AVXS-101 Topline Phase 1 Clinical Trial Results

Fourth Quarter and Full Year 2016 Financial and Operating Results

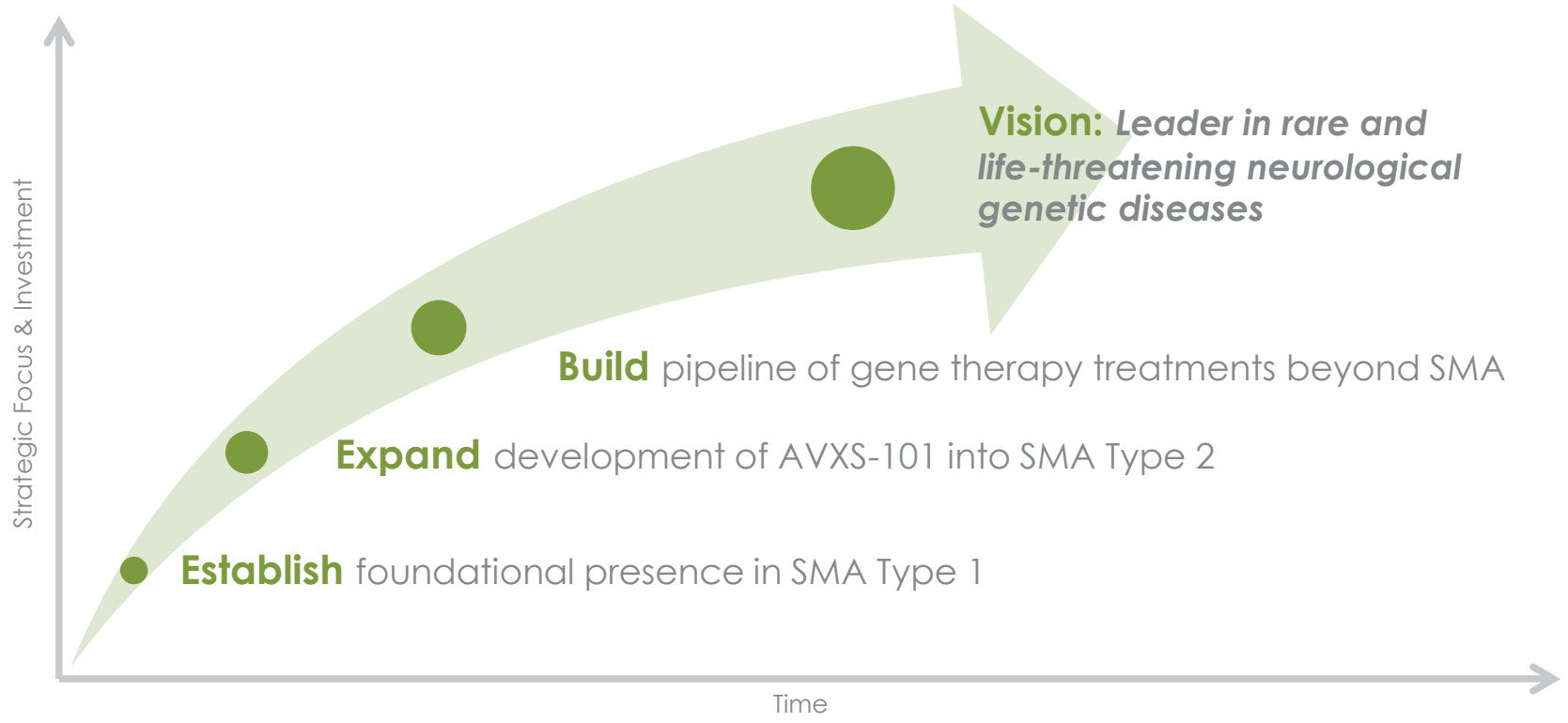
March 16, 2017

Disclaimers

Forward-Looking Statements

This presentation contains forward-looking statements, including statements about: the timing, progress and results of preclinical studies and clinical trials for AVXS-101, including statements regarding the timing of initiation of studies or trials and related preparatory work, our expectations regarding timing for meetings with regulatory agencies, our manufacturing strategy and developments, key regulatory and development milestones and our research and development programs. These statements involve substantial known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation.

