Treated with ZOLGENSMA at ~5 weeks old[1]

Pictured here at ~10 months old

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suspension for intravenous infusion

Meet Lucy

SHE HAS SMA AND THIS IS HER STORY

Lucy was diagnosed with spinal muscular atrophy (SMA) at 11 days old after she was flagged by newborn screening in her state.[1] Learn about her experience with early diagnosis and ZOLGENSMA treatment.

SCROLL DOWN

Indication and Important Safety Information

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: Serious Liver Injury and Acute Liver Failure

Cases of acute liver failure with fatal outcomes have been reported. Acute serious liver injury, acute liver failure, and elevated aminotransferases can also 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. Administer systemic corticosteroid to all patients before and after ZOLGENSMA infusion. Continue to monitor liver function for at least 3 months after infusion, and at other times as clinically indicated. If acute serious liver injury or acute liver failure is suspected, promptly consult a pediatric gastroenterologist or hepatologist.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.

Lucy's EARLY DIAGNOSIS

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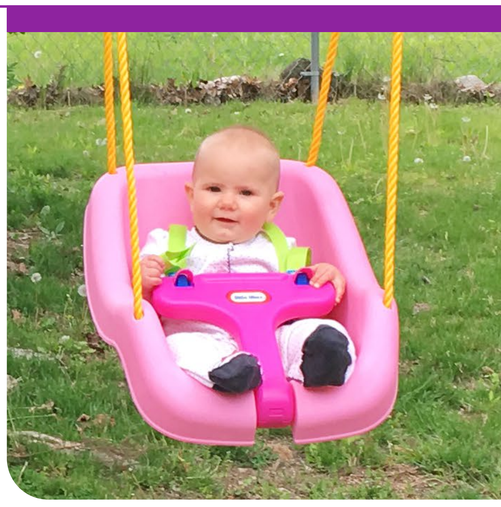
BIRTH

Lucy's SMA was diagnosed through newborn screening in her state[1]

- Before her diagnosis, Lucy's parents had never heard of SMA and didn't know they were both genetic carriers[1]
- A genetic test confirmed that Lucy had 2 copies of the backup *SMN2* gene, which aligns with an SMA Type 1 diagnosis[1]



The importance of newborn screening

As of February 2023, 48 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]

~4 WEEKS OLD

Lucy's parents researched and considered treatment options alongside their neurologist[1]

> ***"Our doctor wanted Lucy to receive ZOLGENSMA because she saw very promising results. She said that it stops the disease progression."[1]***
>
> **– Ashley, mother of Lucy**

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

Systemic Immune Response

Patients with underlying active infection, either acute or chronic uncontrolled, could be at an increased risk of serious systemic immune response. Administer ZOLGENSMA to patients who are clinically stable in their overall health status (e.g., hydration and nutritional status, absence of infection). Postpone ZOLGENSMA in patients with infections until the infection has resolved and the patient is clinically stable.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.

~5 WEEKS OLD

Lucy

WAS TREATED AT ~5 WEEKS OLD

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Lucy was presymptomatic before treatment and showed no signs of SMA[1]

Baseline testing is required for all patients before ZOLGENSMA treatment[5]

- Anti-AAV9 antibody titers ≤1:50[5]
- Liver function,[a] creatinine, complete blood count (including hemoglobin and platelet count), and troponin-I[5]

One day before ZOLGENSMA treatment, Lucy started a corticosteroid regimen[1]

Due to increased risk of serious systemic immune response, administer ZOLGENSMA to patients who are clinically stable in their overall baseline health status[5]

[a]Clinical exam, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, albumin, prothrombin time, partial thromboplastin time (PTT), and international normalized ratio (INR).

AFTER ZOLGENSMA TREATMENT: ~2 MONTHS OLD

Lucy's liver enzymes were elevated after treatment[1]

- Her doctors monitored her lab results until liver enzyme levels returned to baseline[1,5]

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

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.

