phase 1 STRONG trial in SMA Type 2 and Phase 3 STR1VE trial in Type 1 were fully enrolled. Additionally, the Phase 3 STR1VE-EU trial was initiated in Europe.
- Please see the chart below for more details on the clinical development program.

5. When will updated clinical trial data be announced?

- We expect to have robust data from our AVXS-101 clinical development program at the American Academy of Neurology annual meeting in early May 2019, including from the Phase 1 STRONG study in SMA Type 2, Phase 3 STR1VE study in SMA Type 1, as well as data from our study of pre-symptomatic SMA patients known as SPR1NT.

6. Are you planning to seek approval of AVXS-101 in other regions?





- Yes, we are currently working with the health authorities of several additional countries to understand their requirements for filing a new drug application. These health

authorities will use the information collected in our clinical studies to help determine whether AVXS-101 could be approved in their respective country.

7. Who should I contact to see if my child is eligible for a clinical trial with AVXS-101?

- For more information regarding eligibility criteria for our clinical trials, please view the listings on ClinicalTrials.gov or www.studysmanow.com. You may also contact us at medinfo@avexis.com.

Overview of AVXS-101 Clinical Development Program (as of October 2018)

Study Name	Where	Who	Administration	Status
	U.S.	<ul style="list-style-type: none"> • 20 patients with SMA Type 1 • Less than six months of age 	Intravenous (IV) infusion	Enrollment complete
	Europe	<ul style="list-style-type: none"> • 30 patients with SMA Type 1 • Less than six months of age 	IV	Enrolling – Italy and UK currently activated
	Global	<ul style="list-style-type: none"> • 44 patients with two or three copies of <i>SMN2</i> • Less than six weeks of age and pre-symptomatic 	IV	Enrolling – U.S., Canada and Australia currently activated
	U.S.	<ul style="list-style-type: none"> • 27 infants and children who are symptomatic with the bi-allelic deletion of <i>SMN1</i> and three copies of <i>SMN2</i> without the <i>SMN2</i> genetic modifier • Older than six months and less than five years old 	Intrathecal (IT) injection	Enrollment complete
REACH	Global	<ul style="list-style-type: none"> • Data from STRONG (the first study of AVXS-101 delivered through IT injection) will help determine the final study design 	IT	Planned