Our Strategy



Overview of SMA

SMA is a devastating orphan disease that results in motor neuron loss and progressive weakness; it is the most common genetic cause of infant death

- Incidence: ~1 in 10,000 live births
- Caused by reduced SMN (survival motor neuron) protein levels from loss of/defective SMN1 gene
- SMA divided into sub-categories, Type 1- 4, with Type 1 being most severe
  - Severity correlates with # of copies of SMN2 backup gene

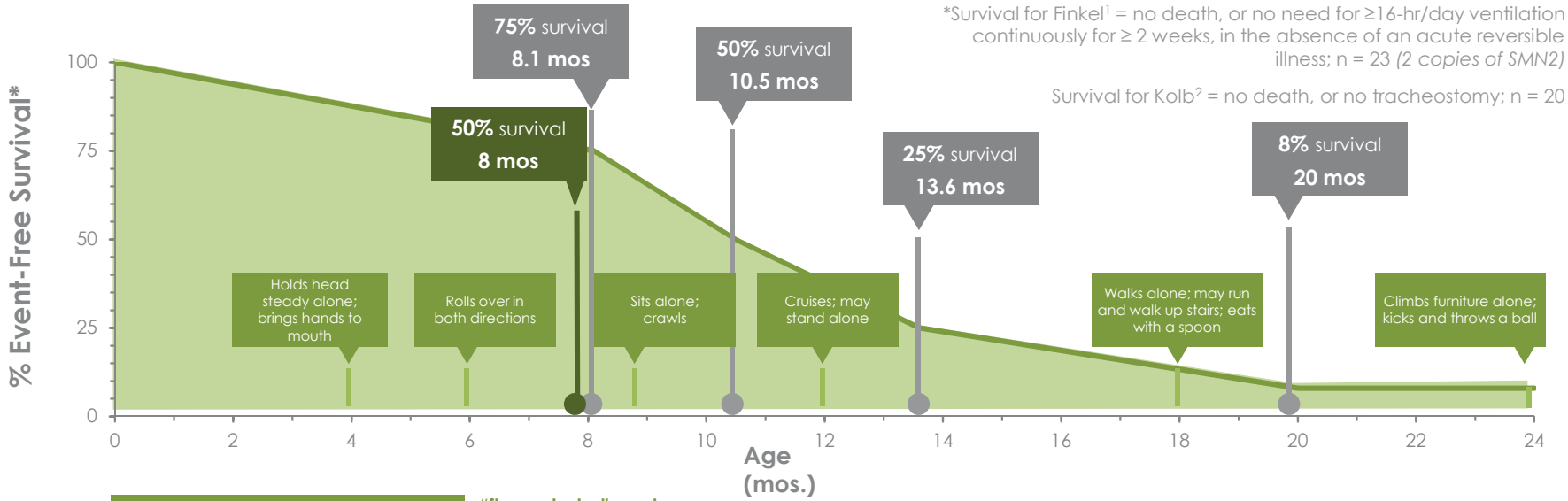
SMA Types: A Devastating Disease

	TYPE 1	TYPE 2	TYPE 3	TYPE 4
SMN2 Copy Number	Two	Three or Four	Three or Four	Four to Eight
Onset	Before 6 Months	6-18 Months	Early childhood to early adulthood (juvenile)	Adulthood (20s-30s) usually after 30
Incidence per Live Birth	Approximately 60%	Approximately 27%	Approximately 13%	Uncommon; limited information available
Developmental Milestones	• Will never be able to sit without support • Difficulty breathing & swallowing • Can't crawl/will never walk	• Will never be able to walk or stand without support	• Stand alone and walk but may lose ability to walk in 30s-40s	• Stand alone and walk but may lose ability to walk in 30s-40s (Same as Type 3)
Survival	• <10% Event free* by two years of age	• 68% alive at age 25	• Normal	• Normal

