

# Some things get everywhere

In spinal muscular atrophy (SMA) treatment, that's what you want



**Evrysdi is an oral, non-invasive treatment designed to produce SMN protein throughout the body.\***

\*This was observed when Evrysdi was studied in animals.

**Now approved  
in tablet form**

For illustrative purposes only.

SMN=survival motor neuron.

## What is Evrysdi?

Evrysdi is a prescription medicine used to treat spinal muscular atrophy (SMA) in children and adults.

## Important Safety Information

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are pregnant or plan to become pregnant, as Evrysdi may harm your unborn baby. Ask your healthcare provider for advice before taking this medicine

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
Type 2 or 3

Results:  
Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

Safety

Support





# The first and only oral treatment for SMA

Evrysdi is a small molecule designed to reach parts of the body that need SMN protein, such as the brain and spinal cord, muscles, larynx, GI system, and heart\*

\*This was observed when Evrysdi was studied in animals.

**Evrysdi is made to fit your lifestyle—  
it's non-invasive, so you have  
flexibility in how you plan your day**

- ✓ Delivered to your door
- ✓ No needles, sedation, or hospital stays required
- ✓ No required monitoring or laboratory testing

“ I love that Evrysdi is an oral treatment I can take at home. Living with a disability is already challenging, and I wanted to find **an option with proven results.**

—**Janelle**, living with Type 2 SMA ”



GI=gastrointestinal; SMN=survival motor neuron.

## Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are a woman who can become pregnant:
    - Before you start your treatment with Evrysdi, your healthcare provider may test you for pregnancy
    - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping Evrysdi

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## Two oral options you can take everywhere\*

Evrysdi tablets have the same demonstrated results and safety as the liquid form

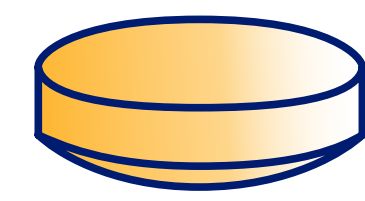


### Liquid

For illustrative purposes only.



\*If refrigeration is not available, Evrysdi liquid can be kept at room temperature up to 104°F for a combined total of 5 days. Please refer to the Instructions for Use for additional information about storage and administration.



### Tablet<sup>†</sup>



<sup>†</sup>Evrysdi 5-mg tablets are approved for people aged 2 years and older who weigh at least 44 lb (20 kg). The tablets cannot be taken with feeding tubes.

Treatment designed with **your needs in mind**

“ I love to hang out with my friends and family, cook, catch a movie, or go out to eat. Evrysdi just works in my life because **I'm not confined by taking my medication in one place.**

—Shaniqua, living with Type 3 SMA “



### Important Safety Information (continued)

• Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:

◦ are a woman who can become pregnant:

- **Pregnancy Registry.** There is a pregnancy registry for women who take Evrysdi during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving Evrysdi, tell your healthcare provider right away. Talk to your healthcare provider about registering with the Evrysdi Pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling **1-833-760-1098** or visiting <https://www.evrysdipregnancyregistry.com>.

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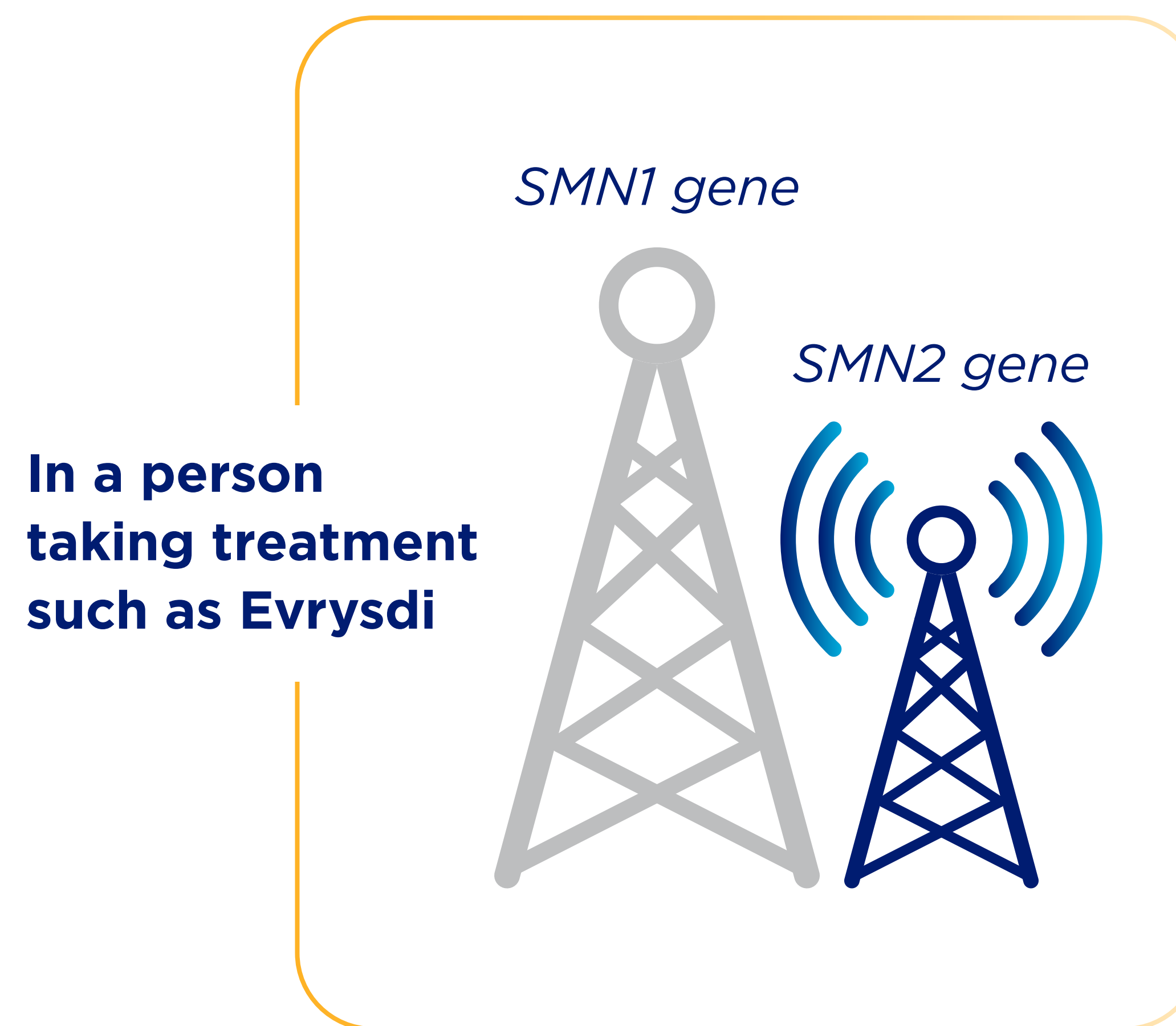
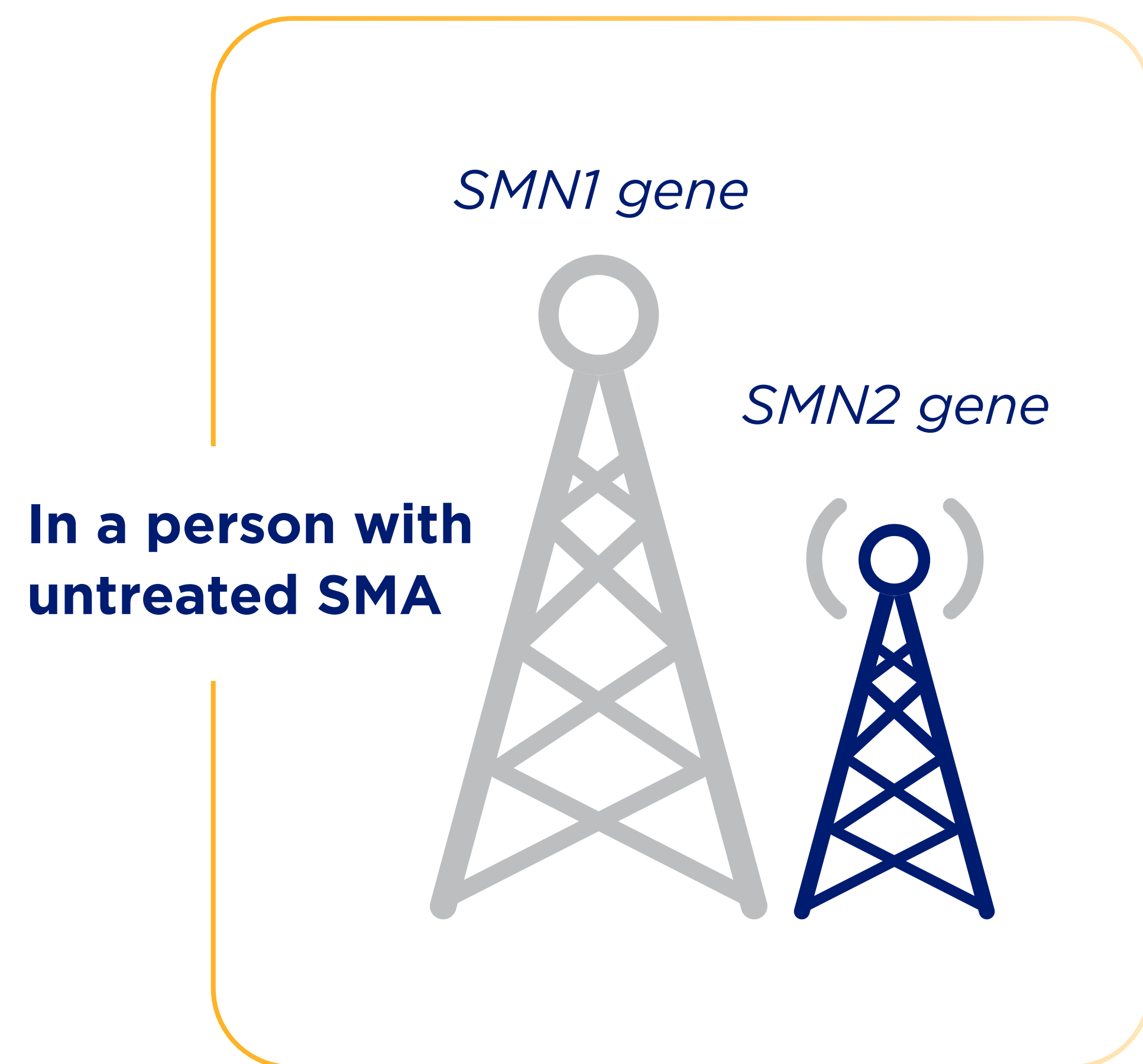


# Understanding SMA

SMA is a genetic disorder that leads to a shortage of SMN protein, which your muscles need to function

There are 2 genes, *SMN1* and *SMN2*, that play a role in creating SMN protein. Think of the *SMN1* gene as the main cell tower and the *SMN2* gene as a backup cell tower, both working together to produce SMN protein.

- In SMA, the main cell tower doesn't function properly, and the backup cell tower can't send enough of the right signals to make up for the lack of SMN protein production
- The number of backup cell towers varies for everyone, but the fewer you have, the more severe your SMA may be



**Some disease-modifying treatments for SMA, such as Evrysdi, can help the backup cell tower send the right signals to produce more SMN protein**

SMN=survival motor neuron.

## Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are an adult male. Evrysdi may affect a man's ability to have children (fertility). Ask a healthcare provider for advice before taking this medicine
  - are breastfeeding or plan to breastfeed. It is not known if Evrysdi passes into breast milk and may harm your baby

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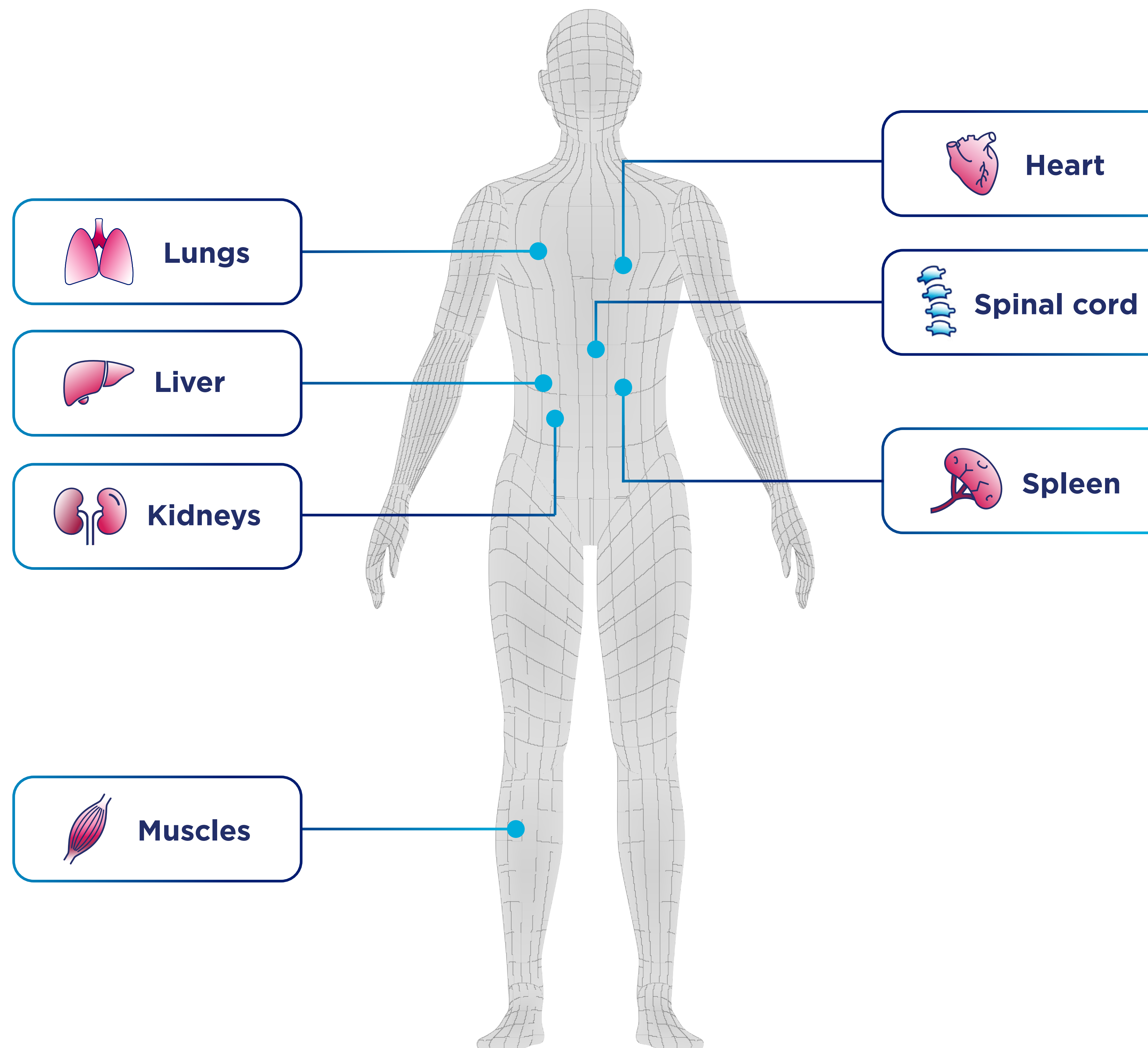
Support





# SMN protein can be found nearly everywhere in the body

This protein plays an important role in helping parts of our body function properly, such as:



SMN=survival motor neuron.

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# Designed to go everywhere

Evrysdi helps produce SMN protein throughout the body

Evrysdi is a small molecule that is taken orally and designed to reach areas of the body that need SMN protein, such as\*:

Brain  
and Spinal  
Cord

Muscles

Larynx

GI System

Heart

“ We heard that Evrysdi was designed to go throughout the body and could be taken at home. **It was absolutely the right choice for Bear.**  
—Erin, mom to Bear,  
who is living with Type 2 SMA ”



\*This was observed when Evrysdi was studied in animals.

GI=gastrointestinal; SMN=survival motor neuron.

## Important Safety Information (continued)

- **Tell your healthcare provider about all the medicines you take**
- If you were prescribed Evrysdi for Oral Solution, you should receive Evrysdi from the pharmacy as a liquid. If the medicine in the bottle is a powder, **do not use it.** Contact your pharmacist for a replacement
- Avoid getting Evrysdi on your skin or in your eyes. If Evrysdi gets on your skin, wash the area with soap and water. If Evrysdi gets in your eyes, rinse your eyes with water

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# Evrysdi works daily for a consistent impact on SMN protein levels

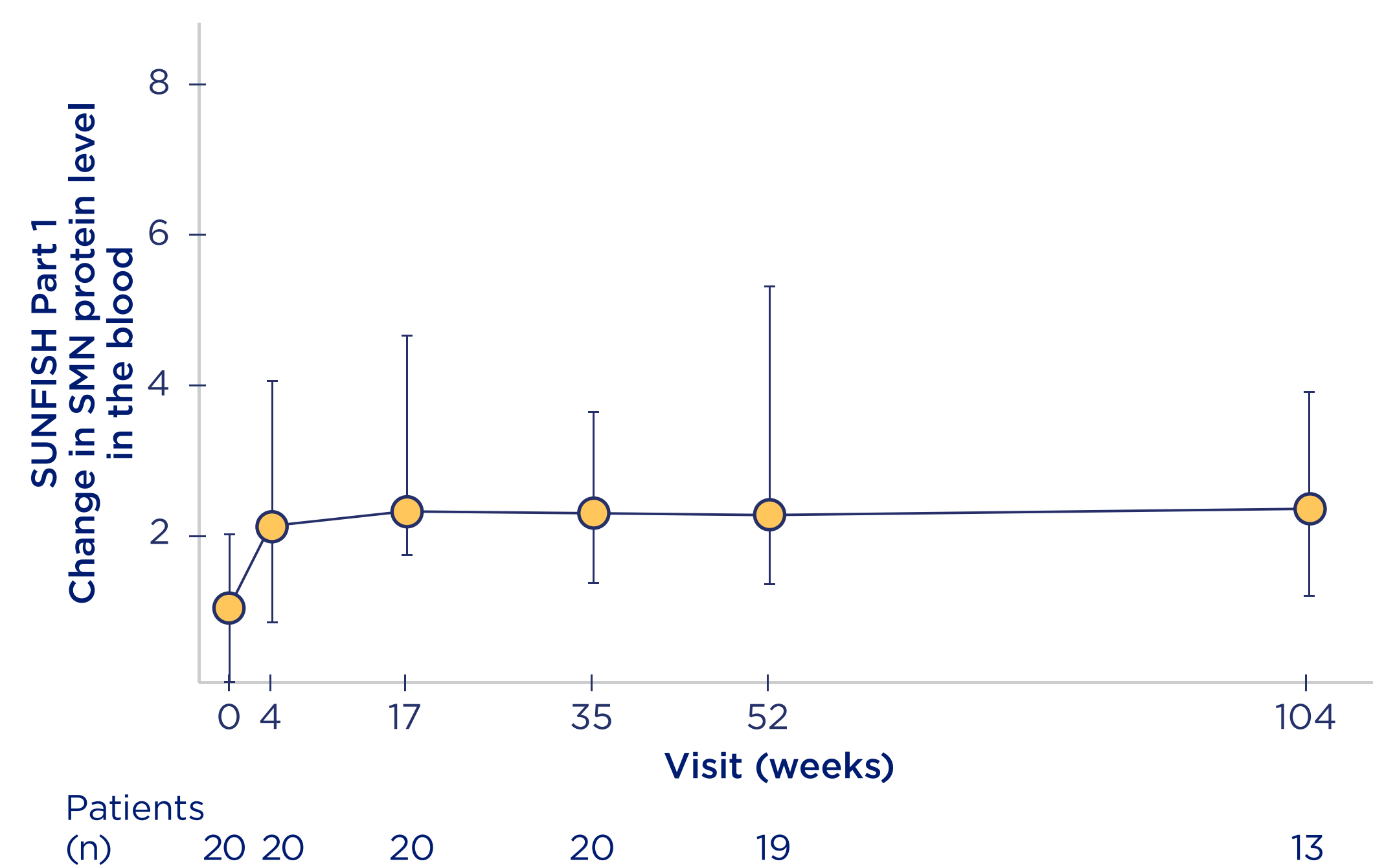
Within 4 weeks of treatment with Evrysdi, SMN protein levels in the blood **approximately doubled**

Results were maintained throughout 2 years across all SMA types studied\*

## Infants with Type 1 SMA†



## Adults and children with Type 2 or 3 SMA†



## Previously treated adults, children, and infants with Type 1, 2, or 3 SMA†



\*Types 1, 2, and 3 SMA. No data available in presymptomatic SMA (under 2 months).

