Indication

ZOLGENSMA is an adeno-associated virus vector-based gene therapy indicated for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *survival motor neuron 1 (SMN1)* gene.

Limitations of Use

The safety and effectiveness of repeat administration or the use in patients with advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence) has not been evaluated with ZOLGENSMA.

Important Safety Information

**BOXED WARNING: Acute Serious Liver Injury and Acute Liver Failure**

Acute serious liver injury, acute liver failure, and elevated aminotransferases can occur with ZOLGENSMA. Patients with preexisting liver impairment may be at higher risk. Prior to infusion, assess liver function of all patients by clinical examination and laboratory testing (e.g., hepatic aminotransferases [aspartate aminotransferase (AST) and alanine aminotransferase (ALT)], total bilirubin, and prothrombin time). Administer a systemic corticosteroid to all patients before and after ZOLGENSMA infusion. Continue to monitor liver function for at least 3 months after infusion.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.
The importance of newborn screening

As of June 28, 2021, 38 states screen for SMA as part of their newborn screening process. SMA was added to the federal Recommended Uniform Screening Panel (RUSP) in 2018, though screening for SMA has yet to be implemented in every state. Newborn screening allows for children to be diagnosed and treated as early as possible.²,³

The efficacy of ZOLGENSMA was evaluated in STR1VE, a completed Phase 3 trial.⁴ Learn more about this study on the following pages or visit ZOLGENSMA-hcp.com.

Important Safety Information

WARNINGS AND PRECAUTIONS

Thrombocytopenia

Transient decreases in platelet counts, some of which met the criteria for thrombocytopenia, were typically observed within the first two weeks after ZOLGENSMA infusion. Monitor platelet counts before ZOLGENSMA infusion and on a regular basis for at least 3 months afterwards.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.
Lucy was presymptomatic before treatment and showed no signs of SMA

Baseline testing is required for all patients before ZOLGENSMA treatment:
- Anti-AAV9 antibody titers ≤1:50
- Liver function, creatinine, complete blood count (including hemoglobin and platelet count), and troponin-I

One day before ZOLGENSMA treatment, Lucy started a corticosteroid regimen.
Due to increased risk of serious systemic immune response, treatment in patients with concurrent infections should be postponed until unresolved.

Lucy’s liver enzymes were elevated after treatment:
- Her doctors monitored her lab results until liver enzyme levels returned to baseline.

Per the regimen detailed in the Full Prescribing Information, treatment with systemic corticosteroids before and after ZOLGENSMA infusion is required. Assess liver function, platelet count, and troponin-I for at least 3 months following infusion.

Important Safety Information
WARNINGS AND PRECAUTIONS

Thrombotic Microangiopathy
Cases of thrombotic microangiopathy (TMA) were reported approximately 1 week after ZOLGENSMA infusion. Obtain baseline creatinine and complete blood count before ZOLGENSMA infusion. Following infusion, monitor for thrombocytopenia as well as other signs and symptoms of TMA. Consult a pediatric hematologist and/or pediatric nephrologist immediately to manage if clinically indicated.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.
Results and outcomes vary among children based on several factors, including how far their SMA symptoms had progressed prior to receiving treatment.

Lucy has maintained respiratory function¹
- She is able to breathe independently without any kind of respiratory support³

She picks up her own drink. She’s crawling, she’s climbing all over the furniture. She loves to dance. She loves to laugh.”¹
– Ashley, mother of Lucy

Lucy has achieved many developmental milestones¹
- She can sit supported in her high chair¹
- She is able to stand both supported and independently for several seconds¹

For her to be treated so young, to meet so many of these milestones, for us it exceeded anything we could have expected.”¹
– Ashley, mother of Lucy

Results and outcomes vary among children based on several factors, including how far their SMA symptoms had progressed prior to receiving treatment.

Important Safety Information
WARNINGS AND PRECAUTIONS
Elevated Troponin-I
Increases in cardiac troponin-I levels were observed following ZOLGENSMA infusion. Monitor troponin-I before ZOLGENSMA infusion and on a regular basis for at least 3 months afterwards.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.
CONSIDER ZOLGENSMA
The one-time-only dose to stop SMA progression

ZOLGENSMA is:
• Designed to treat the genetic cause of SMA (mutations in the SMN1 gene) by providing a working copy of the human SMN gene5
  - ZOLGENSMA is designed not to integrate into the patient’s genome7
• Designed for continuous SMN protein expression with self-complementary DNA and a continuous promoter, which provide rapid activation and expression of the SMN transgene5,8
• Designed for targeted delivery with a non-replicating, adeno-associated virus (AAV9) capsid that can cross the blood-brain barrier into non-dividing motor neurons5,7
  - AAV9 vectors are not known to cause disease in humans7

The safety and efficacy of ZOLGENSMA has been evaluated in completed trials and continues to be evaluated in ongoing trials, including a long-term follow-up.4,9-11
To learn more about the ZOLGENSMA clinical trials, go to ZOLGENSMA-hcp.com.