*Event = Death or ≥16-hr/day ventilation continuously for ≥ 2 wks, in the absence of an acute reversible illness

Natural History of SMA Type 1

More than 90% of SMA Type 1 patients will not survive or will need permanent ventilation support by age 2



*Survival for Finkel[1] = no death, or no need for ≥16-hr/day ventilation continuously for ≥ 2 weeks, in the absence of an acute reversible illness; n = 23 *(2 copies of SMN2)*

Survival for Kolb[2] = no death, or no tracheostomy; n = 20

Onset of SMA Type 1 by 6 months

Symptoms may present

"floppy baby" syndrome
muscle weakness (legs more than arms)
poor head control
belly breathing
bulbar muscle weakness (weak cry, difficulty swallowing, aspiration)
will never sit unsupported
loss of motor function:

- **NeuroNEXT -- CHOP INTEND decrease of 10.5 points/yr.**
- **PNCR -- CHOP INTEND decrease of 1.27 points/yr.**

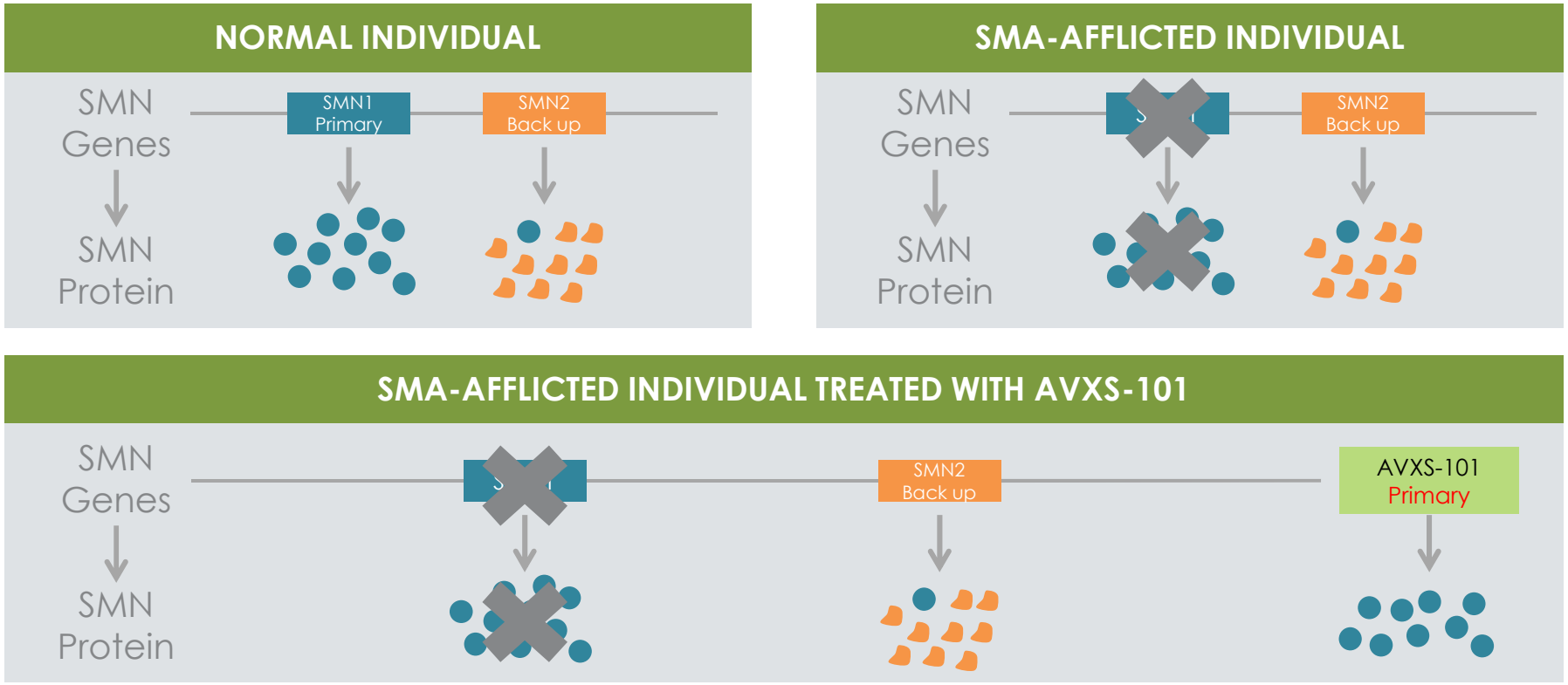
Milestone for a healthy infant

SMA Type 1 survival rates per Finkel[1]