†Evrysdi recommended dose.

SMN=survival motor neuron.

### Important Safety Information (continued)

• **The most common side effects of Evrysdi include:**

- For later-onset SMA: fever, diarrhea, rash
- For infantile-onset SMA: fever; diarrhea; rash; runny nose, sneezing and sore throat (upper respiratory infection); lung infection (lower respiratory infection); constipation; vomiting; cough

These are not all of the possible side effects of Evrysdi. For more information on the risk and benefits profile of Evrysdi, ask your healthcare provider or pharmacist.

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# No matter where you are in your journey with SMA, Evrysdi can make a difference

“ Since SMA is progressive, the longer you go without treatment, the weaker you become. **Every day matters.**

—Tanner, basketball coach,  
living with Type 2 SMA”

“ Because Evrysdi is working daily in her body to make SMN protein, **it is giving her the opportunity to thrive in a way we never thought possible.**

—Amber, mom to Payton,  
who is living with Type 1 SMA”



SMN=survival motor neuron.

## Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are pregnant or plan to become pregnant, as Evrysdi may harm your unborn baby. Ask your healthcare provider for advice before taking this medicine
  - are a woman who can become pregnant:
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# Evrysdi has been well studied and proven safe and effective across SMA types\*

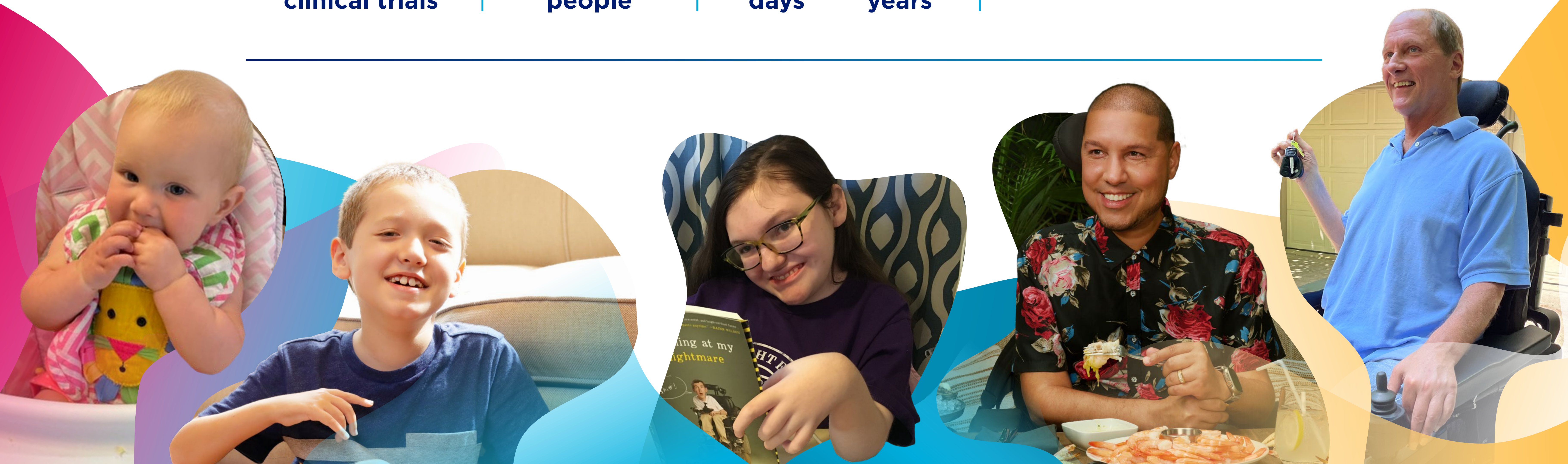
FDA APPROVED SINCE 2020

Studied in  
**4**  
clinical trials

including  
**490+**  
people

people aged  
**16 — 60**  
days years

with presymptomatic  
and Types 1, 2,  
and 3 SMA<sup>†</sup>



\*Types 1, 2, 3 and presymptomatic SMA.

<sup>†</sup>RAINBOWFISH is an open-label study in 26 newborns younger than 6 weeks (at first dose). These newborns were genetically diagnosed with SMA and had not yet shown symptoms (presymptomatic SMA). FIREFISH is a 2-part, open-label study in 62 infants aged 2 to 7 months with Type 1 SMA. SUNFISH is a 2-part, placebo-controlled study in 231 adults and children aged 2 to 25 years with Type 2 or 3 SMA. JEWELFISH is an open-label safety study in 174 people aged 1 to 60 years with Type 1, 2, or 3 SMA that were previously treated with approved or investigational SMA medications.

## Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are a woman who can become pregnant:
    - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping Evrysdi

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# Studied in the most inclusive clinical trial program in SMA

Participants enrolled across all studies included a range of attributes:

✓ broad range of physical ability

✓ able to walk\*

✓ severe scoliosis

✓ previous treatment with approved or investigational SMA medications

✓ unable to walk

✓ joint contractures



// I love the Evrysdi community because it's so diverse. It's great to see the different perspectives and cultural backgrounds, and everyone is just trying to get the information that we need to be successful.

—Jose, living with Type 3 SMA //

\*In SUNFISH Part 1, 9 people were able to walk; in JEWELFISH, 15.

## Important Safety Information (continued)

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◦ are a woman who can become pregnant:

– **Pregnancy Registry.** There is a pregnancy registry for women who take Evrysdi during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving Evrysdi, tell your healthcare provider right away. Talk to your healthcare provider about registering with the Evrysdi Pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling **1-833-760-1098** or visiting

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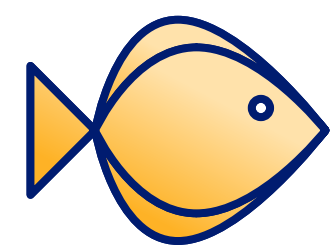
Liquid and  
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SUNFISH PART 2

## Powerful results for everyday life

Study in adults and children  
with later-onset SMA

**Shaniqua**, living with  
Type 3 SMA



### Important Safety Information (continued)

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  - are an adult male. Evrysdi may affect a man's ability to have children (fertility). Ask a healthcare provider for advice before taking this medicine
  - are breastfeeding or plan to breastfeed. It is not known if Evrysdi passes into breast milk and may harm your baby

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## Take action against later-onset SMA

It's important to remember that SMA is a progressive disease that **slowly weakens muscles over time**. While you might not notice these subtle changes on a daily basis, they can prevent you from completing everyday tasks on your own.

// **The progression of SMA can be slow.** You don't realize that something is happening to you until you try to do something that you used to be able to do and go 'Oh, I can't do that anymore.'

—Angela, living with Type 2 SMA //



Whether you or someone you care for has started and stopped treatment or has yet to start treating later-onset SMA, **Evrydsi can help preserve or improve motor function and strength.**

// My biggest encouragement to other adults with SMA would be to **seek out treatment.**

—Jim, living with Type 3 SMA //



### Important Safety Information (continued)

- **Tell your healthcare provider about all the medicines you take**
- If you were prescribed Evrydsi for Oral Solution, you should receive Evrydsi from the pharmacy as a liquid. If the medicine in the bottle is a powder, **do not use it**. Contact your pharmacist for a replacement
- Avoid getting Evrydsi on your skin or in your eyes. If Evrydsi gets on your skin, wash the area with soap and water. If Evrydsi gets in your eyes, rinse your eyes with water

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# A closer look at the SUNFISH study

A 2-part, placebo-controlled study in adults and children with Type 2 or 3 SMA

## The study included

# 231

adults and children with Type 2 or 3 SMA



### The main measurement recorded after 1 year of taking Evrysdi:

Change in motor function\* with Evrysdi, compared with placebo†

Additional measurement after 1 year of taking Evrysdi:

Change in upper limb function‡ with Evrysdi, compared with placebo†

## SUNFISH PART 1

# 51

 adults and children (aged 2 to 24 years)

- Explored the dose and safety of Evrysdi
- Included 9 people **who could walk**

## SUNFISH PART 2

# 180

 adults and children (aged 2 to 25 years)

- Measured the safety and effectiveness of the recommended dose of Evrysdi (in 120 people), compared with placebo (in 60 people)
- Included 180 people who **were not able to walk**, 120 people **with scoliosis** (57 with severe scoliosis), and people **with and without joint contractures**

The majority of people in the SUNFISH study would not have qualified for prior SMA studies

\*Measured by the MFM-32 scale.

†Adults and children not taking Evrysdi took a placebo, a substance that has no active medication and is often used in studies.

‡Measured by the RULM scale.

MFM-32=Motor Function Measure-32 Item; RULM=Revised Upper Limb Module.

### Important Safety Information (continued)

• **The most common side effects of Evrysdi include:**

- For later-onset SMA: fever, diarrhea, rash
- For infantile-onset SMA: fever; diarrhea; rash; runny nose, sneezing and sore throat (upper respiratory infection); lung infection (lower respiratory infection); constipation; vomiting; cough

These are not all of the possible side effects of Evrysdi. For more information on the risk and benefits profile of Evrysdi, ask your healthcare provider or pharmacist.

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# How Evrysdi was studied in people with later-onset SMA

The effectiveness of Evrysdi in later-onset SMA was studied using 2 measurements

## Measuring important daily functions

The **Motor Function Measure-32 Items (MFM-32)** scale is designed to capture changes in head, trunk, and limb motor movements using 32 elements in a broad range of people, including those who can and cannot walk. It uses 3 main categories:



Standing/  
transfer  
movements



Upper/lower body  
movements



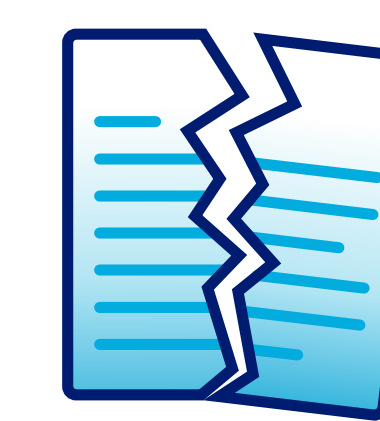
Hand/foot  
movements

## Evaluating the ability to perform daily tasks

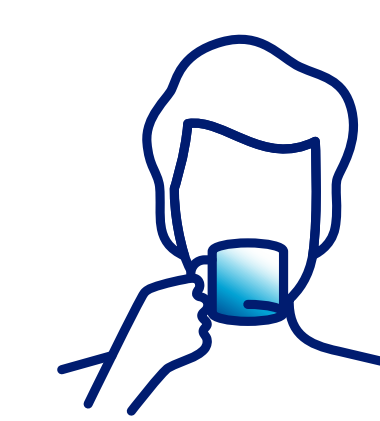
The **Revised Upper Limb Modular (RULM)** was specifically designed for people 2.5 years and older living with SMA to evaluate strength in arm movements and the ability to perform specific tasks. It includes tests such as:



Pick up objects,  
like coins/tokens



Tear paper



Raise cup  
to mouth



Open plastic  
container

## Important Safety Information (continued)

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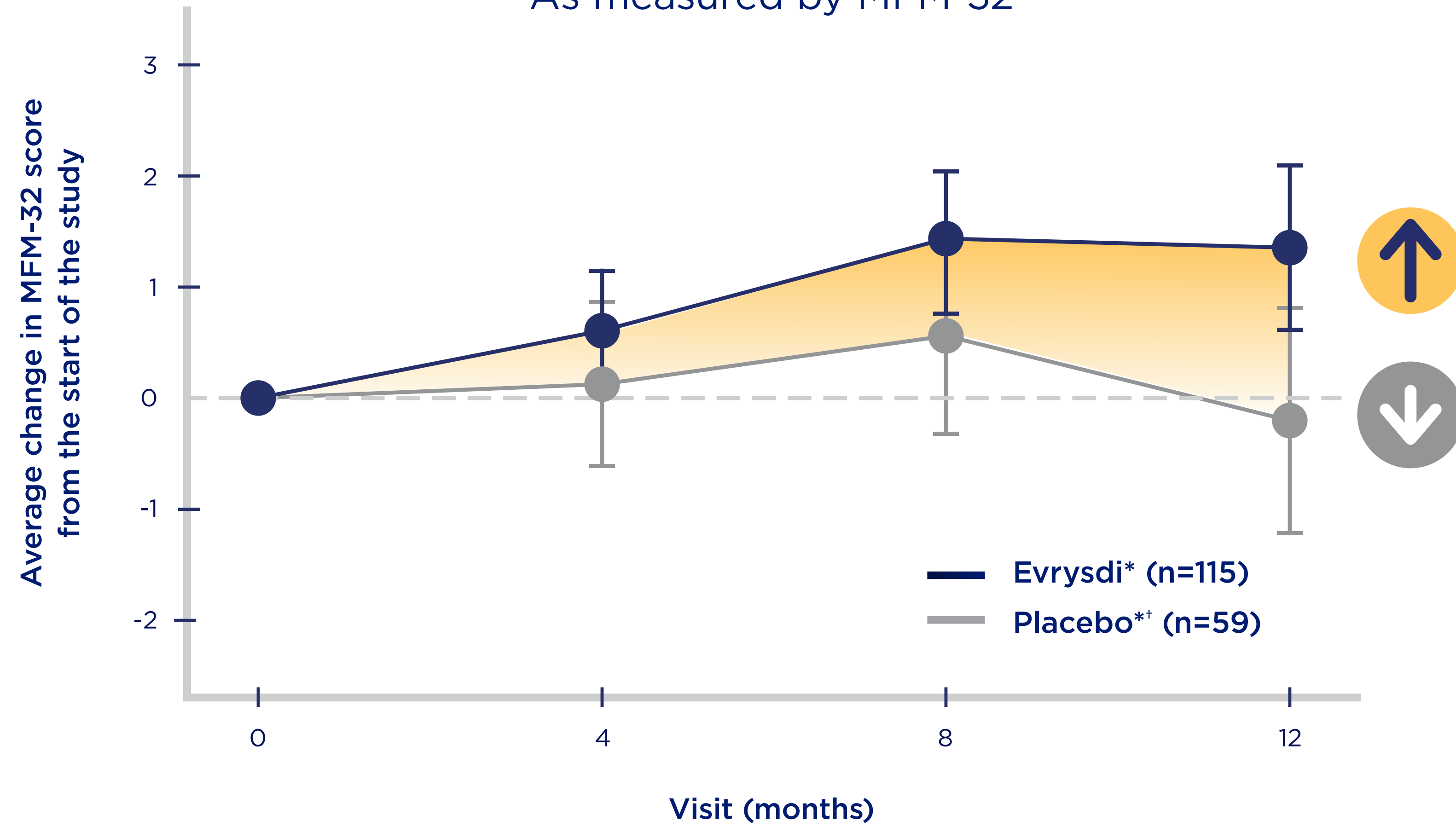


EVERYWHERE



# Helping preserve daily function

**Change in motor function score over 1 year vs placebo**  
As measured by MFM-32



**Average score increased 1.36 points with Evrysdi**  
**Average score decreased 0.19 points with placebo**  
 1.55-point estimated improvement vs placebo  
 (95% CI: 0.30, 2.81;  $P=0.0156$ )<sup>†</sup>

**It's great to see Shaniqua continue to cook and put her clothes on herself.** She is better able to use her arms to move from her wheelchair onto the shower chair and take a shower.  
**—Adriane, mom to Shaniqua,** who is living with Type 3 SMA



\*In some studies, including this one, if someone's data cannot be collected on time for any reason, that person's progress cannot be counted in that part of the study. This chart includes only the information that was collected on time.  
 \*\*Adults and children not taking Evrysdi took a placebo, a substance that has no active medication and is often used in studies.  
 †This 95% CI means that we are 95% confident that the actual average change in MFM-32 with Evrysdi will be between 0.30 and 2.81 points higher than with placebo.

CI=confidence interval; MFM-32=Motor Function Measure-32 Items.

### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
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    - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping Evrysdi

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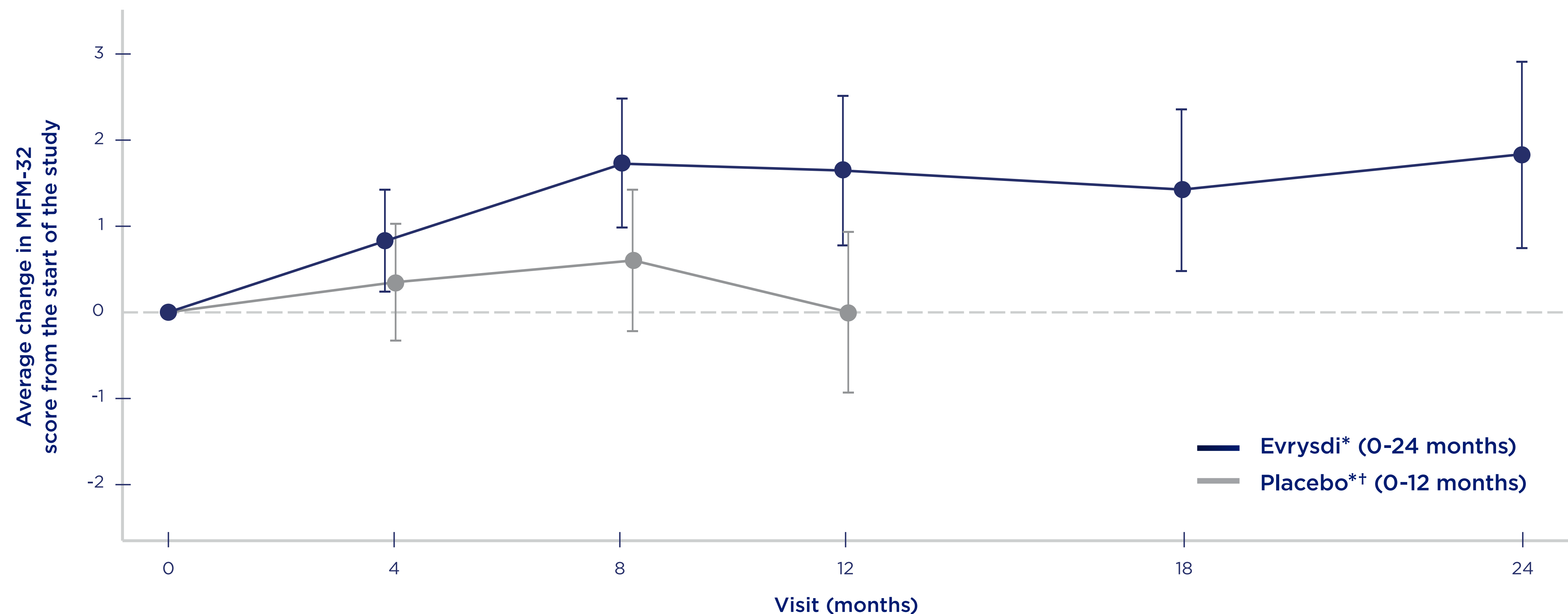
Support





# EXPLORATORY OBSERVATIONS SUGGEST Increase in motor function observed at 1 year was maintained at 2 years

Change in motor function score over 2 years  
As measured by MFM-32



Evrysdi (n)	115	113	113	112	107	103
Placebo (n)	59	57	58	58	NA	NA

**1.83-point average change** in MFM-32 score from the start of the study with Evrysdi

This information is considered **exploratory**, which means the clinical study was not specifically designed to demonstrate that Evrysdi caused these results. Data should be interpreted with caution.

\*Adults and children not taking Evrysdi took a placebo, a substance that has no active medication and is often used in studies. People in this group received placebo for 12 months followed by Evrysdi for 12 months. The period of time on Evrysdi is not included in this chart. The follow-up period was not placebo controlled.

MFM-32=Motor Function Measure-32 Items; NA=not applicable.

## Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are a woman who can become pregnant:
    - **Pregnancy Registry.** There is a pregnancy registry for women who take Evrysdi during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving Evrysdi, tell your healthcare provider right away. Talk to your healthcare provider about registering with the Evrysdi Pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling **1-833-760-1098** or visiting <https://www.evrysdipregnancyregistry.com>.

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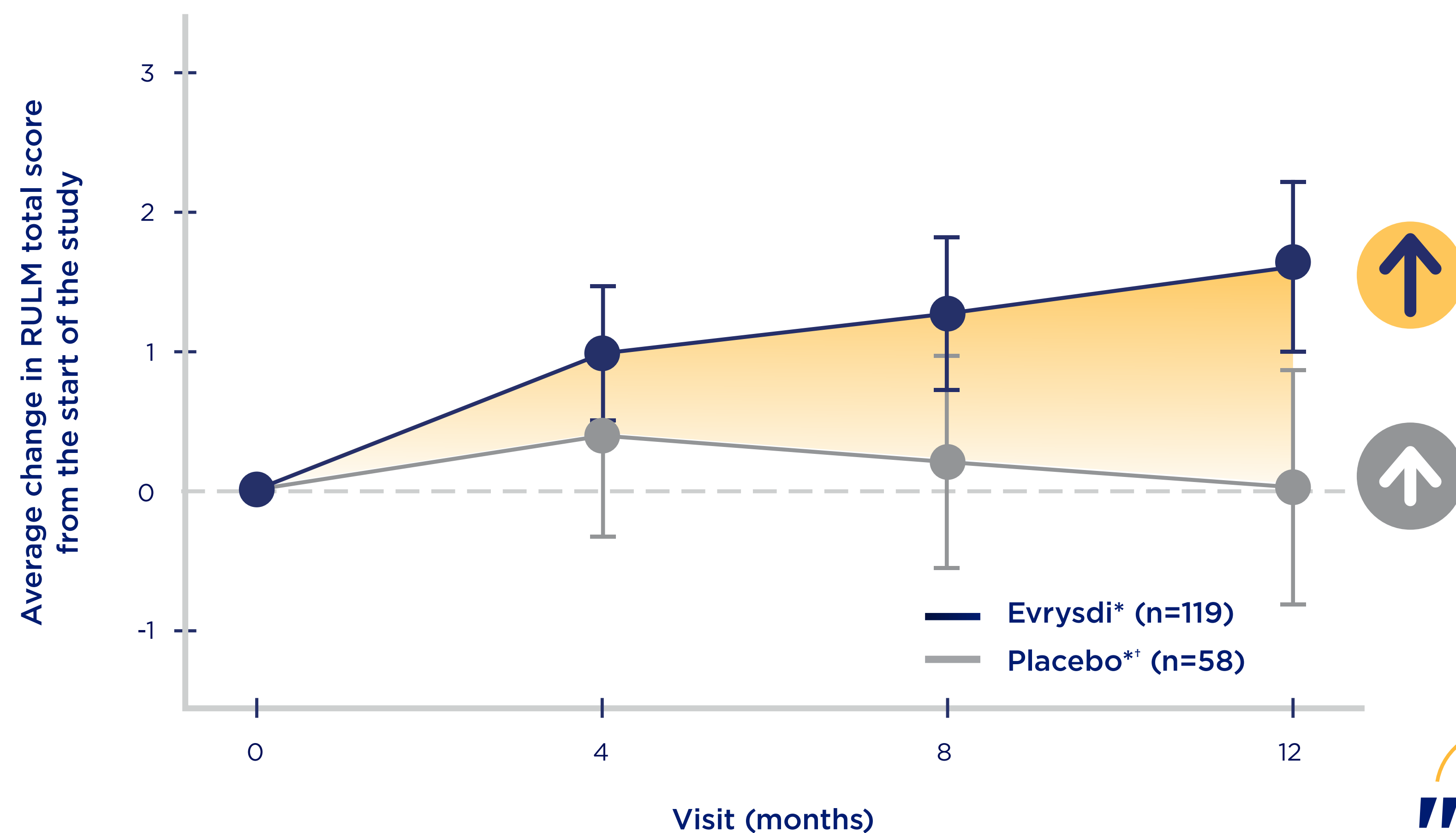


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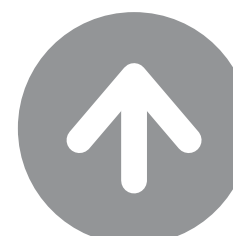


# Evrysdi enabled meaningful improvement of upper limb function

Change in upper limb score over 1 year vs placebo\*†  
As measured by RULM



**Average score increased 1.61 points with Evrysdi**  
**Average score increased 0.02 points with placebo**



1.59-point estimated improvement vs placebo  
(95% CI: 0.55, 2.62; P=0.0469)†



“ I’m really happy with my results on Evrysdi. Every time I go to the neurologist, I do a motor function test, and the last time I went, I actually went up a point! **I was able to tear a piece of paper, and it was the best sound I’d ever heard.** ”  
—Angela, living with Type 2 SMA

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†Adults and children not taking Evrysdi took a placebo, a substance that has no active medication and is often used in studies.

‡This 95% CI means that we are 95% confident that the actual average change in RULM with Evrysdi will be between 0.55 and 2.62 points higher than with placebo.

CI=confidence interval; RULM=Revised Upper Limb Module.

## Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are an adult male. Evrysdi may affect a man’s ability to have children (fertility). Ask a healthcare provider for advice before taking this medicine
  - are breastfeeding or plan to breastfeed. It is not known if Evrysdi passes into breast milk and may harm your baby

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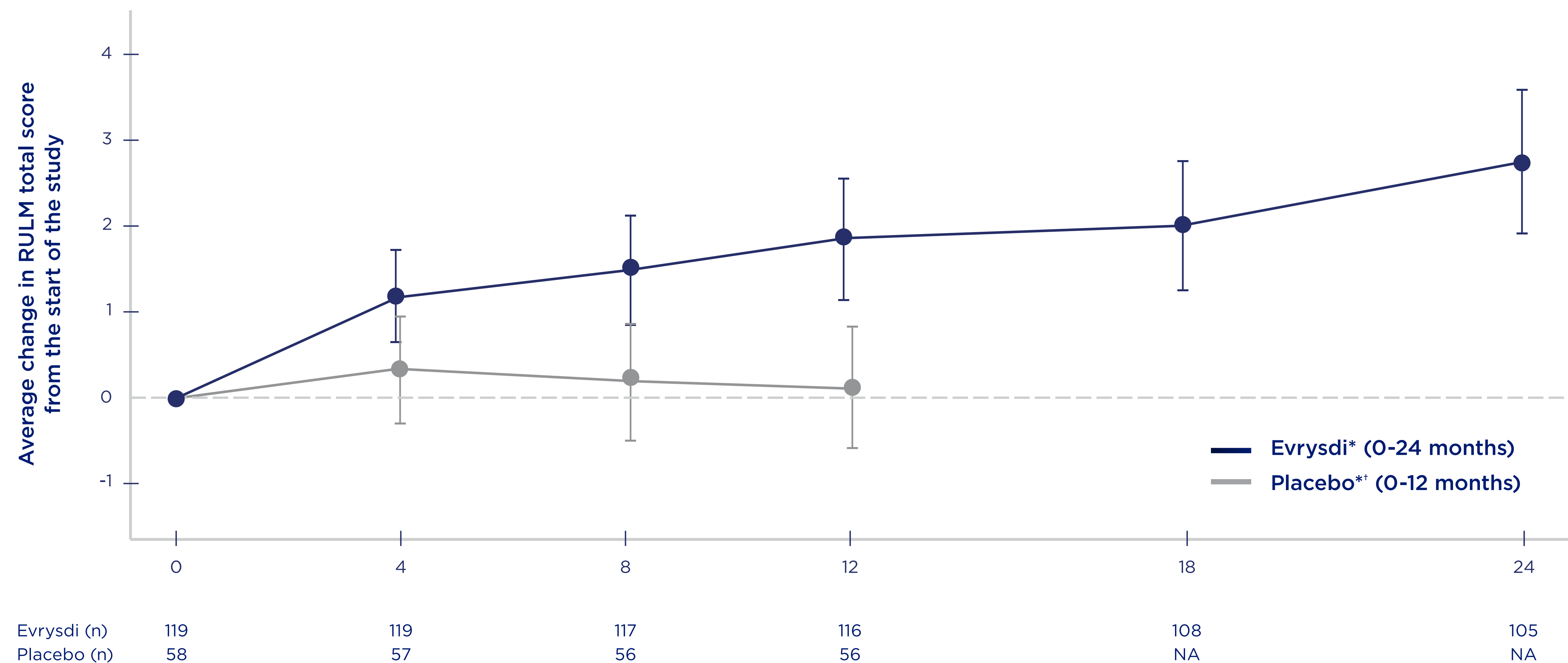


EVERYWHERE



# EXPLORATORY OBSERVATIONS SUGGEST Improvement in upper limb function observed at 1 year was maintained at 2 years

Change in upper limb score over 2 years  
As measured by RULM



**2.79-point average change** in RULM score from the start of the study with Evrysdi

This information is considered **exploratory**, which means the clinical study was not specifically designed to demonstrate that Evrysdi caused these results. Data should be interpreted with caution.

\*In some studies, including this one, if someone's data cannot be collected on time for any reason, that person's progress cannot be counted in that part of the study. This chart includes only the information that was collected on time.  
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 NA=not applicable; RULM=Revised Upper Limb Module.

### Important Safety Information (continued)

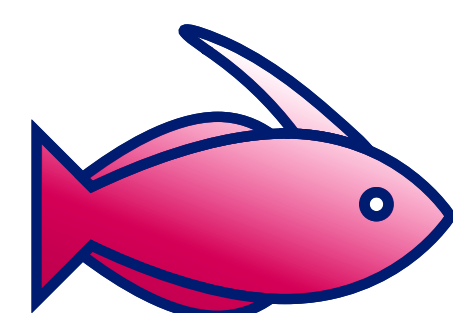
- Tell your healthcare provider about all the medicines you take
- If you were prescribed Evrysdi for Oral Solution, you should receive Evrysdi from the pharmacy as a liquid. If the medicine in the bottle is a powder, **do not use it**. Contact your pharmacist for a replacement
- Avoid getting Evrysdi on your skin or in your eyes. If Evrysdi gets on your skin, wash the area with soap and water. If Evrysdi gets in your eyes, rinse your eyes with water

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE





FIREFISH

## Redefining Possibilities

Study in infants with Type 1 SMA



Etta received a one-time disease-modifying treatment at 26 days old, prior to beginning Evrysdi at around 6 months.

Etta, living with Type 1 SMA

### Important Safety Information (continued)

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Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

Safety

Support





# A closer look at the FIREFISH study

A 2-part, open label study in infants with Type 1 SMA

## The study included

# 62

infants with Type 1 SMA



## The main measurement recorded after 1 year of taking Evrysdi:

- **Sitting without support for at least 5 seconds\***
- **Survival without permanent breathing support<sup>†</sup>**

# 58

 infants (aged 2 to 7 months)

who received the recommended dose of Evrysdi in Parts 1 and 2 were included in a pooled analysis that evaluated the effectiveness of Evrysdi

### PART 1

Explored the recommended dose of Evrysdi in 21 infants (aged 3 to 7 months)

### PART 2

Measured the safety and effectiveness of Evrysdi in 41 infants (aged 2 to 7 months) at the recommended dose

\*Measured by Item 22 of the Bayley Scales of Infant and Toddler Development-Third Edition (BSID-III) gross motor scale.

<sup>†</sup>Permanent support was defined as having a tracheostomy (a surgery where a tube is inserted in the front of the throat into the windpipe) or more than 21 days of either non-invasive ventilation support (16 or more hours a day) or being intubated (a procedure where a breathing tube is inserted down the throat and into the windpipe) to help with breathing, in the absence of an acute reversible event.

## Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are pregnant or plan to become pregnant, as Evrysdi may harm your unborn baby. Ask your healthcare provider for advice before taking this medicine
  - are a woman who can become pregnant:
    - Before you start your treatment with Evrysdi, your healthcare provider may test you for pregnancy

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE

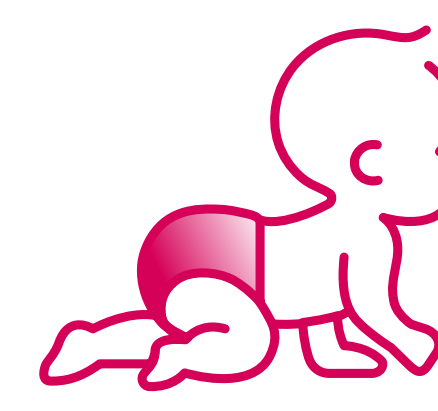


# Measuring important milestones

The effectiveness of Evrysdi in infantile-onset SMA was observed using 2 measurements

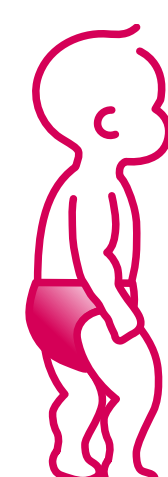
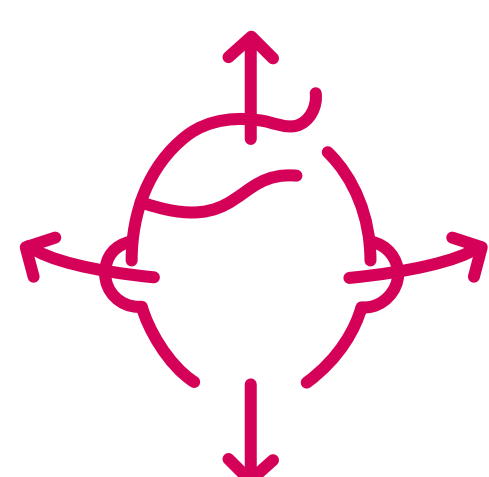
## Primary scale:

The **Bayley Scales of Infant and Toddler Development-Third Edition (BSID-III)** assesses a range of physical abilities, such as sitting, rolling, and crawling.



## Additional scale:

The **Hammersmith Infant Neurological Examination-Module 2 (HINE-2)** assesses 8 developmental milestones for infants, including head control, sitting, voluntary grasp, ability to kick, rolling, crawling, standing, and walking.



## Other measurements included:

- Ability to breathe without permanent support\*
- Ability to feed orally (exploratory)
- Ability to swallow (exploratory)

\*Permanent support was defined as having a tracheostomy (a surgery where a tube is inserted in the front of the throat into the windpipe) or more than 21 days of either non-invasive ventilation support (16 or more hours a day) or being intubated (a procedure where a breathing tube is inserted down the throat and into the windpipe) to help with breathing, in the absence of an acute reversible event.

## Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are a woman who can become pregnant:
    - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping Evrysdi

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
Type 2 or 3

Results:  
Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

Safety

Support





# Changing the course of SMA

Infants with Type 1 SMA exceeded expectations for development compared with infants who did not receive treatment



## FIREFISH PART 2 MAIN MEASUREMENT

AFTER 1 YEAR

**29%**

of infants (12/41)\*

## FIREFISH PARTS 1 AND 2 POOLED ANALYSIS

AFTER 1 YEAR

**33%**

of infants (19/58)\*

AFTER 2 YEARS

**60%**

of infants (35/58)\*

were able to sit without support **for at least 5 seconds**, as measured by BSID-III

Infants with Type 1 SMA are **typically not able to sit on their own without treatment**

Payton received a one-time disease-modifying treatment at 4 months old, prior to beginning Evrysdi at around 12 months.