Important Safety Information
ADVERSE REACTIONS
The most commonly observed adverse reactions (incidence ≥5%) in clinical studies were elevated aminotransferases and vomiting.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.
The efficacy of ZOLGENSMA was evaluated in STR1VE, a completed, open-label, single-arm, multicenter, Phase 3 clinical trial of patients with SMA Type 1 (N=22; genetically confirmed bi-allelic SMN1 deletion, 1-2 copies of SMN2, and <6 months of age at symptom onset and treatment)4

Survival: 91% (20/22) of patients were alive and free of permanent ventilation at the 14-months-of-age study visit, a primary endpoint, and at 18 months of age2,a-c

Sitting independently: 59% (13/22) of patients were sitting without support for ≥30 seconds at the 18-months-of-age study visit, a primary endpoint1,a

• Patients with SMA Type 1 in historical controls do not typically achieve or maintain motor milestones13

Ability to thrive: 41% (9/22) of patients met criteria for ability to thrive at 18 months of age, a secondary endpoint12,d

Respiratory support: 68% (15/22) of patients did not require noninvasive respiratory support at any point during the study12

• 4/22 patients required ventilatory support as assessed by Trilogy BiPAP data alone at 18 months of age, a secondary endpoint12

Motor function improvements: The mean CHOP INTEND score increased from 32 points (range 18–52) at baseline to 53.5 (range 42–60) at 14 months (n=11)12

• Mean CHOP INTEND scores increased as early as month 1, and scores were maintained or improved through the end of the study12

Results and outcomes vary among children based on several factors, including how far their SMA symptoms had progressed prior to receiving treatment.

4One patient was initially classified as presymptomatic and removed from the intent-to-treat (ITT) population. The patient was later confirmed to be symptomatic at the time of treatment and was included in the final ITT analysis.3

1One patient died at 7.8 months from respiratory failure which was deemed unrelated to treatment. One patient withdrew consent at 11.9 months; this patient required permanent ventilation at 11 months prior to withdrawing consent.2

One patient discontinued participation at the age of 18.0 months before the month 18 end-of-study visit due to an adverse event of respiratory distress deemed unrelated to treatment. The patient was alive and without permanent ventilation at 18 months of age and was included in the final analysis.3

5Ability to thrive was defined as ability to tolerate thin liquids as demonstrated through a formal swallowing test, maintenance of weight (≥3rd percentile for age and gender, as defined by WHO guidelines), and independence from mechanical or non-oral nutritional support.13

Important Safety Information

WARNINGS AND PRECAUTIONS

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All 14 patients with 2 copies of SMN2 and all 15 patients with 3 copies of SMN2 were alive.

In SPR1NT, event is defined as death or the requirement of permanent ventilation in the absence of acute reversible illness and perioperatively.

Event-free survival at 14 months of age is a secondary endpoint for patients with 2 copies of SMN2.

Bayley-III, gross motor subtest item 26. WHO MGRS established windows of achievement (1%–99%): 3.8–9.2 months for sitting without support.

Age-appropriate time periods were defined according to the WHO Multicenter Growth Reference Study (MGRS) established windows of achievements for the development of motor milestones.

Bayley-III, gross motor subtest item 40. WHO MGRS established windows of achievement (1%–99%): 6.9–16.9 months for standing alone.

All patients were required to be able to swallow thin liquids and be free from ventilatory support at baseline. Ventilation support includes either invasive or noninvasive respiratory support, cough assist, or BiPAP.

SPR1NT is an ongoing, open-label, single-arm, Phase 3 clinical trial of ZOLGENSMA in presymptomatic patients with SMA. The study enrolled 29 patients with 2 copies (n=14) or 3 copies (n=15) of SMN2 who were ≤6 weeks of age at time of treatment. Data are from the June 2020 data cut.

Survival: **100% (29/29)** of patients were alive and free of permanent ventilation.

Sitting independently: **79% (11/14)** of patients with 2 copies of SMN2 achieved sitting without support for ≥30 seconds (Bayley), a primary endpoint for this cohort.

- **10 of 11** achieved this milestone within an age-appropriate time period.

Standing alone: **53% (8/15)** of patients with 3 copies of SMN2 achieved standing alone for ≥3 seconds (Bayley), a primary endpoint for this cohort.

- **8 of 8** achieved this milestone within an age-appropriate time period.

Nutritional support: **100% (29/29)** of patients did not require nutritional support.

Respiratory support: **100% (29/29)** of patients were free of ventilatory support.

Results and outcomes vary among children based on several factors, including how far their SMA symptoms had progressed prior to receiving treatment.

Important Safety Information

**WARNINGS AND PRECAUTIONS**

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Indication and Important Safety Information

Indication

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WARNINGS AND PRECAUTIONS

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Important Safety Information (cont’d)

WARNINGS AND PRECAUTIONS (cont’d)

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