SMA Type 1 survival rate per Kolb[2]

1. PNCR (Finkel)
2. NeuroNEXT (Kolb)

AVXS-101 Targets the Primary SMN Gene

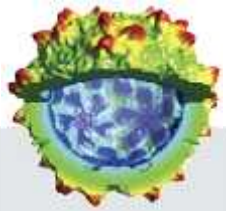


Our Solution: AVXS-101

An Innovative Treatment Approach for SMA

Gene therapy is the right approach for SMA: Monogenic mutation that drives the pathology

Recombinant AAV9 Capsid Shell



scAAV ITR	Continuous Promoter	Human SMN Transgene	scAAV ITR

KEY COMPONENTS	PURPOSE
Recombinant AAV9 Capsid Shell	• Ability to deliver across the blood brain barrier (BBB) and into the spinal cord - Avoids the need for intrathecal delivery when treating infants • Non-replicating virus does not modify the existing DNA of the patient.
scAAV ITR (Self-complementary DNA technology)	• Enables rapid onset of effect which is key in a quickly deteriorating population
Continuous Promoter	• Activates the transgene to allow for continuous and sustained SMN expression
Human SMN Transgene	• Full copy of a stable, functioning SMN gene that is introduced into the cell's nucleus

Rendering adapted from DiMattia et al. Structural Insight into the Unique Properties of Adeno-Associated Virus Serotype 9. J. *Virol*. June 2012.

Children with SMA Type 1 Do Not Reach Any Major Motor Milestones

Developmental Milestones in Type 1 Spinal Muscular Atrophy
De Sanctis et al. *Neuromuscular Disorders, Nov-2016*

DESIGN

- Retrospective Study from large multi-center datasets (US and EU)
- Patients (n=33) have **genetically confirmed homozygous deletion of exon 7 in SMN1 gene**; categorized according to Dubowitz's decimal classification (confirmation of SMN1 status and clinical observations)
- Study visits at baseline, every 2-3 months until the age of 12 months, and every 6 months thereafter, when possible
- Hammersmith Infant Neurological Examination (HINE) used to assess intermediate steps leading to full achievement of milestones

CONCLUSIONS

- **Prolongation of survival with supportive care does not impact achievement of motor milestones** in SMA Type 1 infants
- SMA Type 1 infants with **symptom onset <6 months**:
  - **Will not reach any major motor milestones, such as sitting, crawling, standing, and walking**
  - Any early intermediate milestones in 1B patients will be quickly lost
- The **highest milestone achieved is seen in the child's first visit followed by a rapid decline**
- **Any improvement or achievement of milestones not usually achieved in a child with SMA Type 1** in a drug intervention trial **can be attributed to the drug** and not due to survival or enhanced standard of care

Clinical Study Closeout – January 20, 2017

AVXS-101 PHASE 1 TRIAL OVERVIEW – SMA TYPE 1

Study Site
Nationwide Children's

Principal Investigator
Jerry R. Mendell, M.D.

Trial Design
Open-label, dose-escalation

Route of Administration
One-time intravenous infusion through peripheral limb vein
Prednisolone 1 mg/kg 1 day Pre-GT

KEY ENROLLMENT CRITERIA

Inclusion

- 9 months of age / 6 months of age[1] and younger at day of vector infusion with SMA Type 1 as defined by the following features:
  - **Bi-allelic SMN1 gene deletion or point mutations**
    - **All enrolled patients carry bi-allelic SMN1 deletions, confirmed by independent laboratory**
  - **2 copies of SMN2**
  - **Onset of disease at birth to 6 months of age**
  - Hypotonia by clinical evaluation with delay in motor skills, poor head control, round shoulder posture and hypermobility of joints

