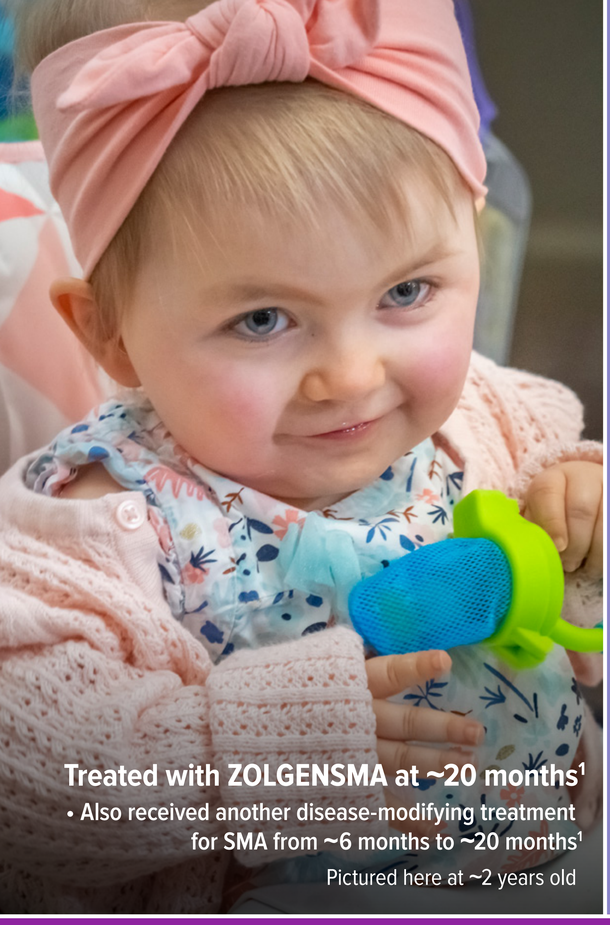

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Meet Maisie

SHE HAS SMA TYPE 1 AND THIS IS HER STORY

Maisie showed signs of spinal muscular atrophy (SMA), including hypotonia, shortly after birth.[1] She was diagnosed with SMA Type 1 at ~6 months old.[1]

Discover why Maisie's mother Ciji wanted one-time-only gene therapy for her daughter,[1] and their journey to 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.

Maisie's journey TO A DIAGNOSIS

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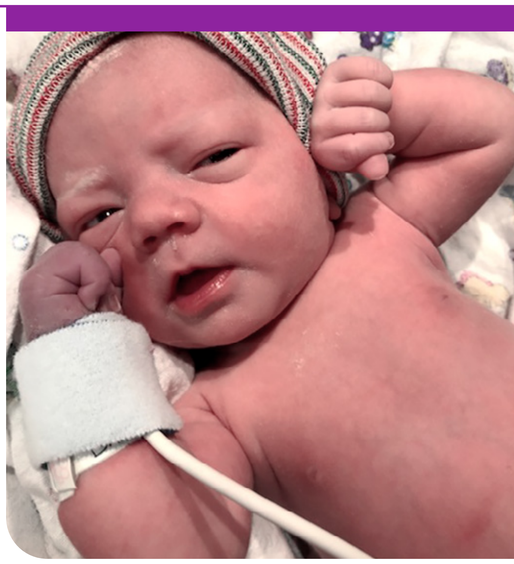
BIRTH

As a newborn, Maisie showed signs of hypotonia and other concerning symptoms[1]

"From day 1, I knew something wasn't right with her. She wasn't moving her legs. She would just lay there…she…got weaker. And weaker. And she eventually just quit eating."[1]

– Ciji, mother of Maisie



~6 WEEKS OLD

Maisie's symptoms continued and Ciji shared her concerns with her pediatrician[1]

"When she was 6 weeks old, I told the doctor…she's very weak. Like she's not holding herself up at all. Like she's a bag of mush."[1]

– Ciji, mother of Maisie

~4-6 MONTHS OLD

Maisie was referred to a physical therapist[1]

- At ~4 months old, Maisie started physical therapy for low muscle tone[1]
- Over the next ~2 months, she continued to have difficulty eating and showed a lack of head control[1]

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.

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~5 MONTHS OLD

Because she continued to get weaker, Maisie was sent for additional testing[1]

> *"We realized there was a serious problem and, the doctors… were not recognizing that there was a valid issue. And, so we took Maisie to our physical therapist…she encouraged us and helped advocate to get Maisie to Denver to seek additional testing."*[1]
>
> – Ciji, mother of Maisie

Maisie received
A DIAGNOSIS AND STARTED TREATMENT[1]

5 MONTHS, 3 WEEKS OLD

One week before she turned 6 months old, Maisie was diagnosed with SMA Type 1[1]

- A genetic test confirmed Maisie has SMA Type 1, with a bi-allelic deletion of *SMN1* and 2 copies of *SMN2*[1]
- At the time of diagnosis, there was one FDA-approved treatment and ZOLGENSMA was in clinical trials[1]
- Maisie was almost 6 months old and she did not qualify for the ZOLGENSMA clinical trials[1]

> *"At the time, Maisie didn't qualify for the [ZOLGENSMA] clinical trial and so, because we knew that the SMA would continue to progress and she would continue to decline, we started the other treatment that was FDA approved."*[1]
>
> – Ciji, mother of Maisie

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.