Evrysdi has helped Payton hit certain milestones, including her ability to sit independently.

—Amber, mom to Payton, who is living with Type 1 SMA

\*Infants taking the recommended dose of Evrysdi.

### Important Safety Information (continued)

• Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:

◦ are a woman who can become pregnant:

– **Pregnancy Registry.** There is a pregnancy registry for women who take Evrysdi during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving Evrysdi, tell your healthcare provider right away. Talk to your healthcare provider about registering with the Evrysdi Pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling **1-833-760-1098** or visiting

<https://www.evrysdipregnancyregistry.com>.

Please see additional **Important Safety Information** throughout and full **Prescribing Information**.

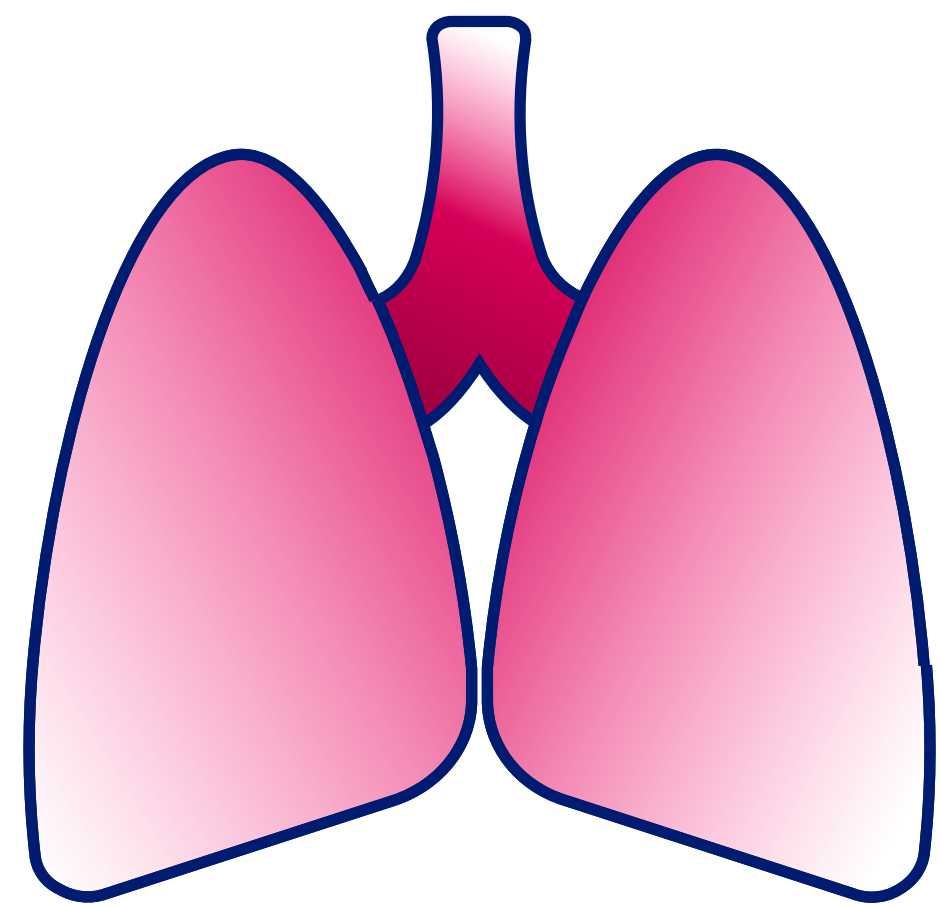


EVERYWHERE



# Slowing the progression of SMA

## EVRYSDI PROLONGED SURVIVAL



AFTER 1 YEAR

**87%**

of infants (54/62)\*

AFTER 2 YEARS

**84%**

of infants (52/62)\*

were alive and **able to breathe without permanent support**<sup>†</sup>

Without treatment, **no more than 25%** of infants with Type 1 SMA **are expected to survive beyond 14 months without permanent breathing support**

“ **Evrysdi helps get Etta closer to whatever milestones she can achieve in her life.**

**—Natalie, mom to Etta,**  
who is living with Type 1 SMA



\*Infants taking Evrysdi (all dose strengths).

<sup>†</sup>Permanent support was defined as having a tracheostomy (a surgery where a tube is inserted in the front of the throat into the windpipe) or more than 21 days of either non-invasive ventilation support (16 or more hours a day) or being intubated (a procedure where a breathing tube is inserted down the throat and into the windpipe) to help with breathing, in the absence of an acute reversible event.

### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are an adult male. Evrysdi may affect a man’s ability to have children (fertility). Ask a healthcare provider for advice before taking this medicine
  - are breastfeeding or plan to breastfeed. It is not known if Evrysdi passes into breast milk and may harm your baby



EVERYWHERE

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



Overview

Results:  
Type 2 or 3

Results:  
Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

Safety

Support





EXPLORATORY OBSERVATIONS SUGGEST

# Infants taking Evrysdi were able to breathe without permanent support and sit, and some were able to stand



AFTER 5 YEARS

**62%**

of infants (36/58)<sup>\*†</sup>  
were able to sit  
without support for  
at least 5 seconds

As measured by BSID-III

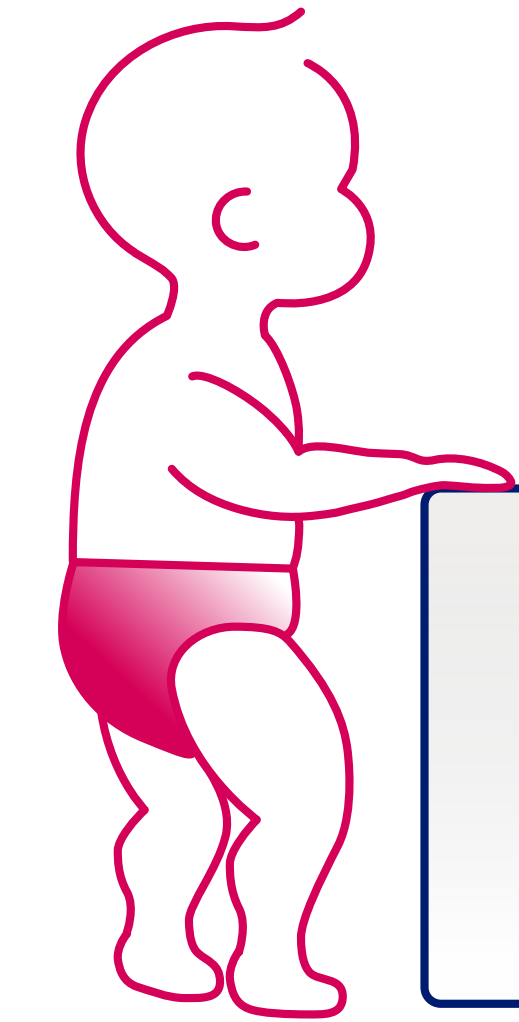


AFTER 5 YEARS

**59%**

of infants (34/58)<sup>\*†</sup>  
were able to sit  
without support for  
at least 30 seconds

As measured by BSID-III



AFTER 5 YEARS

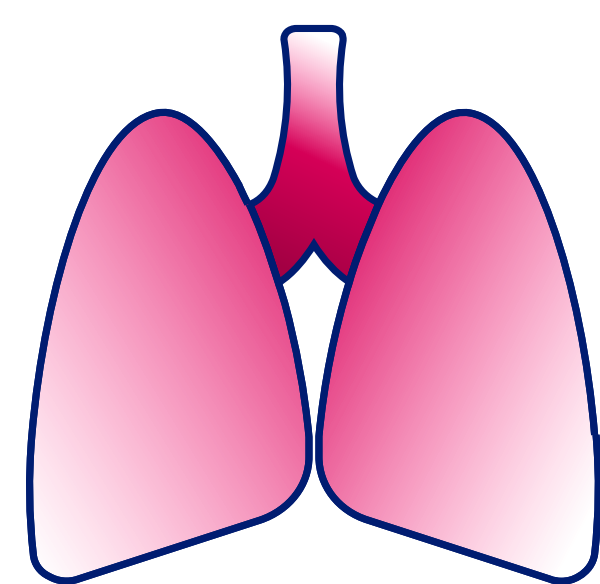
**21%**

of infants (12/58)<sup>\*†</sup>  
were able to stand

- 5/58 could stand supporting weight
- 3/58 could stand with support
- 4/58 could stand unaided

As measured by HINE-2

**EVRYSDI PROLONGED SURVIVAL** Recommended-dose cohort (n=58)<sup>\*</sup>



AFTER 5 YEARS

**81%**

of infants

were alive and able to breathe without permanent support<sup>‡§</sup>

This information is considered **exploratory**, which means the clinical study was not specifically designed to demonstrate that Evrysdi caused these results. Data should be interpreted with caution.



Etta, living with Type 1 SMA

<sup>\*</sup>Infants taking the recommended dose of Evrysdi.

<sup>†</sup>The analyses at Year 1 and Year 5 include the pooled population with children from Part 1 (high-dose cohort, n=17) and all children from Part 2 (n=41). Results at Year 1 (data cutoff: November 14, 2019) are based on the assessment of 2 independent central readers, and those at Year 5 (data cutoff: December 22, 2023) are based on the assessment of the site clinical evaluator. Any children not assessed were included as non-responders (BSID-III, n=11; HINE-2, n=10).

<sup>‡</sup>Percentage based on statistical analysis.

<sup>§</sup>Permanent support was defined as having a tracheostomy (a surgery where a tube is inserted in front of the throat into the windpipe) or more than 21 days of either non-invasive ventilation support (16 or more hours a day) or being intubated (a procedure where a breathing tube is inserted down the throat and into the windpipe) to help with breathing, in the absence of an acute reversible event. BSID-III=Bayley Scales of Infant and Toddler Development-Third Edition; HINE-2=Hammersmith Infant Neurological Examination-Module 2.

**Important Safety Information (continued)**

- **Tell your healthcare provider about all the medicines you take**
- If you were prescribed Evrysdi for Oral Solution, you should receive Evrysdi from the pharmacy as a liquid. If the medicine in the bottle is a powder, **do not use it**. Contact your pharmacist for a replacement
- Avoid getting Evrysdi on your skin or in your eyes. If Evrysdi gets on your skin, wash the area with soap and water. If Evrysdi gets in your eyes, rinse your eyes with water

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
Type 2 or 3

Results:  
Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

Safety

Support





# EXPLORATORY OBSERVATIONS SUGGEST Infants taking Evrysdi had better feeding and swallowing abilities compared with infants without treatment\*

OF THE INFANTS TAKING THE RECOMMENDED DOSE, **AFTER 5 YEARS:**

**91%**

of infants (42/46)

**were able to feed orally<sup>†</sup>**

**96%**

of infants (46/48)

**were able to swallow<sup>†</sup>**

**Payton**, living with Type 1 SMA



Without treatment, **87% of infants** with Type 1 SMA **typically require feeding support** via a feeding tube by 18 months old

This information is considered **exploratory**, which means the clinical study was not specifically designed to show a treatment effect on feeding and swallowing. Data should be interpreted with caution.

\*Includes infants who could eat by mouth or in combination with a feeding tube.  
†These calculations are based on the number of patients assessed for feeding or swallowing at 5 years.

### Important Safety Information (continued)

• **The most common side effects of Evrysdi include:**

- For later-onset SMA: fever, diarrhea, rash
- For infantile-onset SMA: fever; diarrhea; rash; runny nose, sneezing and sore throat (upper respiratory infection); lung infection (lower respiratory infection); constipation; vomiting; cough

These are not all of the possible side effects of Evrysdi. For more information on the risk and benefits profile of Evrysdi, ask your healthcare provider or pharmacist.

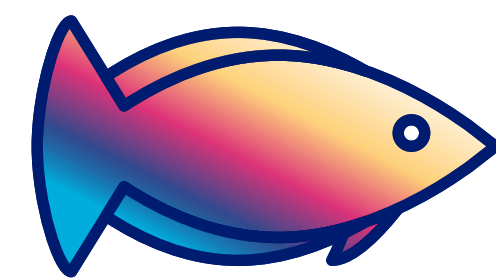
Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Ava at 8 months old, 2023  
living with presymptomatic SMA



RAINBOWFISH

## Milestones that matter

Study in newborns with  
presymptomatic SMA



### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are pregnant or plan to become pregnant, as Evrysdi may harm your unborn baby. Ask your healthcare provider for advice before taking this medicine
  - are a woman who can become pregnant:
    - Before you start your treatment with Evrysdi, your healthcare provider may test you for pregnancy

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
Type 2 or 3

Results:  
Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

Safety

Support





## A closer look at the RAINBOWFISH study

An open-label study in newborns with presymptomatic SMA or infants who have been diagnosed but not yet shown symptoms

Infants were evaluated according to the number of *SMN2* copies that they had. Having fewer *SMN2* copies generally indicates more severe SMA\*



**Main measurement**  
after 1 year of taking Evrysdi:  
**Sitting without support for at least 5 seconds<sup>†</sup>**

### The study included

**8** infants with 2 *SMN2* copies

**26** infants (study total)  
younger than 6 weeks at first dose

- **The study total included infants with 2 or more *SMN2* copies**
- **As a result, the total population represents a wider range of SMA severity**

\**SMN2* is a gene that provides instructions for making SMN protein.

<sup>†</sup>Measured by Item 22 of the Bayley Scales of Infant and Toddler Development-Third Edition (BSID-III).

*SMN2*=survival motor neuron 2.

### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are a woman who can become pregnant:
    - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping Evrysdi

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
Type 2 or 3

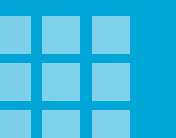
Results:  
Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

Safety

Support



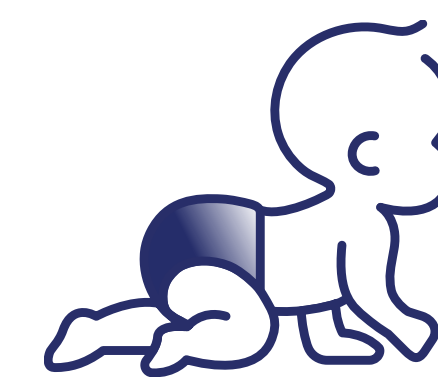
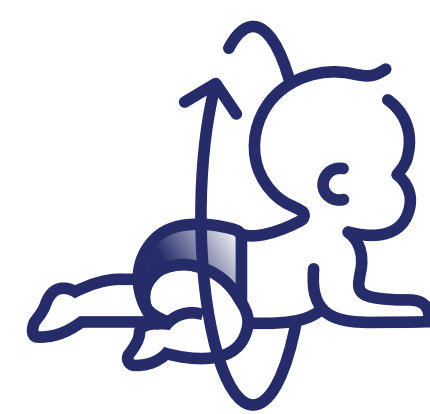


## Measuring important milestones

The effectiveness of Evrysdi in presymptomatic SMA was observed using 2 measurements

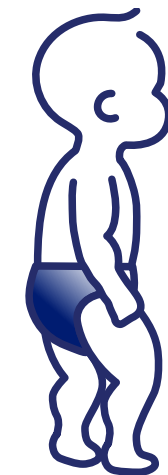
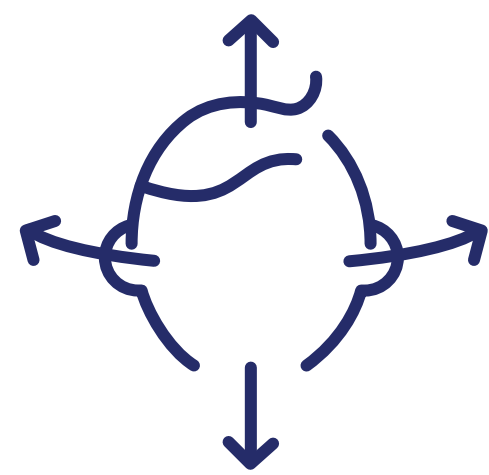
### Primary scale:

The **Bayley Scales of Infant and Toddler Development-Third Edition (BSID-III)** assesses a range of physical abilities, such as sitting, rolling, and crawling.



### Additional scale:

The **Hammersmith Infant Neurological Examination-Module 2 (HINE-2)** assesses 8 developmental milestones for infants, including head control, sitting, voluntary grasp, ability to kick, rolling, crawling, standing, and walking.



### Other measurements included:

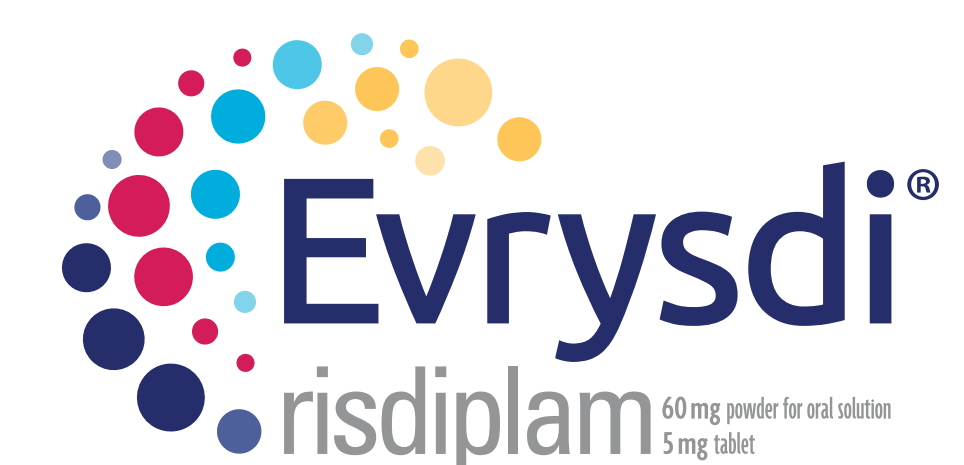
- Ability to breathe without permanent support\*
- Ability to feed orally (exploratory)
- Ability to swallow (exploratory)

\*Permanent support was defined as having a tracheostomy (a surgery where a tube is inserted in the front of the throat into the windpipe) or more than 21 days of either non-invasive ventilation support (16 or more hours a day) or being intubated (a procedure where a breathing tube is inserted down the throat and into the windpipe) to help with breathing, in the absence of an acute reversible event.

### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are a woman who can become pregnant:
    - **Pregnancy Registry.** There is a pregnancy registry for women who take Evrysdi during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving Evrysdi, tell your healthcare provider right away. Talk to your healthcare provider about registering with the Evrysdi Pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling **1-833-760-1098** or visiting <https://www.evrysdipregnancyregistry.com>.

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
Type 2 or 3

Results:  
Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

Safety

Support





# Evrysdi helped infants with a wide range of SMA severity sit without support

## AFTER 1 YEAR OF TREATMENT

### INFANTS WITH 2 SMN2 COPIES (n=8)



# 88%

of infants (7/8)

**were able to sit without support for at least 5 seconds**

### TOTAL INFANTS IN STUDY (N=26)



# 96%

of infants (25/26)

**were able to sit without support for at least 5 seconds**

- 81% of infants (21/26) were able to sit without support for at least 30 seconds

As measured by BSID-III

Ava at 12 months old, 2023  
living with presymptomatic SMA



BSID-III=Bayley Scales of Infant and Toddler Development-Third Edition; SMN2=survival motor neuron 2.

### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are an adult male. Evrysdi may affect a man's ability to have children (fertility). Ask a healthcare provider for advice before taking this medicine
  - are breastfeeding or plan to breastfeed. It is not known if Evrysdi passes into breast milk and may harm your baby

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
Type 2 or 3

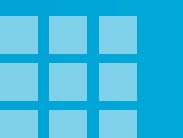
Results:  
Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

Safety

Support





# EXPLORATORY OBSERVATIONS SUGGEST Evrysdi helped infants continue to achieve key milestones at 2 years of treatment

## AFTER 2 YEARS OF TREATMENT

INFANTS WITH 2 *SMN2* COPIES (n=5)\*



**100%**

of infants (5/5)\*  
were able to sit without support for at least 5 seconds

TOTAL INFANTS IN STUDY (N=23)\*



**100%**

of infants (23/23)  
were able to sit without support for at least 5 seconds

- 91% of infants (21/23)\*\* were able to sit without support for at least 30 seconds

### As measured by BSID-III

These results reflect the impact of Evrysdi alongside an infant's natural development.

This information is considered **exploratory**, which means the clinical study was not specifically designed to measure treatment effect at 2 years. Data should be interpreted with caution.

\*Excludes 3 infants who withdrew before the Year 2 assessment to receive a one-time disease-modifying treatment.

\*\*For infants with 3 *SMN2* copies, the clinical site evaluator results differed from the 2 independent central readers. The site clinical evaluator results were 13/13 infants were able to sit without support for ≥30 seconds, while the 2 independent central readers results were 12/13 infants. For infants with ≥4 *SMN2* copies, the clinical site evaluator results differed from the 2 independent central readers. The site clinical evaluator results were 5/5 infants were able to sit without support for ≥30 seconds, while the 2 independent central readers results were 4/5 infants. The 2 independent reader results are reported here.

BSID-III=Bayley Scales of Infant and Toddler Development-Third Edition; *SMN2*=survival motor neuron 2.

### Important Safety Information (continued)

- Tell your healthcare provider about all the medicines you take
- If you were prescribed Evrysdi for Oral Solution, you should receive Evrysdi from the pharmacy as a liquid. If the medicine in the bottle is a powder, **do not use it**. Contact your pharmacist for a replacement
- Avoid getting Evrysdi on your skin or in your eyes. If Evrysdi gets on your skin, wash the area with soap and water. If Evrysdi gets in your eyes, rinse your eyes with water

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



# Evrysdi helped infants sit, stand, or walk independently

**AFTER 1 YEAR OF TREATMENT**  
TOTAL INFANTS IN STUDY (N=26)\*



**96%**  
of infants (24/25)  
**were able to sit**



**84%**  
of infants (21/25)  
**were able to stand**

- 13/25 could stand unaided
- 8/25 could stand with support



**48%**  
of infants (12/25)  
**were able to walk independently**

**As measured by HINE-2**

\*One infant could not be assessed for HINE-2 at the 1-year visit.  
HINE-2=Hammersmith Infant Neurological Examination-Module 2.

**Important Safety Information (continued)**

- **The most common side effects of Evrysdi include:**
  - For later-onset SMA: fever, diarrhea, rash
  - For infantile-onset SMA: fever; diarrhea; rash; runny nose, sneezing and sore throat (upper respiratory infection); lung infection (lower respiratory infection); constipation; vomiting; cough

These are not all of the possible side effects of Evrysdi. For more information on the risk and benefits profile of Evrysdi, ask your healthcare provider or pharmacist.

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
Type 2 or 3

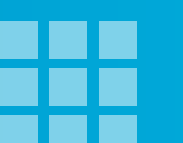
Results:  
Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

Safety

Support





## EXPLORATORY OBSERVATIONS SUGGEST

**Two years of treatment with Evrysdi helped infants achieve motor milestones****AFTER 2 YEARS OF TREATMENT**

TOTAL INFANTS IN STUDY (N=23)\*

**100%**of infants (23/23)  
**were able to sit****96%**of infants (22/23)  
**were able to stand****87%**of infants (20/23)<sup>†</sup>  
**were able to walk independently**

- 21/23 could stand unaided
- 1/23 could stand with support

**As measured by HINE-2**

These results reflect the impact of Evrysdi alongside an infant's natural development.

This information is considered **exploratory**, which means the clinical study was not specifically designed to show a treatment effect on HINE-2 assessments. Data should be interpreted with caution.

\*Excludes 3 infants who withdrew before the Year 2 assessment to receive a one-time disease modifying treatment.

<sup>†</sup>One child could not be assessed at Year 2.

HINE-2=Hammersmith Infant Neurological Examination, Module 2.

**Important Safety Information (continued)**

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are pregnant or plan to become pregnant, as Evrysdi may harm your unborn baby. Ask your healthcare provider for advice before taking this medicine
  - are a woman who can become pregnant:
    - Before you start your treatment with Evrysdi, your healthcare provider may test you for pregnancy

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
Type 2 or 3Results:  
Type 1Results:  
PresymptomaticLiquid and  
Tablet

Safety

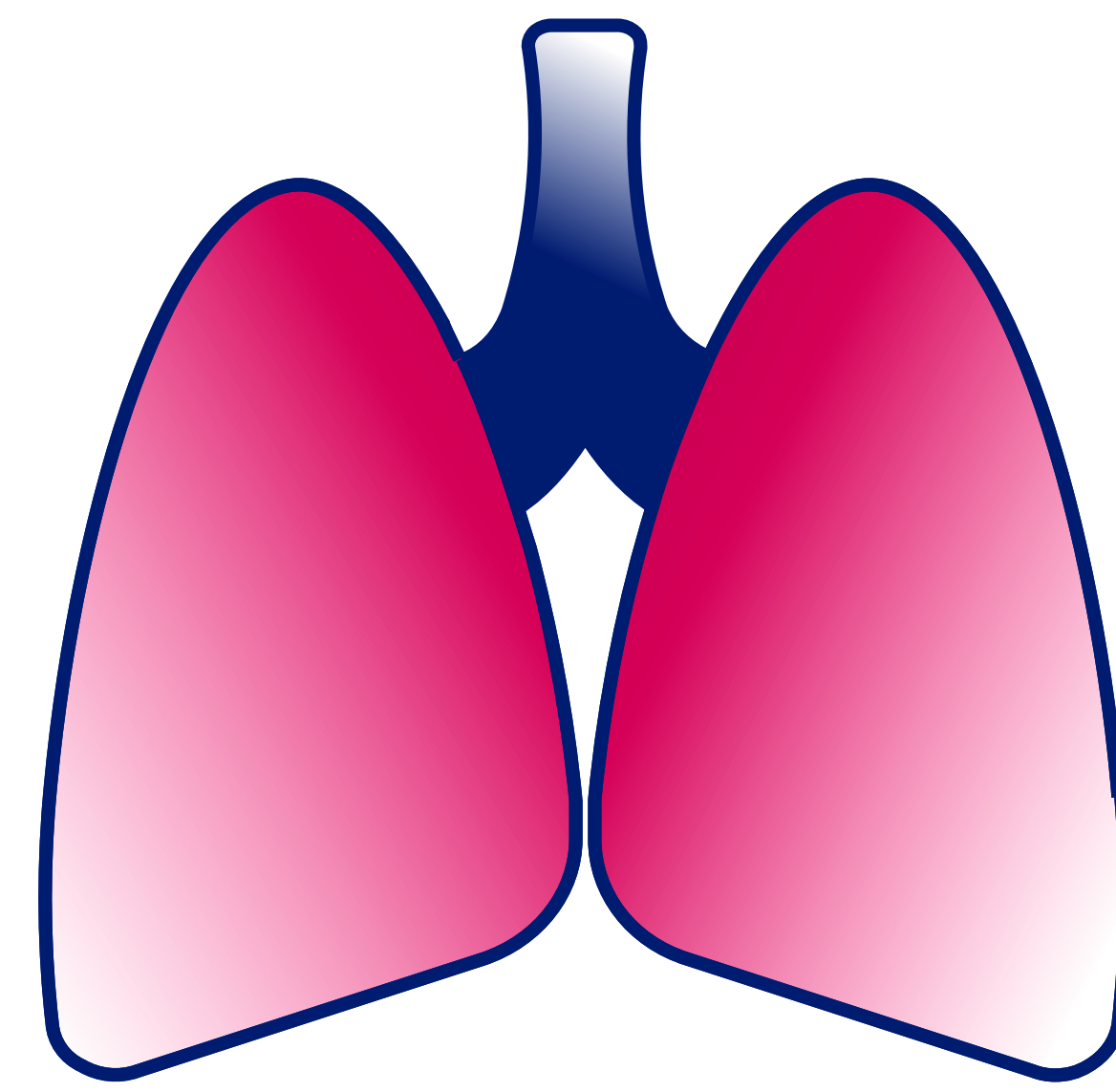
Support





## Evrysdi helped infants survive

**AFTER 1 YEAR OF TREATMENT**  
TOTAL INFANTS IN STUDY (N=26)



**100%**  
of infants (26/26)  
were alive without  
permanent support\*

Exploratory assessments suggest that after **2 years** of treatment (N=23),<sup>†</sup>  
**100% of infants (23/23) were alive without permanent support**

This information is considered **exploratory**, which means the clinical study was not specifically designed to show a treatment effect on survival without permanent support. Data should be interpreted with caution.

\*Permanent support was defined as having a tracheostomy (a surgery where a tube is inserted in the front of the throat into the windpipe) for more than 21 days of either non-invasive ventilation support (16 or more hours a day) or being intubated (a procedure where a breathing tube is inserted down the throat and into the windpipe) to help with breathing, in the absence of an acute reversible event.

<sup>†</sup>Excludes 3 infants who withdrew before the Year 2 assessment to receive a one-time disease-modifying treatment.

### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are a woman who can become pregnant:
    - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping Evrysdi

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
Type 2 or 3

Results:  
Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

Safety

Support





EXPLORATORY OBSERVATIONS SUGGEST

# Presymptomatic infants taking Evrysdi were able to feed orally and swallow

**AFTER 2 YEARS OF TREATMENT**

TOTAL INFANTS IN STUDY (N=23)\*

# 100%

of infants (23/23)

**were able to  
exclusively feed orally**

# 100%

of infants (23/23)

**were able to swallow**

This information is considered **exploratory**, which means the clinical study was not specifically designed to show a treatment effect on feeding and swallowing. Data should be interpreted with caution.

\*Excludes 3 infants who withdrew before the Year 2 assessment to receive a one-time disease-modifying treatment. The 3 infants were able to swallow and feed orally at their last assessments.

### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**

- are a woman who can become pregnant:

- **Pregnancy Registry.** There is a pregnancy registry for women who take Evrysdi during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving Evrysdi, tell your healthcare provider right away. Talk to your healthcare provider about registering with the Evrysdi Pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling **1-833-760-1098** or visiting

<https://www.evrysdipregnancyregistry.com>.

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
Type 2 or 3

Results:  
Type 1

Results:  
Presymptomatic

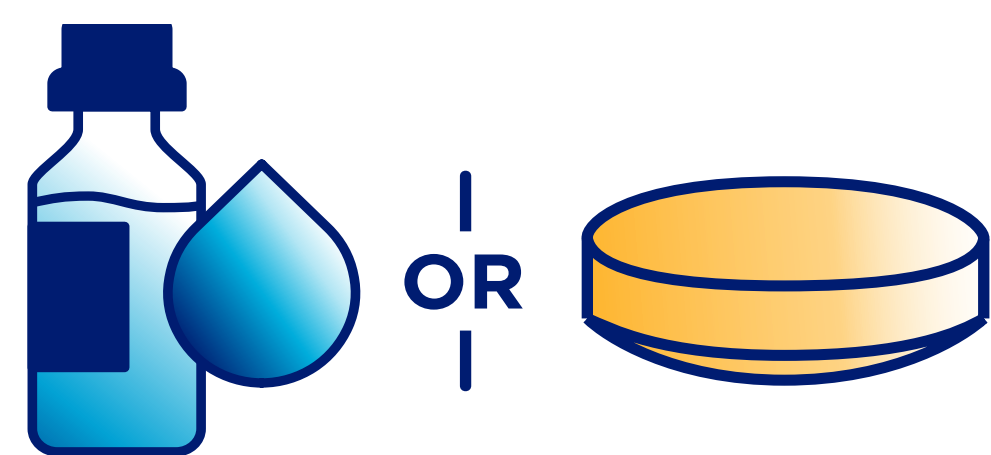
Liquid and  
Tablet

Safety

Support







## More choices

Evrysdi tablets have the same demonstrated results and safety as the liquid form

“ Since I’m on the go a lot, I’m able to take Evrysdi with me.\*  
—Jose, living with Type 3 SMA ”



\*If refrigeration is not available, Evrysdi liquid can be kept at room temperature up to 104°F (40°C) for a combined total of 5 days. Store Evrysdi tablets at room temperature, between 68°F to 77°F (20°C to 25°C). Excursions permitted between 59°F to 86°F (15°C to 30°C). Keep the bottle tightly closed in order to protect from moisture. Please refer to the Dosage and Administration section of the Prescribing Information for additional information about storage and administration.

### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are an adult male. Evrysdi may affect a man’s ability to have children (fertility). Ask a healthcare provider for advice before taking this medicine
  - are breastfeeding or plan to breastfeed. It is not known if Evrysdi passes into breast milk and may harm your baby



EVERYWHERE

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



Overview

Results:  
Type 2 or 3

Results:  
Type 1

Results:  
Presymptomatic

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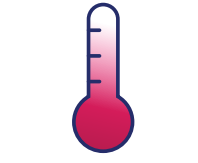

Support





## Two non-invasive treatment options to choose from

Your experience with SMA might be different from others—that's why having options in how you take Evrysdi is important

	 Liquid	 <b>NOW APPROVED:</b> Tablet
 <b>Eligibility</b>	For <b>any age or weight</b>	Must be <b>≥2 years of age and weigh ≥20 kg (44 lb)</b>
 <b>Use with feeding tube</b>	<b>Yes</b>	<b>No</b>
 <b>Administration</b>	Taken via <b>oral syringe</b>	May be <b>swallowed whole with water</b> or <b>mixed with non-chlorinated drinking water (eg, filtered water, bottled water)</b>
 <b>Days' supply</b>	Dependent on dosage	<b>30 days</b> per bottle
 <b>Storage</b>	<b>Refrigerate</b> 36°F to 46°F (2°C to 8°C)	<b>Room temperature</b> , 68°F to 77°F (20°C to 25°C)
 <b>Obtaining Evrysdi</b>	Shipped <b>directly to your door</b> from a specialty pharmacy	



Looking for more information on the Evrysdi treatment options?  
**Speak to your doctor** to find out if this oral treatment is right for you

### Important Safety Information (continued)

- **Tell your healthcare provider about all the medicines you take**
- If you were prescribed Evrysdi for Oral Solution, you should receive Evrysdi from the pharmacy as a liquid. If the medicine in the bottle is a powder, **do not use it**. Contact your pharmacist for a replacement
- Avoid getting Evrysdi on your skin or in your eyes. If Evrysdi gets on your skin, wash the area with soap and water. If Evrysdi gets in your eyes, rinse your eyes with water

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



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## Designed to fit your lifestyle

“ I am passionate about my independence. I am able to work a full time job, drive a modified vehicle, volunteer on the weekends, and attend concerts. **Evrysdi helps me maintain the motor function needed to do these things.**

—Ira, living with Type 2 SMA “



“ I think choice is always important in any situation, but most certainly when it comes to your body. **Evrysdi for me is taking action.**

—Angela, living with Type 2 SMA “



### Important Safety Information (continued)

#### • The most common side effects of Evrysdi include:

- For later-onset SMA: fever, diarrhea, rash
- For infantile-onset SMA: fever; diarrhea; rash; runny nose, sneezing and sore throat (upper respiratory infection); lung infection (lower respiratory infection); constipation; vomiting; cough

These are not all of the possible side effects of Evrysdi. For more information on the risk and benefits profile of Evrysdi, ask your healthcare provider or pharmacist.

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



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# The Evrysdi community is *everywhere* **16,000+** people globally, including people up to 75 years of age<sup>\*†</sup>



EVERYWHERE

\*Based on individuals with SMA receiving Evrysdi worldwide as of August 2024.

†Clinical trials of Evrysdi did not include people aged 65 and older to determine whether they respond differently from those who are younger.



Markers represent countries where Evrysdi is approved

As of November 2024.

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



Overview

Results:  
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## What the community is saying

// **The reason I switched to Evrysdi was that I wanted a medication that fit my lifestyle.** I like how Evrysdi is non-invasive and I don't have to worry about going to a hospital or doctor's office to take my dose.

—Janelle, living with Type 2 SMA //

// **Since starting Evrysdi, I have noticed changes in my motor function.** This has made such a difference in my daily life.

—Shaniqua, living with Type 3 SMA //

// **Etta is able to eat foods that she was having a hard time swallowing** before starting treatment.

—Natalie, mom to Etta, who is living with Type 1 SMA //



Individual results may vary.

### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are pregnant or plan to become pregnant, as Evrysdi may harm your unborn baby. Ask your healthcare provider for advice before taking this medicine
  - are a woman who can become pregnant:
    - Before you start your treatment with Evrysdi, your healthcare provider may test you for pregnancy

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
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Type 1

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# Extensively studied, with a consistent safety profile across all approved doses

## The most common side effects include:

### IN INFANTS with Type 1 SMA (infantile-onset)

- fever
- diarrhea
- rash
- runny nose, sneezing and sore throat (upper respiratory infection)
- lung infection (lower respiratory infection)
- constipation
- vomiting
- cough

### IN ADULTS AND CHILDREN with Type 2 or 3 SMA (later-onset)

- fever
- diarrhea
- rash

The safety profile for presymptomatic infants is consistent with the safety profile for symptomatic SMA patients treated with Evrysdi in clinical studies

No one in the clinical studies permanently stopped taking Evrysdi because of side effects of treatment.\*  
These are not all of the possible side effects of Evrysdi.

**For more information on the risk and benefit profile of Evrysdi, ask your healthcare provider or pharmacist.**

Ongoing studies are exploring the safety of Evrysdi in individuals who previously received a different SMA treatment.

You may report side effects to the FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

You may also report side effects to Genentech at 1-888-835-2555.

\*As of March 27, 2024

FDA=Food and Drug Administration.

### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are a woman who can become pregnant:
    - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping Evrysdi

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
Type 2 or 3

Results:  
Type 1

Results:  
Presymptomatic

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Support





# Important Safety Information

## What is Evrysdi?

Evrysdi is a prescription medicine used to treat spinal muscular atrophy (SMA) in children and adults.

## Important Safety Information



- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**

- are pregnant or plan to become pregnant, as Evrysdi may harm your unborn baby. Ask your healthcare provider for advice before taking this medicine
- are a woman who can become pregnant:
  - Before you start your treatment with Evrysdi, your healthcare provider may test you for pregnancy
  - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping Evrysdi
  - **Pregnancy Registry.** There is a pregnancy registry for women who take Evrysdi during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving Evrysdi, tell your healthcare provider right away. Talk to your healthcare provider about registering with the Evrysdi Pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling [1-833-760-1098](tel:1-833-760-1098) or visiting <https://www.evrysdipregnancyregistry.com>.



- are an adult male. Evrysdi may affect a man's ability to have children (fertility). Ask a healthcare provider for advice before taking this medicine



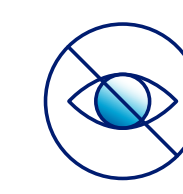
- are breastfeeding or plan to breastfeed. It is not known if Evrysdi passes into breast milk and may harm your baby



- **Tell your healthcare provider about all the medicines you take**



- If you were prescribed Evrysdi for Oral Solution, you should receive Evrysdi from the pharmacy as a liquid. If the medicine in the bottle is a powder, **do not use it**. Contact your pharmacist for a replacement



- Avoid getting Evrysdi on your skin or in your eyes. If Evrysdi gets on your skin, wash the area with soap and water. If Evrysdi gets in your eyes, rinse your eyes with water



- **The most common side effects of Evrysdi include:**

- For later-onset SMA: fever, diarrhea, rash
- For infantile-onset SMA: fever; diarrhea; rash; runny nose, sneezing and sore throat (upper respiratory infection); lung infection (lower respiratory infection); constipation; vomiting; cough

These are not all of the possible side effects of Evrysdi. For more information on the risk and benefits profile of Evrysdi, ask your healthcare provider or pharmacist.

You may report side effects to the FDA at [1-800-FDA-1088](tel:1-800-FDA-1088) or [www.fda.gov/medwatch](http://www.fda.gov/medwatch). You may also report side effects to Genentech at [1-888-835-2555](tel:1-888-835-2555).



EVERYWHERE

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



Overview

Results:  
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# The MySMA Support™ team is here for you

MySMA Support\* is a support service from Genentech that's here to help.



**We can answer your questions about Evrysdi**, help you navigate insurance coverage, explain potential financial assistance options, and help coordinate the preparation and delivery of your Evrysdi, even when traveling.



**When you reach out, you will be connected to a Partnership and Access Liaison (PAL)**—your local Genentech representative who supports people living with SMA and their caregivers. A PAL can provide in-person or virtual support based on your preference and connect you to helpful resources.

**The MySMA Support team, including the PAL, does not provide medical advice and is not a substitute for your medical team.**

Your healthcare provider should always be your main resource for any questions about your health and medical care.



Sign up to stay connected

\*Enrollment in MySMA Support through the Evrysdi Start Form is mandatory to receive assistance through the program. Participation in MySMA Support is not necessary to receive treatment with Evrysdi.

## Important Safety Information (continued)

• **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**

◦ are a woman who can become pregnant:

- **Pregnancy Registry.** There is a pregnancy registry for women who take Evrysdi during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving Evrysdi, tell your healthcare provider right away. Talk to your healthcare provider about registering with the Evrysdi Pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling **1-833-760-1098** or visiting <https://www.evrysdipregnancyregistry.com>.

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



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# We call them PALs because they're here to help

Local support for your journey with SMA is on standby



Shaniqua, living with Type 3 SMA

**Talk to a PAL in person, over the phone, or online.**

Connect with a local PAL by visiting **Evrysdi.com/PAL** or calling **(833) 387-9734**

(Monday-Friday, 9 am to 8 pm ET)

If refrigeration is not available, Evrysdi liquid can be kept at room temperature up to 104°F for a combined total of 5 days. Please refer to the Instructions for Use for additional information about storage and administration.

## Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are an adult male. Evrysdi may affect a man's ability to have children (fertility). Ask a healthcare provider for advice before taking this medicine
  - are breastfeeding or plan to breastfeed. It is not known if Evrysdi passes into breast milk and may harm your baby

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



EVERYWHERE



Overview

Results:  
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Results:  
Type 1

Results:  
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CONSIDER EVRYSDI:

# Designed to go everywhere\*

so you have the flexibility  
to do the same†

\*When studied in animals, Evrysdi was distributed throughout the body.



Two **oral, non-invasive** forms:  
liquid and tablet

- ✓ **No needles, sedation, or hospital stays**
- ✓ Small molecule designed to **reach the brain and spinal cord\***
- ✓ **Works daily** for a consistent impact on SMN protein levels in the blood

**Talk to your doctor to see if Evrysdi is right for you and your lifestyle**

†If refrigeration is not available, Evrysdi liquid can be kept at room temperature up to 104°F (40°C) for a combined total of 5 days. Store Evrysdi tablets at room temperature, between 68°F to 77°F (20°C to 25°C). Excursions permitted between 59°F to 86°F (15°C to 30°C). Keep the bottle tightly closed in order to protect from moisture. Please refer to the Dosage and Administration section of the Prescribing Information for additional information about storage and administration. SMN=survival motor neuron.

## Important Safety Information (continued)

- **Tell your healthcare provider about all the medicines you take**
- If you were prescribed Evrysdi for Oral Solution, you should receive Evrysdi from the pharmacy as a liquid. If the medicine in the bottle is a powder, **do not use it**. Contact your pharmacist for a replacement
- Avoid getting Evrysdi on your skin or in your eyes. If Evrysdi gets on your skin, wash the area with soap and water. If Evrysdi gets in your eyes, rinse your eyes with water

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).

**Genentech**  
A Member of the Roche Group

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EVERYWHERE



Overview

Results:  
Type 2 or 3

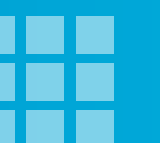
Results:  
Type 1

Results:  
Presymptomatic

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Safety

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# APPENDIX



EVERYWHERE

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



Overview

Results:  
Type 2 or 3

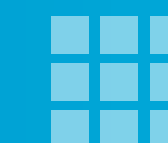
Results:  
Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

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# More adults and children experienced a $\geq 3$ -point change with Evrysdi compared with placebo after 1 year

## SUNFISH PART 2

**Change in motor function score after 1 year\***  
As measured by MFM-32

Improvement ( $\geq 3$ -point change)	
Evrysdi	Placebo
<b>38%<sup>†</sup></b> (44/115)	<b>24%<sup>‡</sup></b> (14/59)

Stabilization <sup>§</sup> or improvement ( $\geq 0$ -point change)	
Evrysdi	Placebo
<b>70%</b> (80/115)	<b>54%</b> (32/59)

P=0.0469

<sup>§</sup>Results in stabilization were not one of the main measurements and were only considered supportive. This means it was not designed to show a treatment effect so conclusions cannot be drawn.

A 3-point change may represent the ability to perform an everyday task. Depending on their starting score, for some, this could mean having the ability to wash their face, put on pants, or get into bed

\*In some studies, including this one, if someone's data cannot be collected on time for any reason, that person's progress cannot be counted in that part of the study. This chart includes only the information that was collected on time.  
<sup>†</sup>95% CI: 28.9, 47.6. This CI (confidence interval) means that we are 95% confident that the actual average change in MFM-32 with Evrysdi will be between 28.9 and 47.6 points.  
<sup>‡</sup>95% CI: 12.0, 35.4. This CI means that we are 95% confident that the actual average change in MFM-32 with placebo will be between 12.0 and 35.4 points.  
 MFM-32=Motor Function Measure-32 Items.

### Important Safety Information (continued)

- **The most common side effects of Evrysdi include:**
  - For later-onset SMA: fever, diarrhea, rash
  - For infantile-onset SMA: fever; diarrhea; rash; runny nose, sneezing and sore throat (upper respiratory infection); lung infection (lower respiratory infection); constipation; vomiting; cough

These are not all of the possible side effects of Evrysdi. For more information on the risk and benefits profile of Evrysdi, ask your healthcare provider or pharmacist.

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).

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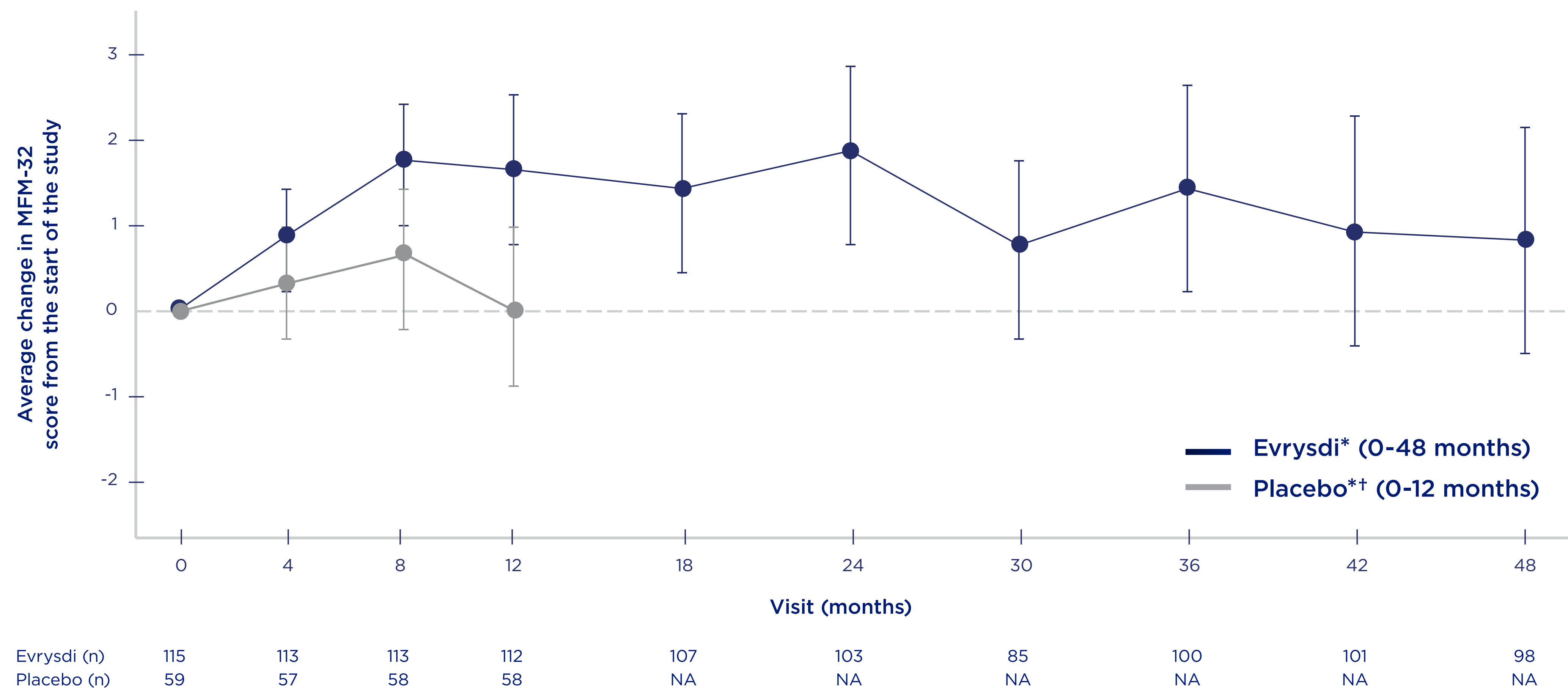


EVERYWHERE



# EXPLORATORY OBSERVATIONS SUGGEST Increase in motor function at 1 year was maintained at 4 years

**Change in motor function score after 4 years**  
As measured by MFM-32



0.84-point average change in MFM-32 score from the start of the study with Evrysdi

This information is considered **exploratory**, which means the clinical trial was not specifically designed to measure these results. Data should be interpreted with caution.

\*In some studies, including this one, if someone's data cannot be collected on time for any reason, that person's progress cannot be counted in that part of the study. This chart includes only the information that was collected on time.

\*\*Adults and children not taking Evrysdi took a placebo, a substance that has no active medication and is often used in studies. People in this group received placebo for 12 months followed by Evrysdi for 36 months. The period of time on Evrysdi is not included in this chart. The follow-up period was not placebo controlled. After 24 months, participants had the opportunity to enter the open-label extension portion of the study.

MFM-32=Motor Function Measure-32 Items; NA=not applicable.

## Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are pregnant or plan to become pregnant, as Evrysdi may harm your unborn baby. Ask your healthcare provider for advice before taking this medicine
  - are a woman who can become pregnant:
    - Before you start your treatment with Evrysdi, your healthcare provider may test you for pregnancy

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).

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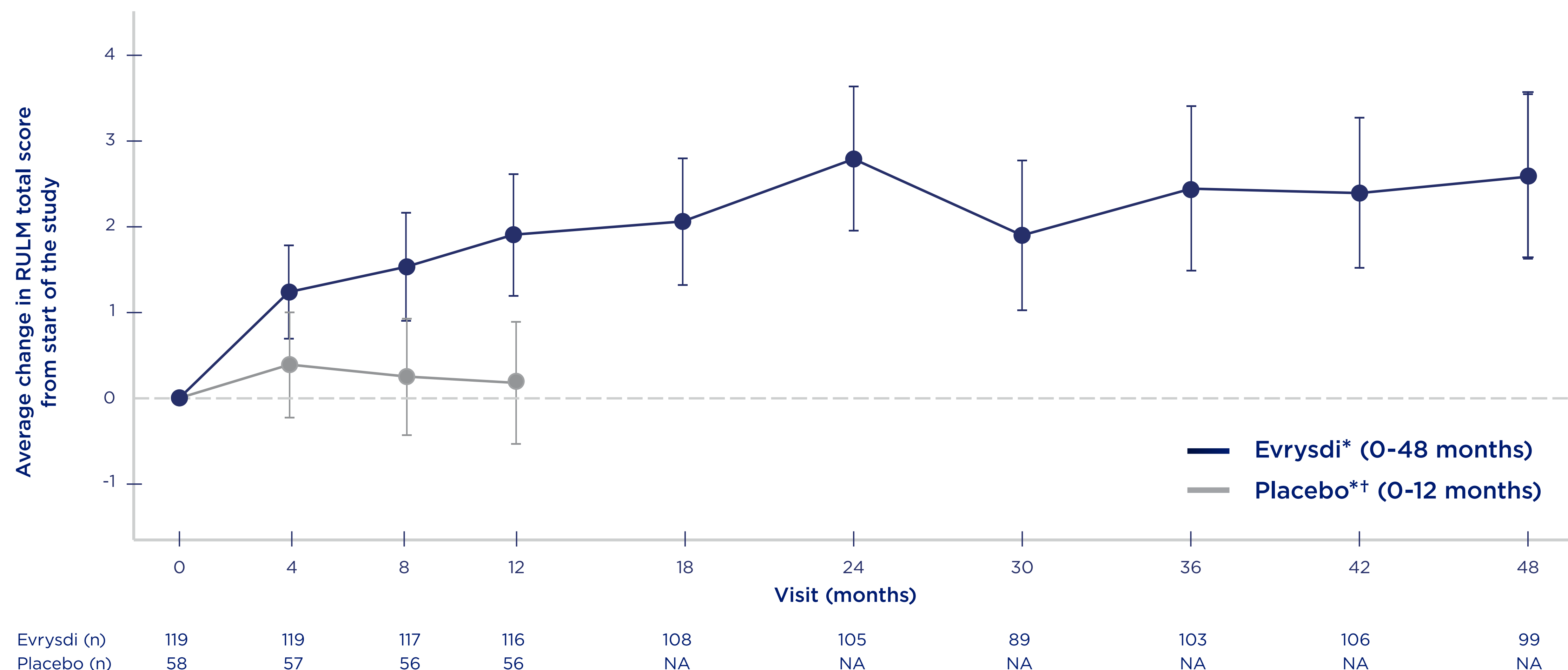


EVERYWHERE



# EXPLORATORY OBSERVATIONS SUGGEST Improvement in upper limb function at 1 year was maintained at 4 years

**Change in upper limb score over 4 years**  
As measured by RULM



2.58-point average change in RULM score from the start of the study with Evrysdi

This information is considered **exploratory**, which means the clinical trial was not specifically designed to measure these results. Data should be interpreted with caution.

\*In some studies, including this one, if someone's data cannot be collected on time for any reason, that person's progress cannot be counted in that part of the study. This chart includes only the information that was collected on time.

\*\*Adults and children not taking Evrysdi took a placebo, a substance that has no active medication and is often used in studies. People in this group received placebo for 12 months followed by Evrysdi for 36 months. The period of time on Evrysdi is not included in this chart. The follow-up period was not placebo controlled. After 24 months, participants had the opportunity to enter the open-label extension portion of the study.

NA stands for not applicable; RULM stands for the Revised Upper Limb Module (RULM) assessment.

### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are a woman who can become pregnant:
    - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping Evrysdi

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).

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EVERYWHERE



## SUNFISH PART 2

### Side effects occurring in $\geq 5\%$ of adults and children receiving Evrysdi and with an incidence of $\geq 5\%$ compared with placebo (N=180)

Side effect	Evrysdi (n=120)	Placebo (n=60)
Fever	22%	17%
Diarrhea	17%	8%
Rash	17%	2%
Mouth and canker sores	7%	0%
Joint pain	5%	0%
Urinary tract infection	5%	0%

Based on data collected through September 6, 2019.