~1 YEAR OLD

Lucy

~1 YEAR POST ZOLGENSMA TREATMENT

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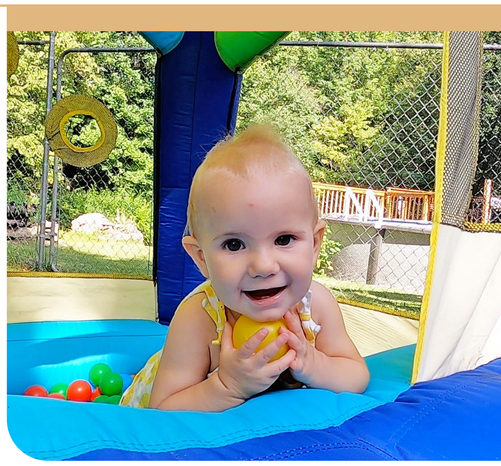
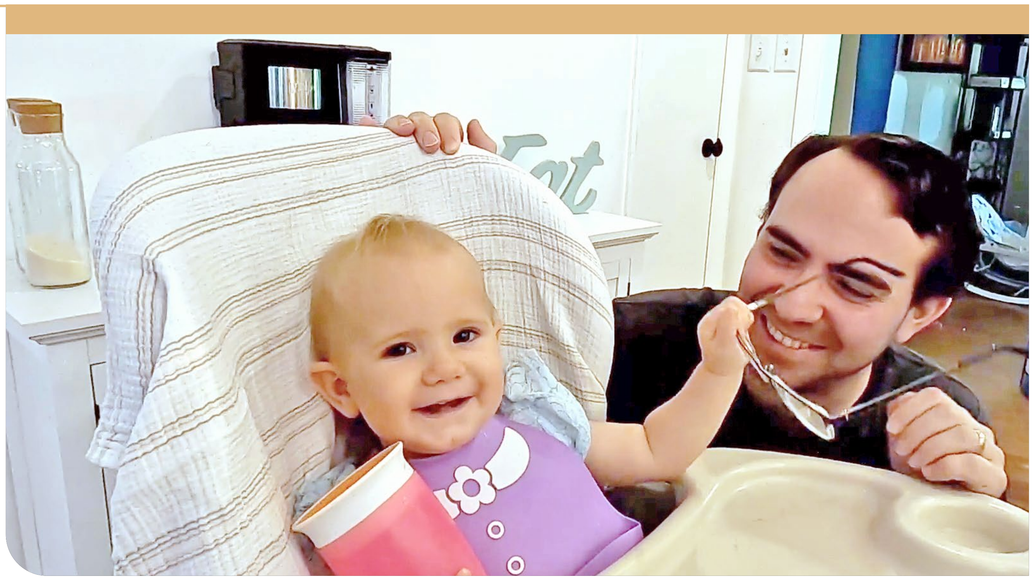
Lucy has maintained respiratory function[1]

- She is able to breathe independently without any kind of respiratory support[1]



> *"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 milestones[1]

- She can sit supported in her high chair[1]
- She is able to stand both supported and independently for several seconds[1]

> *"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 progressed before receiving treatment.

Important Safety Information

WARNINGS AND PRECAUTIONS

Thrombotic Microangiopathy

Cases of thrombotic microangiopathy (TMA) were reported to occur generally within the first two weeks after ZOLGENSMA infusion. TMA can result in life-threatening or fatal outcomes. Obtain baseline creatinine and complete blood count before ZOLGENSMA infusion. Following infusion, monitor platelet counts closely as well as other signs and symptoms of TMA. Consult a pediatric hematologist and/or pediatric nephrologist immediately to manage as clinically indicated.

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~1 YEAR OLD

Lucy is still supported by a medical team[1]

- For patients with SMA, a multidisciplinary care team is important to ongoing treatment. Depending on their needs, patients may see physical, occupational, and other therapists[6]

> ***"Lucy does receive physical therapy every week. It's important because it allows us to continually track her progression and make sure she's continuing to meet her milestones."[1]***
>
> **– Steve, father of Lucy**

CONSIDER ZOLGENSMA

The one-time-only dose to stop SMA progression[5]

ZOLGENSMA is:

- **Designed to treat the genetic cause of SMA** (mutations in the *SMN1* gene) by providing a working copy of the human *SMN* gene[5]
  - ZOLGENSMA is designed not to integrate into the patient's genome[7]
- **Designed for continuous SMN protein expression** with self-complementary DNA and a continuous promoter, which provide rapid activation and expression of the *SMN* transgene[5,8]
- **Designed for targeted delivery** with a non-replicating, adeno-associated virus (AAV9) capsid that can cross the blood-brain barrier into non-dividing motor neurons[5,7]
  - AAV9 vectors are not known to cause disease in humans[7]

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

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. Consider consultation with a cardiologist if troponin elevations are accompanied by clinical signs or symptoms.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.