Exclusion

- Active viral infection (includes HIV or serology positive for hepatitis B or C)
- Use of invasive ventilatory support (tracheotomy)* or pulse oximetry <95% saturation
- Patients with Anti-AAV9 antibody titers >1:50 as determined by ELISA binding immunoassay
- Abnormal laboratory values considered to be clinically significant
- **Patients with the c.859G>C mutation in SMN2 exon 7 (predicted mild phenotype)[2]**

*Patients may be put on non-invasive ventilatory support (BiPAP) for <16 hours/day at discretion of their physician or study staff.
Clinicaltrials.gov Identifier = NCT02122952
[1] Inclusion criteria was 9 months of age and younger for the first nine patients. 6 months of age and younger for the last six patients.
[2] Exclusion criteria related to c.859G>C was confirmed for all patients by an independent laboratory.

OBJECTIVES

Primary

- Safety and Tolerability

Secondary

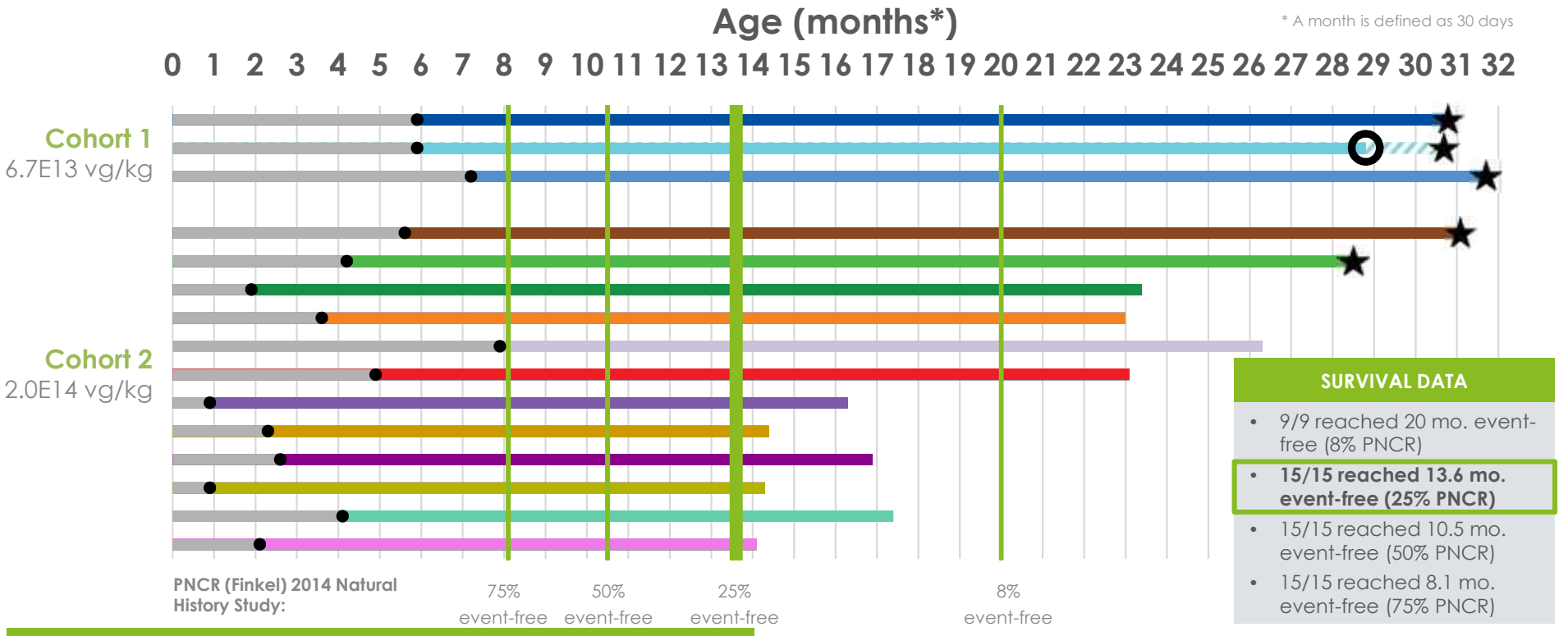
- **Time from birth until death or time to ≥16-hour ventilation continuously for ≥2 weeks** in the absence of an acute reversible illness or perioperatively
- **Video confirmed achievement of ability to sit unassisted***