Fever, diarrhea, and rash were the most common side effects reported more frequently than placebo that occurred in at least 10% of people taking Evrysdi.

#### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are a woman who can become pregnant:
    - **Pregnancy Registry.** There is a pregnancy registry for women who take Evrysdi during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving Evrysdi, tell your healthcare provider right away. Talk to your healthcare provider about registering with the Evrysdi Pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling **1-833-760-1098** or visiting <https://www.evrysdipregnancyregistry.com>.

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).

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EVERYWHERE



## SUNFISH PART 2

### Safety observations over 4 years

	<b>Placebo</b> 0-12 months (n=60)*	<b>Evrysdi</b> 0-12 months (n=120)	<b>Evrysdi</b> 12-24 months (n=117)	<b>Evrysdi</b> 24-36 months (n=116)	<b>Evrysdi</b> 36-48 months (n=112)
<b>Most common side effects, % (n)<sup>†</sup></b>					
Upper respiratory tract infection	30.0% (18)	31.7% (38)	16.2% (19)	8.6% (10)	17.9% (20)
Cold	25.0% (15)	25.8% (31)	22.2% (26)	9.5% (11)	5.4% (6)
Fever	16.7% (10)	20.8% (25)	13.7% (16)	9.5% (11)	8.0% (9)
Headache	16.7% (10)	20.0% (24)	10.3% (12)	7.8% (9)	3.6% (4)
Diarrhea	8.3% (5)	16.7% (20)	8.5% (10)	6.0% (7)	3.6% (4)
Vomiting	23.3% (14)	14.2% (17)	13.7% (16)	6.9% (8)	7.1% (8)
Cough	20.0% (12)	14.2% (17)	10.3% (12)	4.3% (5)	2.7% (3)
<b>Most common serious side effects, % (n)</b>					
Pneumonia	3.3% (2)	8.3% (10)	6.8% (8)	1.7% (2)	2.7% (3)
Influenza	0% (0)	0.8% (1)	0.9% (1)	0.9% (1)	0.9% (1)

Based on data collected through September 6, 2019 for Evrysdi 0-12 months and placebo 0-12 months.

Based on data collected through September 30, 2020 for Evrysdi 12-24 months.

Based on data collected through September 6, 2021 for Evrysdi 24-36 months.

Based on data collected through September 6, 2022 for Evrysdi 36-48 months.

No treatment-related side effects leading to permanent withdrawal or treatment discontinuation over 4 years<sup>†</sup>

\*People in the placebo group received placebo for 12 months followed by Evrysdi. The Evrysdi period for this group is not shown.

<sup>†</sup>One person withdrew from the trial after the September 6, 2021, clinical cut-off date because of a side effect (elevated liver enzymes) that was initially reported as related to Evrysdi and then reassessed after stopping treatment as unrelated to Evrysdi.

#### Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are an adult male. Evrysdi may affect a man's ability to have children (fertility). Ask a healthcare provider for advice before taking this medicine
  - are breastfeeding or plan to breastfeed. It is not known if Evrysdi passes into breast milk and may harm your baby

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).

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EVERYWHERE



# Safety information in infants with Type 1 SMA

The most common side effects of Evrysdi for infantile-onset SMA include:

- fever
- diarrhea
- rash
- runny nose, sneezing and sore throat (upper respiratory infection)
- lung infection (lower respiratory infection)
- constipation
- vomiting
- cough

**No treatment-related side effects leading to withdrawal or treatment discontinuation over 5 years**

## FIREFISH PART 1 AND 2

Side effects occurring in ≥10 infants receiving Evrysdi over 5 years

Side effects	Evrysdi (n=58)
Upper respiratory tract infection	64%
Fever	64%
Pneumonia	50%
Cold	28%
Diarrhea	28%
Constipation	26%
Vomiting	21%
Cough	21%
COVID-19	21%
Runny nose	21%
Bronchitis	19%
Respiratory tract infection	19%
Influenza	17%
Urinary tract infection	17%

Based on data collected through December 22, 2023.

### Important Safety Information (continued)

- **Tell your healthcare provider about all the medicines you take**
- If you were prescribed Evrysdi for Oral Solution, you should receive Evrysdi from the pharmacy as a liquid. If the medicine in the bottle is a powder, **do not use it**. Contact your pharmacist for a replacement
- Avoid getting Evrysdi on your skin or in your eyes. If Evrysdi gets on your skin, wash the area with soap and water. If Evrysdi gets in your eyes, rinse your eyes with water

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).

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EVERYWHERE



Overview

Results: Type 2 or 3

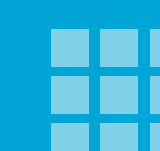
Results: Type 1

Results: Presymptomatic

Liquid and Tablet

Safety

Support





# Safety information in infants with presymptomatic SMA

- The most common side effects in adults and children with Type 2 or 3 SMA (later-onset) were fever, rash, and diarrhea
- The most common side effects in infants with Type 1 SMA (infantile-onset) were fever, upper respiratory infection (runny nose, sneezing and sore throat), lower respiratory infection (lung infection), constipation, vomiting, and cough
- The safety profile for presymptomatic infants is consistent with the safety profile for symptomatic SMA patients treated with Evrysdi in clinical studies

**No treatment-related side effects leading to withdrawal or treatment discontinuation over 2 years**

### Important Safety Information (continued)

- **The most common side effects of Evrysdi include:**
  - For later-onset SMA: fever, diarrhea, rash
  - For infantile-onset SMA: fever; diarrhea; rash; runny nose, sneezing and sore throat (upper respiratory infection); lung infection (lower respiratory infection); constipation; vomiting; cough

These are not all of the possible side effects of Evrysdi. For more information on the risk and benefits profile of Evrysdi, ask your healthcare provider or pharmacist.

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).

## RAINBOWFISH

### Side effects occurring in ≥5 infants receiving Evrysdi over 2 years

Side effects	Evrysdi (N=26)
Teething	42%
Stomach flu	39%
COVID-19	35%
Diarrhea	35%
Eczema	31%
Fever	31%
Constipation	23%
Upper respiratory tract infection	23%
Vomiting	23%
Nasal congestion	19%
Cold	19%
Respiratory tract infection viral	19%
Runny nose	19%
Viral infection	19%

Based on data collected through March 27, 2024.

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EVERYWHERE



# JEWELFISH description of study participants

**All participants**  
(N=174)

Baseline characteristics		
Age at enrollment, years		
Median (range)		<b>14.0 (1-60)</b>
>18 years, % (n)		<b>36% (63)</b>
Gender, % (n)		
Male		<b>55% (95)</b>
SMA type, % (n)		
1		<b>9% (15)</b>
2		<b>62% (108)</b>
3		<b>29% (51)</b>
SMN2 copy number, % (n)		
1		<b>2% (3)</b>
2		<b>8% (13)</b>
3		<b>78% (136)</b>
4		<b>13% (22)</b>

**All participants**  
(N=174)

Disease severity		
Scoliosis, % (n)		
Yes		<b>83% (139)<sup>*†</sup></b>
>40° curvature		<b>39% (66)<sup>*†</sup></b>
Hip - partial or complete dislocation, % (n)		
Yes		<b>30% (51)<sup>*†</sup></b>
Motor function assessment scores at baseline		
Motor function at baseline, % (n)		
Nonsitters		<b>34% (59)<sup>‡</sup></b>
Sitters		<b>57% (100)<sup>‡</sup></b>
Walkers		<b>9% (15)</b>
Baseline HFMSE total score <10, % (n)		
Yes		<b>63% (105)<sup>*†</sup></b>

JEWELFISH is an open-label safety study in 174 people aged 1 to 60 years with Type 1, 2, or 3 SMA who were previously treated with other approved or investigational SMA medications.<sup>§</sup>

\*Only reported for people aged 2 to 60 years.

<sup>†</sup>n=168.

<sup>‡</sup>For people younger than 2 years, baseline motor milestones were evaluated by the HINE-2.

<sup>§</sup>All but 3 patients enrolled in JEWELFISH received previous treatment; these 3 patients were previously enrolled in a different trial but received placebo only.

HFMSE=Hammersmith Functional Motor Score Expanded.

## Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are pregnant or plan to become pregnant, as Evrysdi may harm your unborn baby. Ask your healthcare provider for advice before taking this medicine
  - are a woman who can become pregnant:
    - Before you start your treatment with Evrysdi, your healthcare provider may test you for pregnancy

Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).

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EVERYWHERE



# JEWELFISH side effects and serious side effects at 2 years

**All participants**  
(N=174)\*

Side effects occurring in ≥12% of individuals,† % (n)	
Fever (pyrexia)	24% (42)
Upper respiratory tract infection	21% (37)
Headache	18% (31)
Common cold (nasopharyngitis)	16% (27)
Diarrhea	14% (24)
Nausea	13% (22)
Cough	12% (21)
Serious side effects occurring in >2% of individuals,† % (n)	
Pneumonia	3% (5)
Respiratory failure	2% (4)
Respiratory distress	2% (3)
Lower respiratory tract infection	2% (3)
Upper respiratory tract infection	2% (3)

Based on data collected through January 31, 2022.

Evrysdi treatment duration  
in months, median (range):  
26.8 (0.9-59.0)

- The length of time on Evrysdi varies for each person. Therefore, one should not compare the overall rates of common and serious side effects
- The safety findings from JEWELFISH have been consistent with the safety findings in FIREFISH and SUNFISH

\*One person withdrew from the study at baseline; therefore, 173 patients received Evrysdi.

†Multiple occurrences of the same side effects in one person are counted only once.

## Important Safety Information (continued)

- **Before taking Evrysdi, tell your healthcare provider about all of your medical conditions, including if you:**
  - are a woman who can become pregnant:
    - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping Evrysdi

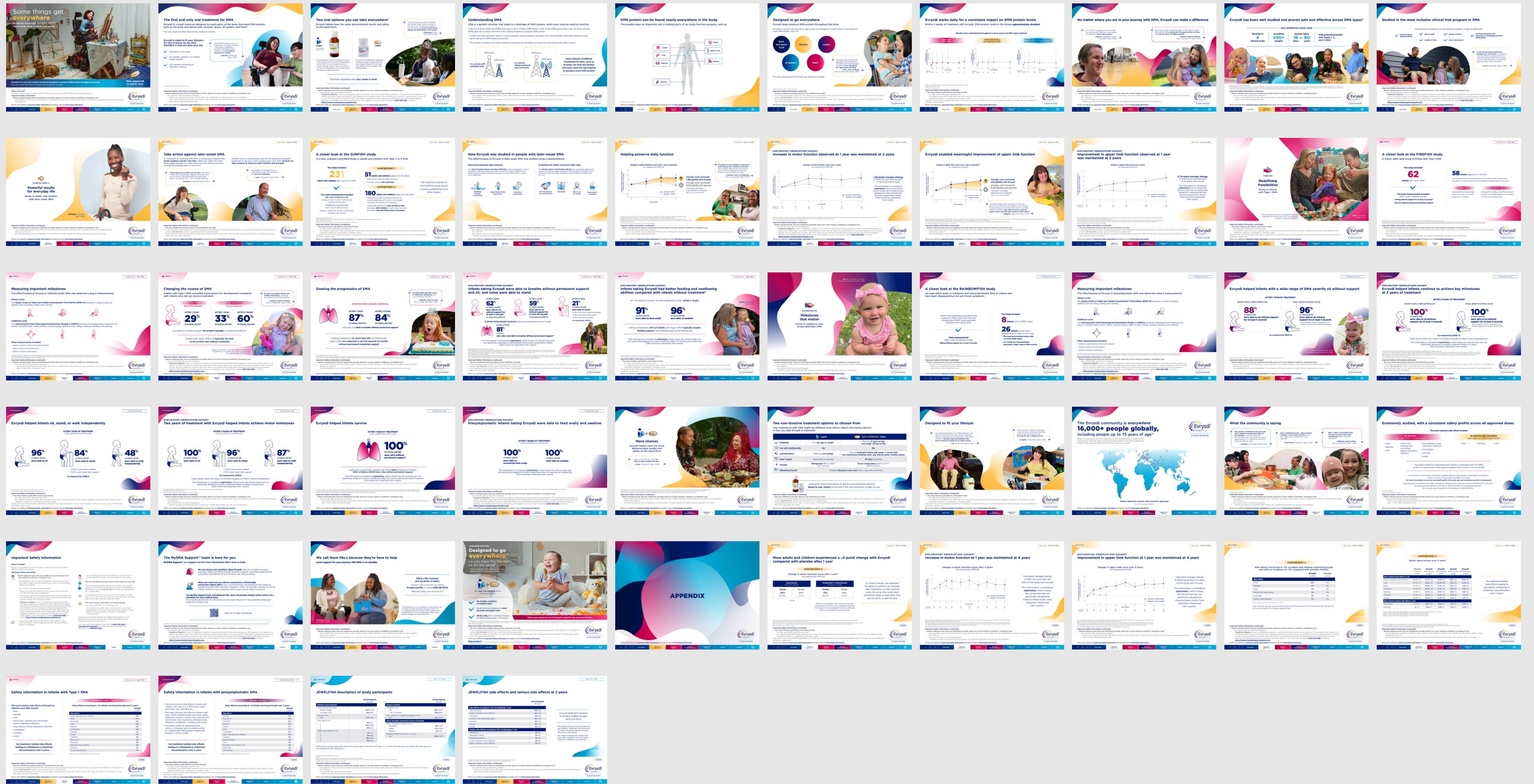
Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).

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EVERYWHERE





Please see additional [Important Safety Information](#) throughout and full [Prescribing Information](#).



Overview

Results:  
Type 2 or 3

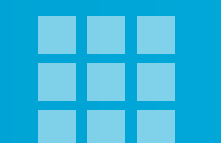
Results:  
Type 1

Results:  
Presymptomatic

Liquid and  
Tablet

Safety

Support





**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use EVRYSDI safely and effectively. See full prescribing information for EVRYSDI.

EVRYSDI® (risdiplam) for oral solution

EVRYSDI® (risdiplam) tablets, for oral use

Initial U.S. Approval: 2020

-----RECENT MAJOR CHANGES-----

Dosage and Administration (2.1, 2.2, 2.4) 2/2025

----- INDICATIONS AND USAGE -----

EVRYSDI is a survival of motor neuron 2 (SMN2) splicing modifier indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. (1)

----- DOSAGE AND ADMINISTRATION -----

- Administer once daily with or without food per the table below (2.1):

Age and Body Weight	Recommended Daily Dosage	Dosage Form
Less than 2 months of age	0.15 mg/kg	EVRYSDI for Oral Solution
2 months to less than 2 years of age	0.2 mg/kg	
2 years of age and older weighing less than 20 kg	0.25 mg/kg	
2 years of age and older weighing 20 kg or more	5 mg	EVRYSDI for Oral Solution or EVRYSDI Tablet

- Swallow EVRYSDI tablet whole with water or dispersed in non-chlorinated drinking water (e.g., filtered water). (2.2)
- Administer EVRYSDI for oral solution with the provided oral syringe. (2.2)

- EVRYSDI for oral solution must be constituted by a healthcare provider prior to dispensing. (2.4)
  - See Full Prescribing Information for important preparation and administration instructions. (2.2, 2.4)
- DOSAGE FORMS AND STRENGTHS -----
- For Oral Solution: 60 mg of risdiplam as a powder for constitution to provide 0.75 mg/mL solution. (3)
  - Tablets: 5 mg

----- CONTRAINDICATIONS -----

None. (4)

----- ADVERSE REACTIONS -----

The most common adverse reactions in later-onset SMA (incidence at least 10% of patients treated with EVRYSDI and more frequent than control) were fever, diarrhea, and rash. (6.1)

The most common adverse reactions in infantile-onset SMA were similar to those observed in later-onset SMA patients. Additionally, adverse reactions with an incidence of at least 10% were upper respiratory tract infection, lower respiratory tract infection, constipation, vomiting, and cough. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----- DRUG INTERACTIONS -----

Avoid coadministration with drugs that are substrates of multidrug and toxin extrusion (MATE) transporters. (7.1)

----- USE IN SPECIFIC POPULATIONS -----

Pregnancy: Based on animal data, may cause fetal harm. (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 2/2025

**FULL PRESCRIBING INFORMATION: CONTENTS\***

- 1 INDICATIONS AND USAGE**
- 2 DOSAGE AND ADMINISTRATION**
  - 2.1 Dosing Information
  - 2.2 Important Administration Instructions
  - 2.3 Missed Dose
  - 2.4 Preparation of Powder for Oral Solution by Healthcare Provider
- 3 DOSAGE FORMS AND STRENGTHS**
- 4 CONTRAINDICATIONS**
- 6 ADVERSE REACTIONS**
  - 6.1 Clinical Trials Experience
- 7 DRUG INTERACTIONS**
  - 7.1 Effect of EVRYSDI on Substrates of Multidrug and Toxin Extrusion (MATE) Protein Transporters
- 8 USE IN SPECIFIC POPULATIONS**
  - 8.1 Pregnancy
  - 8.2 Lactation
  - 8.3 Females and Males of Reproductive Potential
  - 8.4 Pediatric Use
  - 8.5 Geriatric Use
- 11 DESCRIPTION**

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- 13 NONCLINICAL TOXICOLOGY**
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  - 16.1 EVRYSDI for Oral Solution
  - 16.2 EVRYSDI Tablets
- 17 PATIENT COUNSELING INFORMATION**

\* Sections or subsections omitted from the full prescribing information are not listed.



## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

EVERYSDI is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 Dosing Information

EVERYSDI is administered orally once daily with or without food. The recommended dosage is determined by age and body weight (see Table 1). EVERYSDI tablets are available for patients prescribed the 5 mg dose.

**Table 1 Adult and Pediatric Dosing Regimen by Age and Body Weight**

Age and Body Weight	Recommended Daily Dosage	Dosage Form
Less than 2 months of age	0.15 mg/kg	EVERYSDI for Oral Solution
2 months to less than 2 years of age	0.2 mg/kg	
2 years of age and older weighing less than 20 kg	0.25 mg/kg	
2 years of age and older weighing 20 kg or more	5 mg	EVERYSDI for Oral Solution or EVERYSDI Tablet

#### 2.2 Important Administration Instructions

It is recommended that a healthcare provider discuss with the patient or caregiver how to prepare the prescribed daily dose prior to administration of the first dose [*see Instructions for Use for EVERYSDI for Oral Solution and Patient Information*].