STR1VE PHASE 3 CLINICAL TRIAL

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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 age[12,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 endpoint**[1,a]

- Patients with SMA Type 1 in historical controls do not typically achieve or maintain motor milestones[13]

Ability to thrive: **41% (9/22)** of patients met criteria for ability to thrive at 18 months of age, a secondary endpoint[12,d]

Respiratory support: **68% (15/22)** of patients did not require noninvasive respiratory support at any point during the study[12]

- 4/22 patients required ventilatory support as assessed by Trilogy BiPAP data alone at 18 months of age, a secondary endpoint[12]

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 study[12]

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

[a]One 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.[12]

[b]One 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.[12]

[c]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.[12]

[d]Ability 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.[12]

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.

SPR1NT CLINICAL TRIAL

zolgensma® (onasemnogene abeparvovec-xioi) suspension for intravenous infusion

SPR1NT is a completed, 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) and 3 copies (n=15) of *SMN2* who were ≤6 weeks of age at time of treatment[1,11]

The 2-copy cohort reached study end at 18 months of age while the 3-copy cohort reached study end at 24 months of age.[11]

2 COPIES OF *SMN2*

Sitting independently: **100% (14/14)** of patients achieved the primary endpoint of sitting without support for ≥30 seconds (Bayley)[14]

- **11 of 14** achieved at an age-appropriate time[14,a]

Standing alone: **71% (10/14)** of patients achieved standing alone (WHO)[14,b]

Survival: **100% (14/14)** of patients were alive and free of permanent ventilation at 14 months of age, a secondary endpoint, and at study end[14]

Respiratory: **100% (14/14)** of patients were free of ventilation support of any kind at study end[14,c]

Nutrition: **93% (13/14)** of patients were able to maintain weight ≥3rd percentile without need for non-oral or mechanical feeding support at any visit through study end[14]

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

[a]Bayley-III, gross motor subtest item 26. WHO MGRS established window of achievement (1%-99%): 3.8-9.2 months for sitting without support.[14,15]

[b]Independent standing ≥10 seconds assessed by WHO MGRS. WHO MGRS established window of achievement (1%-99%): 6.9-16.9 months for standing alone.[14,15]

[c]Ventilation support includes either invasive or noninvasive respiratory support, cough assist, or BiPAP.[14]

Important Safety Information

WARNINGS AND PRECAUTIONS

Systemic Immune Response

Patients with underlying active infection, either acute or chronic uncontrolled, could be at an increased risk of serious systemic immune response. Administer ZOLGENSMA to patients who are clinically stable in their overall health status (e.g., hydration and nutritional status, absence of infection). Postpone ZOLGENSMA in patients with infections until the infection has resolved and the patient is clinically stable.

Please see accompanying Full Prescribing Information, also available at ZOLGENSMA-hcp.com.

SPR1NT CLINICAL TRIAL

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suspension for intravenous infusion

3 COPIES OF *SMN2*

Standing independently: **100% (15/15)** of patients achieved the primary endpoint of standing alone for ≥3 seconds (Bayley) by study end[1,a]

- **14 of 15** patients achieved at an age-appropriate time[1]

Walking independently: **93% (14/15)** of patients achieved the secondary endpoint of walking alone by study end (Bayley)[1,b]

- **11 of 14** patients achieved at an age-appropriate time[1]

Gross motor development: **100% (10/10)** of patients assessed had gross motor performance similar to same-aged children at 24 months of age[1,c]

Nutrition: **100% (15/15)** of patients did not require feeding support of any kind during the study[1]

Respiratory: **100% (15/15)** of patients did not require ventilatory support of any kind during the study[1,d]