***key developmental milestone achievements assessed and adjudicated by external independent reviewer**

Additional

- CHOP INTEND
- Bayley Motor Scales of Infant/Toddler development – Gross Motor

Event-Free Survival Data – January 20, 2017

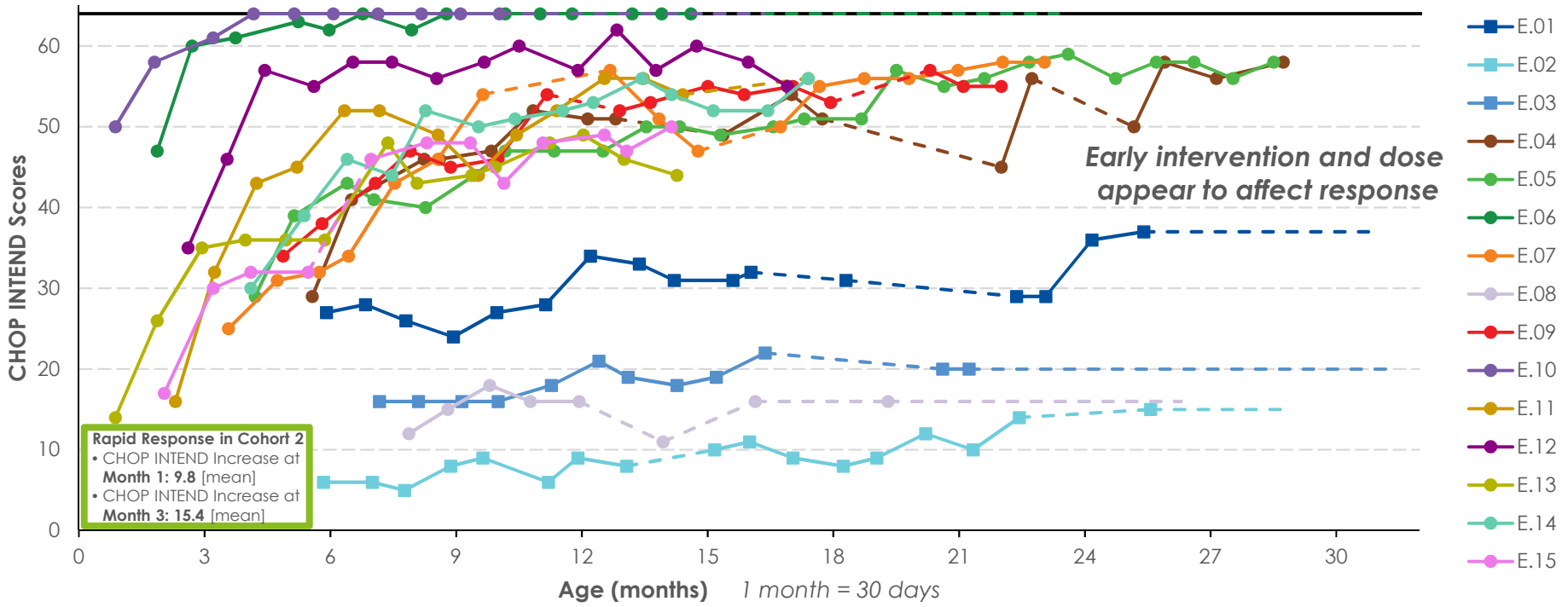


Age at Last Follow-up

Cohort 1*:	30.8 months (median)	30.4 months (mean)
Cohort 2*:	20.2 months (median)	20.7 months (mean)

