

## **AVXS-101 Gene-Replacement Therapy (GRT) in Presymptomatic Spinal Muscular Atrophy (SMA): Study Update**

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**Objective:** To evaluate efficacy and safety of onasemnogene abeparvovec (AVXS-101), an *SMN* GRT, for treatment of presymptomatic newborns with SMA.

**Background:** SMA is a recessive neurodegenerative disease resulting in loss of motor and respiratory function, the genetic root cause of which is biallelic deletion/mutation of *SMN1*. Genomic copies of a structurally similar gene (*SMN2*) modify disease severity. In a phase 1 study, AVXS-101 improved survival and motor function of symptomatic SMA type 1 patients (*2xSMN2*) dosed at  $\leq 6$  months of age. Because motor neuron loss can be insidious and disease progression is rapid, early intervention with disease modifying treatment is critical.

### **Design/Methods:**

SPR1NT is a multicenter, open-label, single-arm, phase 3 study enrolling  $\geq 27$  SMA patients with *2xSMN2* (cohort 1) or *3xSMN2* (cohort 2). Asymptomatic infants aged  $\leq 6$  weeks receive a one-time intravenous infusion of AVXS-101 ( $1.1 \times 10^{14}$  vg/kg). Safety and efficacy are assessed through study end at 18 or 24 months for patients with *2x* or *3xSMN2*, respectively. Primary outcomes are independent sitting for  $\geq 30$  seconds at 18 months (*2xSMN2*) or standing with assistance at 24 months (*3xSMN2*).

### **Results:**

As of September 27, 2018, 7 presymptomatic infants received AVXS-101 (4 female; 6 with *2xSMN2*; 1 with *3xSMN2*). The first patient was infused April 10, 2018. Age at dosing was 8–37 days (median: 12 days; mean: 21 days); mean CHOP-INTEND score was 41.7 (n=6 with data available). Mean increase from baseline in CHOP-INTEND score was 6.8 at day 14 (n=4), 11.0 at month 1 (n=3), 18.0 at month 2 (n=3), and 22.5 at month 3 (n=2). Additional baseline patient data (weight, motor function, maternal AAV9 antibody titers) and clinical follow-up will be presented.

### **Conclusions:**

Preliminary data from SPR1NT show rapid motor function improvements in presymptomatic SMA patients with *2–3xSMN2*, which may be associated with future survival and motor milestone achievement.