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~6 MONTHS OLD

Maisie started a disease-modifying treatment for SMA that required ongoing lumbar punctures multiple times per year[1]

"...it got her to ZOLGENSMA...It got her to the treatment date."[1]

– Ciji, mother of Maisie

Why Maisie's mother wanted ZOLGENSMA

"From the beginning, I wanted ZOLGENSMA...there was never a second thought. The first few things that I learned about ZOLGENSMA was it treated the genetic root cause of SMA and that it was a one-time treatment."[1]

– Ciji, mother of Maisie

~6-18 MONTHS OLD

For ~1 year, Maisie received multiple doses of disease-modifying treatment for SMA and showed improvements[1]

"I could see that it had definitely improved her in some of her areas. Like her arm movements became faster. And she started slightly moving her head...."[1]

– Ciji, mother of Maisie

May 2019: ZOLGENSMA received FDA approval for pediatric patients 2 years and under with SMA[2]

After first being denied coverage for ZOLGENSMA, Ciji appealed and was approved[1]

"The insurance company called me and said...'I'm calling with good news. We're gonna reverse our decision and Maisie's gonna get ZOLGENSMA.' I couldn't breathe. I was so elated."[1]

– Ciji, mother of Maisie

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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~20 MONTHS OLD

Maisie

WAS TREATED WITH ZOLGENSMA AT ~20 MONTHS OLD[1]

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"I'll always remember the day Maisie received ZOLGENSMA."[1]

– Ciji, mother of Maisie

Baseline testing is required for all patients before ZOLGENSMA treatment[2]

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

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

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

Per the regimen detailed in the **Full Prescribing Information,** treatment with systemic corticosteroids before and after ZOLGENSMA infusion is required. Administer ZOLGENSMA to patients who are clinically stable in their overall baseline health status. Postpone ZOLGENSMA in patients with infections until the infection has resolved and the patient is clinically stable.

AFTER ZOLGENSMA TREATMENT: ~20-25 MONTHS OLD

Maisie continued to achieve and maintain motor milestones[1]

- Motor milestones: Head control, rolling over, lifting legs, and sitting without support[1]
- Bulbar function: Laughing and speaking[1]
- Walking with assistance: Maisie is also learning to walk with the help from leg braces and physical therapy[1]

"It's 5 months post dosing with ZOLGENSMA. Maisie is 2 years old. She grabs her toes now and she sticks 'em in her mouth. She sits up and she only wants to sit up."[1]

– Ciji, mother of Maisie

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.

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Since her one-time ZOLGENSMA infusion, Maisie has not received any additional disease-modifying treatments for SMA[1]

- Her SMA is managed with the support of a multidisciplinary team, including physical, speech, and occupational therapy multiple times a week[1]

~25 MONTHS OLD

Maisie

5 MONTHS POST ONE-TIME ZOLGENSMA TREATMENT

"Maisie is doing incredible. She's not requiring her vent. She's moving around so much. She's lifting her legs. She's rolling over. She's getting into things. She's doing things that we never thought possible. She's smiling. She's laughing. She's talking. She sits up and she plays with you…And she's hitting milestones that were once just a dream."[1]

– Ciji, mother of Maisie

"Even though Maisie received treatments, Maisie still has SMA. She still shows plenty of signs of weakness. And limitations. She still struggles to breathe sometimes… it's still hard for her to cough. She's working on strengthening her muscles."[1]

– Ciji, mother of Maisie

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

ADVERSE REACTIONS

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

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> *One of my most memorable moments was, we were driving home from Utah, and she just started going Ma-ma-ma…And I just held her and loved her and was like, yay…you said Mama. I wasn't sure if I was ever gonna hear that."*[1]
>
> **– Ciji, mother of Maisie**

CONSIDER ZOLGENSMA

The one-time-only dose to stop SMA progression

As a one-time gene therapy, ZOLGENSMA is:

- **Designed to treat the cause of SMA** (mutations in *SMN1*) with a working copy of the human *SMN* gene[2]
  - ZOLGENSMA is designed not to integrate into the patient's genome[3]
- **Designed for continuous SMN protein expression** with self-complementary DNA and a continuous promoter, which provide rapid activation and expression of the *SMN* transgene[2,4]
- **Designed for targeted delivery** with a nonreplicating, adeno-associated virus (AAV9) capsid that can cross the blood-brain barrier into nondividing motor neurons[2,3]
  - AAV9 vectors are not known to cause disease in humans[3]

Safety and efficacy of ZOLGENSMA have been evaluated in 4 trials.[4-7]

To learn more about the ZOLGENSMA clinical trials, go to ZOLGENSMA-hcp.com.

Important Safety Information

WARNINGS AND PRECAUTIONS

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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)[5]

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[1,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[8]

Ability to thrive: **41% (9/22)** of patients met criteria for ability to thrive at 18 months of age, a secondary endpoint[1,d]

Respiratory support: **68% (15/22)** of patients did not require noninvasive respiratory support at any point during the study[1]

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

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[1]

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

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) data set included in the Prescribing Information. The patient has been confirmed to be symptomatic at the time of gene therapy and included in the final ITT analysis.[1]

[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 of age; this patient required permanent ventilation at 11 months prior to withdrawal of consent.[1]

[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. Patient was alive and without permanent ventilation at the time of withdrawal.[1]

[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.[1]

Important Safety Information

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Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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References: 1. Data on file. AveXis, Inc. 2020. **2.** ZOLGENSMA [prescribing information]. Bannockburn, IL: Novartis Gene Therapies, Inc; 2023. **3.** 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):985-995.doi:10.1089/hum.2020.138. **4.** 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. **5.** Novartis Gene Therapies, Inc. Gene replacement therapy clinical trial for patients 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. **6.** 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. **7.** 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. **8.** De Sanctis R, Coratti G, Pasternak A, et al. Developmental milestones in type I spinal muscular atrophy. *Neuromuscul Disord.* 2016;26(11):754-759.

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