**reflects age at Last Trial Visit or most recent pulmonary assessment, E.02's age at Pulmonary Event*

CHOP INTEND vs. Age – January 20, 2017



COHORT 1 (n=3)	COHORT 2 (n=12)
Baseline Age (months): 5.9 [median], 6.3 [mean]	Baseline Age (months): 3.1 [median], 3.4 [mean]
Current Age (months): 30.8 [median], 30.4 [mean]	Current Age (months): 20.2 [median], 20.7 [mean]
Mean CHOP INTEND Increase: 7.7 points	Mean CHOP INTEND Increase: 24.7 points

Dashed line denotes missed or partial assessments

Safety Data – January 20, 2017

AVXS-101 appears to have a favorable safety profile and appears to be generally well-tolerated in patients studied to date

SAFETY AND TOLERABILITY OBSERVATIONS

- **No new treatment-related SAEs or AEs observed**
- As previously reported, a total of 5 treatment-related AEs in 4 patients have been reported following monitoring and source verification
  - Treatment-related SAEs and AEs were **clinically asymptomatic** elevated liver function enzymes (LFEs) assessed under CTCAE on the basis on laboratory values and **resolved with prednisolone treatment***
    - 2 were SAEs experienced by 2 patients
    - 3 were AEs experienced by 2 patients
- A total 256 AEs (5 treatment-related AEs and 251 non-treatment related AEs) have been reported following monitoring and source verification
  - 52 SAEs and 204 non-serious AEs
  - 65 AEs have occurred since September 15, 2016
    - 10 disease-related SAEs in 3 patients have occurred since September 15, 2016

*No drug-induced liver injury (DILI) as defined by Hy's Law

Children with SMA Type 1 Never Sit Unassisted

The Natural History of SMA Type 1 is marked by the inability to achieve or maintain developmental milestones

Disease Characteristics

- Disease onset <6 months
- Hypotonia and weakness
- Bulbar muscle weakness
- Difficulty breathing and swallowing
- Inexorable progression to nutritional failure
- Inexorable progression to respiratory failure

Developmental Milestone Prognosis

- Progressive decline in motor function soon after birth
- Rapid loss of any early milestones (e.g. head control, hands to mouth)
- Will never be able to sit unassisted
- Will never be able to roll
- Will never be able to crawl, stand, or walk

Motor Milestone Achievement Assessed and Adjudicated by Independent External Reviewer – January 20, 2017

Cohort 2 2.0e14 vg/kg	Age at GT (mos)	Motor Milestone Achievement							
		Brings hand to mouth	Head control	Partial Roll[a]	Roll[b]	Sitting with assistance	Sitting Unassisted		
							≥ 5 seconds[c]	≥ 10 seconds[d]	≥ 30 seconds[e]
E.04	6	a	a	a	a	a	a		
E.05	4	a	a	a	a	a	a	a	a
E.06	2	a	a	a	a	a	a	a	a
E.07	4	a	a	a	a	a	a	a	
E.08	8	a							
E.09	5	a	a	a	a	a	a	a	a
E.10	1	a	a	a	a	a	a	a	a
E.11	2	a	a	a	a	a	a		
E.12	3	a	a	a	a	a	a	a	a
E.13	1	a	a			a	a	a	
E.14	4	a	a	a	a	a			
E.15	2	a	a			a			

