Treated with ZOLGENSMA at ~6 weeks old[1]

Pictured here at ~1.5 years old

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

Meet Payne

HE HAS SMA AND WAS TREATED PRESYMPTOMATICALLY. THIS IS HIS STORY.

Newborn screening identified spinal muscular atrophy (SMA) before signs appeared.[1] This is his ZOLGENSMA treatment journey.

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.

Payne's
NEWBORN SCREENING AND DIAGNOSIS

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

BIRTH

5 days after he was born, Payne's newborn screening results were reported as positive for SMA[1]

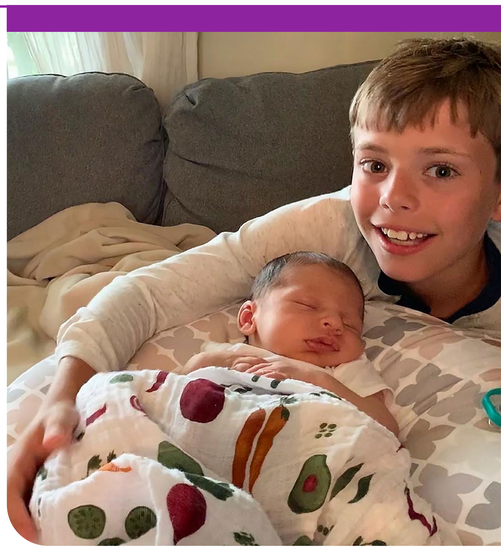
- A genetic test later confirmed a diagnosis for SMA[1]
- Early treatment for SMA is critical in stopping the progressive, irreversible loss of motor neurons[2]
- Newborn screening programs help prevent diagnostic delays[2]

> ***"We live 39 miles from the Iowa state line. Had our family lived 39 miles north we would not know about Payne's condition. We wouldn't have found out until Payne started to lose motor function."***[1]
>
> **– Jim, father of Payne**

~2 WEEKS OLD

Payne's family met with a physical therapist, geneticist, and neurologist[1]

- Through genetic tests, the treatment team confirmed Payne had 4 copies of *SMN2*[1]
- Recommendations from SMA treatment experts advise immediate treatment of children with 4 copies of *SMN2*[3]



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.

~6 WEEKS OLD

Payne

WAS TREATED WITH ZOLGENSMA AT ~6 WEEKS OLD[1]

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

Baseline testing is required for all patients before ZOLGENSMA treatment[4]

- Anti-AAV9 antibody titers ≤1:50[4]
- Liver function,[a] creatinine, complete blood count (including hemoglobin and platelet count), and troponin-I[4]
- Due to increased risk of serious systemic immune response, administer ZOLGENSMA to patients who are clinically stable in their overall baseline health status[4]

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

Before ZOLGENSMA treatment, Payne showed no signs of SMA, such as muscle weakness[1,2]

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.[4]

AFTER ZOLGENSMA TREATMENT: 7 WEEKS OLD

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.

Life After
ZOLGENSMA TREATMENT

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

~2 YEARS OLD

Payne is supported by a multidisciplinary treatment team[1]

- His family planned regular follow-ups at 3 months, 6 months, and 1 year[1]

Payne has not shown any muscle weakness or other signs of SMA[1]

- Payne is achieving milestones and can stand and walk without assistance[1]

"[Payne's] favorite thing to do is jump! He climbs up anything to jump off and is still growing and excelling at all of his milestones. He's a big-time talker."[1]

– Jim, father of Payne

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

OneGene program®

The OneGene Program® supported Payne's family throughout the pre-treatment process

Individualized patient support

The OneGene Program is a comprehensive support program for families and healthcare providers throughout the ZOLGENSMA treatment journey.

To contact the OneGene Program, call 1-855-441-GENE (4363).

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.

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[1,5]

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.[5]

2 COPIES OF *SMN2*

Sitting independently: 100% (14/14) of patients achieved the primary endpoint of sitting without support for ≥30 seconds (Bayley)[6]

- **11 of 14** achieved at an age-appropriate time[6,a]

Standing alone: 71% (10/14) of patients achieved standing alone (WHO)[6,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[6]

Respiratory: 100% (14/14) of patients were free of ventilation support of any kind at study end[6,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[6]

[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.[6,7]

[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.[6,7]

[c]Ventilation support includes either invasive or noninvasive respiratory support, cough assist, or BiPAP.[6]

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.

SPR1NT CLINICAL TRIAL

zolgensma® (onasemnogene abeparvovec-xioi)
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]

[a]Bayley-III, gross motor subtest item 40. WHO MGRS established window of achievement (1%-99%): 6.9-16.9 months for standing alone.[1,7]

[b]Bayley-III, gross motor subtest item 43. WHO MGRS established window of achievement (1%-99%): 8.2-17.6 months for walking alone.[1,7]

[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]).[1,8]

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

CONSIDER ZOLGENSMA

The one-time-only dose to stop SMA progression[4]

ZOLGENSMA is:

- **Designed to treat the genetic root cause of SMA** (deletion or mutation of the *SMN1* gene) by providing a working copy of the human *SMN* gene[4]
  - ZOLGENSMA is designed not to integrate into the patient's genome[9]
- **Designed for continuous SMN protein expression** with self-complementary DNA and a continuous promoter, which provide rapid activation and expression of the *SMN* gene[4,10]
- **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[4,9]
  - AAV9 vectors are not known to cause disease in humans[9]

To learn more about ZOLGENSMA, visit 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.

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

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.

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.

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.

NOVARTIS

© **2023 Novartis Gene Therapies, Inc.**
Bannockburn, IL 60015

03/2023 US-ZOL-22-0094 V2

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

Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

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.

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. 2022. **2.** Kichula EA, Proud CM, Farrar MA, et al. Expert recommendations and clinical considerations in the use of onasemnogene abeparvovec gene therapy for spinal muscular atrophy. *Muscle Nerve.* 2021;64(4):413-427. **3.** Glascock J, Sampson J, Connolly AM, et al. Revised recommendations for the treatment of infants diagnosed with spinal muscular atrophy via newborn screening who have 4 copies of *SMN2*. *J Neuromuscul Dis.* 2020;7(2):97-100. **4**. ZOLGENSMA [prescribing information]. Bannockburn, IL: Novartis Gene Therapies, Inc; 2023. **5.** 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 21, 2023. **6.** Data on file. Novartis Gene Therapies, Inc. 2021. **7.** 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. **8.** Bayley N. *Bayley Scales of Infant and Toddler Development: Administration Manual.* 3rd ed. The Psychological Corporation; 2006. **9.** 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). **10.** 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.

NOVARTIS

© **2023 Novartis Gene Therapies, Inc.**
Bannockburn, IL 60015

For US healthcare professionals only.
03/2023 US-ZOL-22-0094 V2