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

[a]Bayley-III, gross motor subtest item 40. WHO MGRS established window of achievement (1%-99%): 6.9-16.9 months for standing alone.[1,15]

[b]Bayley-III, gross motor subtest item 43. WHO MGRS established window of achievement (1%-99%): 8.2-17.6 months for walking alone.[1,15]

[c]Gross motor function was measured by the Bayley Scales of Infant and Toddler Development and compared to a standardized norm. Normal range: mean ±2 standard deviations (4-16 score [mean=10, SD=3, range of 1-19]).[1,16]

[d]Ventilation support includes either invasive or noninvasive respiratory support, cough assist, or BiPAP.[1]

Important Safety Information

WARNINGS AND PRECAUTIONS

Thrombocytopenia

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Indication and Important Safety Information

Indication

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Important Safety Information

BOXED WARNING: Serious Liver Injury and Acute Liver Failure

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Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Thrombotic Microangiopathy

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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.

References: 1. Data on file. Novartis Gene Therapies, Inc. 2021. **2.** CureSMA. State of Newborn Screening for SMA Report. https://www.curesma.org/wp-content/uploads/2021/06/Cure-SMA_Report-Card-June21_Final.pdf. Accessed February 17, 2023. **3.** CureSMA. Newborn Screening for SMA. https://www.curesma.org/newborn-screening-for-sma. Accessed February 23, 2023. **4.** Novartis Gene Therapies, Inc. Gene replacement therapy clinical trial for participants with spinal muscular atrophy type 1 (STR1VE). https://clinicaltrials.gov/ct2/show/NCT03306277. ClinicalTrials.gov identifier: NCT03306277. Updated August 16, 2022. Accessed February 17, 2023. **5.** ZOLGENSMA [prescribing information]. Bannockburn, IL: Novartis Gene Therapies, Inc; 2023. **6.** Mercuri E, Finkel RS, Muntoni F, et al. Diagnosis and management of spinal muscular atrophy: part 1: recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. *Neuromuscul Disord.* 2018;28(2):103-115. **7.** Brommel CM, Cooney AL, Sinn PL. Adeno-associated virus-based gene therapy for lifelong correction of genetic disease. *Hum Gene Ther.* 2020;31(17-18). doi:10.1089/hum.2020.138. **8.** Mendell JR, Al-Zaidy S, Shell R, et al. Single-dose gene-replacement therapy for spinal muscular atrophy. *N Engl J Med.* 2017;377(18):1713-1722. **9.** Novartis Gene Therapies, Inc. Gene transfer clinical trial for spinal muscular atrophy type 1. https://clinicaltrials.gov/ct2/show/NCT02122952. ClinicalTrials.gov identifier: NCT02122952. Updated September 15, 2022. Accessed February 17, 2023. **10.** Novartis Gene Therapies, Inc. Long-term follow-up study for patients from AVXS-101-CL-101 (START). https://clinicaltrials.gov/ct2/show/NCT03421977. ClinicalTrials.gov identifier: NCT03421977. Updated November 22, 2022. Accessed February 17, 2023. **11.** Novartis Gene Therapies, Inc. Pre-symptomatic study of intravenous onasemnogene abeparvovec-xioi in spinal muscular atrophy (SMA) for patients with multiple copies of SMN2 (SPR1NT). https://clinicaltrials.gov/ct2/show/NCT03505099. ClinicalTrials.gov identifier: NCT03505099. Updated September 7, 2022. Accessed February 17, 2023. **12.** Data on file. AveXis, Inc. 2020. **13.** De Sanctis R, Coratti G, Pasternak A, et al. Developmental milestones in type I spinal muscular atrophy. *Neuromuscul Disord.* 2016;26(11):754-759. **14.** Data on file. Novartis Gene Therapies, Inc. 2021. **15.** WHO Multicentre Growth Reference Study Group. WHO Motor Development Study: windows of achievement for six gross motor development milestones. *Acta Paediatr Suppl.* 2006;450:86-95. **16.** Bayley N. *Bayley Scales of Infant and Toddler Development: Administration Manual.* 3rd ed. The Psychological Corporation; 2006.

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