Two children stand with support, and stand and walk independently

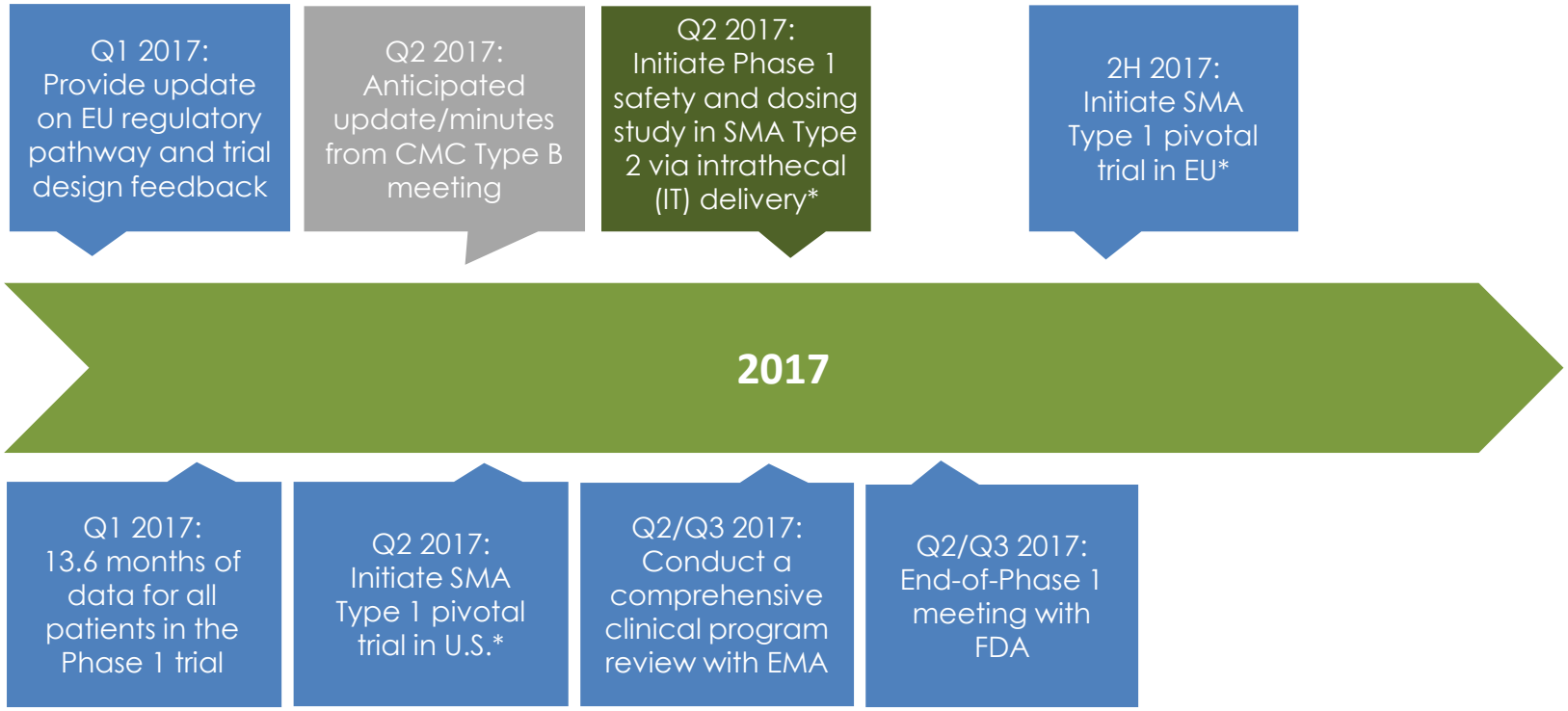
a. Bayley Scales of Infant and Toddler Development, item #20, rolls a minimum 180° from back in only one direction.
b. Bayley Scales of Infant and Toddler Development, item #20, rolls a minimum 180° from back to both left and right.
c. Sitting unassisted for ≥5 seconds is in accordance with the criteria of item 22 in the Bayley Scales of Infant and Toddler Development – gross motor subtest and surpasses the three second count used as a basis for sitting (test item 1) in the Hammersmith Functional Motor Scale – Expanded for SMA (HFMSE).
d. Sitting unassisted for ≥10 seconds is in accordance with the criteria in the World Health Organization – MultiCentre Growth Reference Study.
e. Sitting unassisted for ≥30 seconds defines functional independent sitting and is in accordance with the criteria of item 26 in the Bayley Scales of Infant and Toddler Development – gross motor subtest.

Financial Position *(dollars in millions)*

Cash and cash equivalents of $240.4 million as of December 31, 2016

	Three months ended 12/31/16	Three months ended 12/31/15
R&D Expense	$18.3	$8.7
G&A Expense	$7.2	$4.4
Net Loss	$25.4	$13.2

Company Milestones



*Assumes positive outcome of CMC Type B meeting

Type 1 Program Type 2 Program Manufacturing

Thank You