EVERYSDI is taken orally once daily with or without food at approximately the same time each day.

##### EVERYSDI for Oral Solution

In infants who are breastfed, EVERYSDI for oral solution can be administered before or after breastfeeding. EVERYSDI cannot be mixed with formula or milk.

Instruct patients or caregivers to administer the dose using the reusable oral syringe provided.

EVERYSDI for oral solution must be taken immediately after it is drawn up into the oral syringe. If EVERYSDI is not taken within 5 minutes, EVERYSDI should be discarded from the oral syringe, and a new dose should be prepared.

Instruct patients to drink water after taking EVERYSDI for oral solution to ensure the drug has been completely swallowed.

If the patient is unable to swallow and has a nasogastric or gastrostomy tube, EVERYSDI for oral solution can be administered via the tube. The tube should be flushed with water after delivering EVERYSDI for oral solution [*see Instructions for Use*].

##### EVERYSDI Tablets

Swallow EVERYSDI tablets whole with water. Do not chew, cut, or crush the tablets.

The EVERYSDI tablet can also be dispersed in one teaspoon (5 mL) of room temperature non-chlorinated drinking water (e.g., filtered water). EVERYSDI tablets must not be dispersed in any liquid other than non-chlorinated drinking water. Do not expose the prepared dispersion to sunlight. Swirl the small cup gently for up to 3 minutes until fully mixed (though some particles



will remain). Administer the dispersed tablet immediately. To ensure no particles are left in the small cup, refill it with at least one tablespoon (15 mL) of non-chlorinated drinking water, swirl, and administer immediately again.

EVERYSDI must be taken immediately after it is dispersed in non-chlorinated drinking water. Discard the prepared dispersion if it is not used within 10 minutes of adding non-chlorinated drinking water.

Do not administer the prepared dispersion via a nasogastric or gastrostomy tube. If administration through a nasogastric or gastrostomy tube is required, EVERYSDI for oral solution should be used.

### **2.3 Missed Dose**

If a dose of EVERYSDI is missed, EVERYSDI should be administered as soon as possible if still within 6 hours of the missed dose, and the usual dosing schedule can be resumed on the next day. Otherwise, the missed dose should be skipped, and the next dose should be taken at the regularly scheduled time on the next day.

If a dose is not fully swallowed or vomiting occurs after taking a dose of EVERYSDI, another dose should not be administered to make up for the lost dose. The patient should wait until the next day to take the next dose at the regularly scheduled time.

### **2.4 Preparation of Powder for Oral Solution by Healthcare Provider**

EVERYSDI powder must be constituted to the oral solution by a pharmacist or other healthcare provider prior to dispensing to the patient.

#### Preparation of the EVERYSDI Oral Solution 0.75 mg/mL

The EVERYSDI “Instructions for Constitution” booklet contains more detailed instructions on the preparation of the oral solution [*see Instructions for Constitution*].

Caution should be exercised when handling EVERYSDI powder for oral solution. Avoid inhalation and direct contact with skin or mucous membranes with the dry powder and the constituted solution. If such contact occurs, wash thoroughly with soap and water; rinse eyes with water. Wear disposable gloves during the preparation and cleanup procedure.

1. Gently tap the bottom of the closed glass bottle to loosen the powder.
2. Remove the cap. Do not throw away the cap.
3. Carefully pour 79 mL of purified water into the EVERYSDI bottle to yield the 0.75 mg/mL oral solution. Do not mix EVERYSDI with formula or milk.
4. Insert the press-in bottle adapter into the bottle opening by pushing it down against the bottle lip. Ensure it is completely pressed against the bottle lip.
5. Re-cap the bottle tightly and shake well for 15 seconds. Wait for 10 minutes. You should have obtained a clear solution. If not, shake well again for another 15 seconds or until you have obtained a clear solution.
6. Write the date of expiration of the constituted oral solution (calculated as 64 days after constitution) and the lot number on the bottle label. Peel off the part of the bottle label that has the expiration date of the powder.
7. Put the bottle back in its original carton.
8. Select the appropriate oral syringes (1 mL, 6 mL, or 12 mL) based on the patient’s dosage and remove the other oral syringes from the carton.



9. Dispense with the “Instructions for Use” and FDA-approved patient labeling. Alert patients to read the important handling information described in the Instructions for Use.

### Storage

Keep the constituted oral solution of EVRYSDI in the original amber bottle to protect from light. Store in a refrigerator at 2°C to 8°C (36°F to 46°F). Do not freeze. Discard any unused portion 64 days after constitution. Keep the bottle in an upright position with the cap tightly closed. If refrigeration is not available, EVRYSDI can be kept at room temperature up to 40°C (up to 104°F) for a combined total of 5 days. EVRYSDI can be removed from, and returned to, a refrigerator. The total combined time out of refrigeration should not exceed 5 days.

## **3 DOSAGE FORMS AND STRENGTHS**

EVRYSDI for oral solution: 60 mg as a light yellow, pale yellow, yellow, greyish yellow, greenish yellow, or light green powder for constitution. Following constitution, the volume of the greenish yellow to yellow solution is 80 mL, providing 60 mg/80 mL (0.75 mg/mL) risdiplam.

EVRYSDI tablet: 5 mg as a pale yellow film-coated tablet, round and curved, with EVR debossed on one side.

## **4 CONTRAINDICATIONS**

None.

## **6 ADVERSE REACTIONS**

### **6.1 Clinical Trials Experience**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in clinical trials of another drug and may not reflect the rates observed in practice.

In clinical trials including patients with infantile-onset SMA, later-onset SMA, and pre-symptomatic SMA, a total of 491 patients (51% female, 74% Caucasian) were exposed to EVRYSDI for up to a median duration of 48.1 months (range: 0.6 to 63.4 months), with 231 patients receiving treatment for more than 24 months. At the time of first EVRYSDI dose, 90 (18%) patients were 18 years and older, 119 (24%) were 12 years to less than 18 years, 189 (39%) were 2 years to less than 12 years, 67 (14%) 2 months to less than 2 years, and 26 (5%) were less than 2 months.

#### Clinical Trial in Later-Onset SMA

The safety of EVRYSDI for later-onset SMA is based on data from a randomized, double-blinded, placebo-controlled study (Study 2 Part 2) in patients with SMA Type 2 or 3 (n = 180) [see *Clinical Studies (14.2)*]. The patient population in Study 2 Part 2 ranged in age from 2 to 25 years at the time of the first dose.

The most common adverse reactions (reported in at least 10% of patients treated with EVRYSDI and at an incidence greater than on placebo) in Study 2 Part 2 were fever, diarrhea, and rash. Table 2 lists the adverse reactions that occurred in at least 5% of patients treated with EVRYSDI and at an incidence  $\geq$  5% greater than on placebo in Study 2 Part 2.

**Table 2 Adverse Reactions Reported in  $\geq$  5% of Patients Treated with EVRYSDI and with an Incidence  $\geq$  5% Greater Than on Placebo in Study 2 Part 2**



<b>Adverse Reaction</b>	<b>EVRYSDI (N = 120) %</b>	<b>Placebo (N = 60) %</b>
Fever <sup>1</sup>	22	17
Diarrhea	17	8
Rash <sup>2</sup>	17	2
Mouth and aphthous ulcers	7	0
Arthralgia	5	0
Urinary tract infection <sup>3</sup>	5	0

<sup>1</sup> Includes pyrexia and hyperpyrexia.

<sup>2</sup> Includes rash, erythema, rash maculo-papular, rash erythematous, rash papular, dermatitis allergic, and folliculitis.

<sup>3</sup> Includes urinary tract infection and cystitis.

### Clinical Trial in Infantile-Onset SMA

The safety of EVRYSDI therapy for infantile-onset SMA is based on data from an open-label study in 62 patients (Study 1) [see *Clinical Studies (14.1)*]. The patient population ranged in age from 2 to 7 months at the time of the first EVRYSDI dose (weight range: 4.1 to 10.6 kg).

The most frequent adverse reactions reported in infantile-onset SMA patients treated with EVRYSDI in Study 1 were similar to those observed in later-onset SMA patients in Study 2. Additionally, the following adverse reactions reported in  $\geq 10\%$  of patients were: upper respiratory tract infection (including nasopharyngitis, rhinitis), lower respiratory tract infection (including pneumonia, bronchitis), constipation, vomiting, and cough.

### Clinical Trial in Pre-Symptomatic SMA

The safety of EVRYSDI therapy for pre-symptomatic SMA is based on data from an open-label, single-arm study in 26 patients (Study 3) [see *Clinical Studies (14.3)*]. The patient population ranged in age from 16 to 41 days at the time of the first dose (weight range: 3.1 to 5.7 kg). The safety profile of EVRYSDI in pre-symptomatic patients in Study 3 is consistent with the safety profile for symptomatic SMA patients treated with EVRYSDI in clinical trials.

## **7 DRUG INTERACTIONS**

### **7.1 Effect of EVRYSDI on Substrates of Multidrug and Toxin Extrusion (MATE) Protein Transporters**

Based on in vitro data, EVRYSDI may increase plasma concentrations of drugs eliminated via MATE1 or MATE2-K [see *Clinical Pharmacology (12.3)*], such as metformin. Avoid coadministration of EVRYSDI with MATE substrates. If coadministration cannot be avoided, monitor for drug-related toxicities and consider dosage reduction of the coadministered drug (based on the labeling of that drug) if needed.

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy and fetal/neonatal/infant outcomes in women exposed to EVRYSDI during pregnancy. Physicians are encouraged to



register patients and pregnant women are encouraged to register themselves by calling 1-833-760-1098 or visiting <https://www.evrysdipregnancyregistry.com>.

### Risk Summary

There are no adequate data on the developmental risk associated with the use of EVRYSDI in pregnant women. In animal studies, administration of risdiplam during pregnancy or throughout pregnancy and lactation resulted in adverse effects on development (embryofetal mortality, malformations, decreased fetal body weights, and reproductive impairment in offspring) at or above clinically relevant drug exposures [see *Data*].

The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. In the U.S. general population, the estimated background risk of major birth defect and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Based on animal data, advise pregnant women of the potential risk to the fetus.

### Data

#### *Animal Data*

Oral administration of risdiplam (0, 1, 3, or 7.5 mg/kg/day) to pregnant rats throughout organogenesis resulted in decreased fetal body weights and increased incidences of fetal structural variations at the highest dose tested, which was not associated with maternal toxicity. The no-effect level for adverse effects on embryofetal development (3 mg/kg/day) was associated with maternal plasma exposure (AUC) approximately 2 times that in humans at the maximum recommended human dose (MRHD) of 5 mg.

Oral administration of risdiplam (0, 1, 4, or 12 mg/kg/day) to pregnant rabbits throughout organogenesis resulted in embryofetal mortality, fetal malformations (hydrocephaly), and structural variations at the highest dose tested, which was associated with maternal toxicity. The no-effect dose for adverse effects on embryofetal development (4 mg/kg/day) was associated with maternal plasma exposure (AUC) approximately 4 times that in humans at the MRHD.

When risdiplam (0, 0.75, 1.5, or 3 mg/kg/day) was orally administered to rats throughout pregnancy and lactation, gestation was prolonged in the dams, and delayed sexual maturation (vaginal opening) and impaired reproductive function (decreased numbers of corpora lutea, implantation sites, and live embryos) were observed in female offspring at the highest dose. The no-effect dose for adverse effects on pre- and postnatal development in rats (1.5 mg/kg/day) was associated with maternal plasma exposure (AUC) similar to that in humans at the MRHD.

## **8.2 Lactation**

### Risk Summary

There are no data on the presence of risdiplam in human milk, the effects on the breastfed infant, or the effects on milk production. Risdiplam was excreted in the milk of lactating rats orally administered risdiplam.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for EVRYSDI and any potential adverse effects on the breastfed infant from EVRYSDI or from the underlying maternal condition.



### **8.3 Females and Males of Reproductive Potential**

Studies of risdiplam in juvenile and adult rats and in monkeys demonstrated adverse effects on the reproductive organs, including germ cells, in males at clinically relevant plasma exposures [*see Use in Specific Populations (8.4) and Nonclinical Toxicology (13.1)*].

#### Pregnancy Testing

Pregnancy testing is recommended for females of reproductive potential prior to initiating EVRYSDI [*see Use in Specific Populations (8.1)*].

#### Contraception

EVRYSDI may cause embryofetal harm when administered to a pregnant woman [*see Use in Specific Populations (8.1)*].

#### *Female Patients*

Advise female patients of reproductive potential to use effective contraception during treatment with EVRYSDI and for at least 1 month after her last dose.

#### Infertility

##### *Male Patients*

Male fertility may be compromised by treatment with EVRYSDI [*see Nonclinical Toxicology (13.1)*].

Counsel male patients of reproductive potential receiving EVRYSDI about the potential effects on fertility. Male patients may consider sperm preservation prior to treatment.

### **8.4 Pediatric Use**

The safety and effectiveness of EVRYSDI in pediatric patients (neonates and older) have been established. Use of EVRYSDI for SMA is supported by evidence from adequate and well-controlled studies of EVRYSDI in patients 2 months of age and older with SMA. Use of EVRYSDI for SMA in patients 2 months of age and younger is supported by pharmacokinetic and safety data from pediatric patients 16 days and older, and pharmacokinetic modeling and simulation to identify the dosing regimen [*see Clinical Pharmacology (12.3) and Clinical Studies (14)*].

#### Juvenile Animal Toxicity Data

Oral administration of risdiplam (0, 0.75, 1.5, 2.5 mg/kg/day) to young rats from postnatal day (PND) 4 through PND 31 resulted in decreased growth (body weight, tibia length) and delayed sexual maturation in males at the mid and high dose. The skeletal and body weight deficits persisted after cessation of dosing. Ophthalmic changes consisting of vacuoles in the anterior vitreous were seen at the high dose. Decreases in absolute B lymphocyte counts were observed at all doses after cessation of dosing. Decreases in testis and epididymis weights, which correlated with degeneration of the seminiferous epithelium in the testis, occurred at the mid and high doses; the histopathology findings were reversible, but organ weight persisted after cessation of dosing. Impaired female reproductive performance (decreased mating index, fertility index, and conception rate) was observed at the high dose. A no-effect dose for adverse developmental effects on preweaning rats was not identified. The lowest dose tested (0.75 mg/kg/day) was associated with plasma exposures (AUC) lower than that in humans at the maximum recommended human dose (MRHD) of 5 mg/day.

Oral administration of risdiplam (0, 1, 3, or 7.5 mg/kg/day) to young rats from PND 22 through PND 112 produced a marked increase in micronuclei in the bone marrow, male reproductive organ histopathology (degeneration/necrosis of the seminiferous tubule epithelium,



oligo/aspermia in the epididymis, spermatic granulomas), and adverse effects on sperm parameters (decreased sperm concentration and motility, increased sperm morphology abnormalities) at the highest dose tested. Increases in T lymphocytes (total, helper, and cytotoxic) were observed at the mid and high doses. The reproductive and immune effects persisted after cessation of dosing. The no-effect dose (1 mg/kg/day) for adverse effects on postweaning juvenile rats was associated with plasma exposures (AUC) lower than that in humans at the MRHD.

## 8.5 Geriatric Use

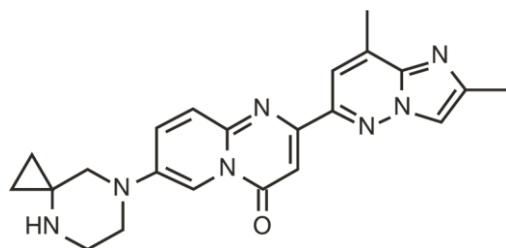
Clinical studies of EVERYSDI did not include patients aged 65 years and older to determine whether they respond differently from younger adult patients.

## 11 DESCRIPTION

EVERYSDI for oral solution and EVERYSDI tablets for oral use contain risdiplam, which is a survival of motor neuron 2 (SMN2)-directed RNA splicing modifier.

The chemical name of risdiplam is 7-(4,7-diazaspiro[2.5]octan-7-yl)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)pyrido-4H-[1,2-a]pyrimidin-4-one. Risdiplam has a molecular weight of 401.46 g/mol. Risdiplam demonstrates pH-dependent aqueous solubility; the greatest solubility is at low pH, and solubility decreases with increasing pH. Risdiplam has a pKa<sub>1</sub> of 3.78 (base) and pKa<sub>2</sub> of 6.62 (base).

The molecular formula of risdiplam is C<sub>22</sub>H<sub>23</sub>N<sub>7</sub>O and the chemical structure is shown below.



EVERYSDI for oral solution is supplied as a powder in an amber glass bottle. Each bottle contains 60 mg of risdiplam. The inactive ingredients of EVERYSDI are: ascorbic acid, disodium edetate dihydrate, isomalt, mannitol, polyethylene glycol 6000, sodium benzoate, strawberry flavor, sucralose, and tartaric acid.

The powder is constituted with purified water to yield 60 mg/80 mL (0.75 mg/mL) of risdiplam after constitution [*see Dosage and Administration (2.4)*].

Each EVERYSDI tablet contains 5 mg of risdiplam. The inactive ingredients of EVERYSDI tablet are colloidal silicon dioxide, crospovidone, mannitol, microcrystalline cellulose, polyethylene glycol 3350, polyvinyl alcohol, sodium stearyl fumarate, strawberry flavor, talc, tartaric acid, titanium dioxide, and yellow iron oxide.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Risdiplam is a survival of motor neuron 2 (SMN2) splicing modifier designed to treat patients with spinal muscular atrophy (SMA) caused by mutations in chromosome 5q that lead to SMN protein deficiency. Using in vitro assays and studies in transgenic animal models of SMA, risdiplam was shown to increase exon 7 inclusion in SMN2 messenger ribonucleic acid (mRNA) transcripts and production of full-length SMN protein in the brain.

In vitro and in vivo data indicate that risdiplam may cause alternative splicing of additional genes, including FOXM1 and MADD. FOXM1 and MADD are thought to be involved in cell



cycle regulation and apoptosis, respectively, and have been identified as possible contributors to adverse effects seen in animals.

## **12.2 Pharmacodynamics**

In clinical trials for infantile-onset SMA and later-onset SMA patients, EVRYSDI led to an increase in SMN protein with a greater than 2-fold median change from baseline within 4 weeks of treatment initiation across all SMA types studied. The increase was sustained throughout the treatment period (of at least 24 months).

### Cardiac Electrophysiology

At the maximum recommended dose, clinically significant QTc interval prolongation was not observed.

## **12.3 Pharmacokinetics**

Pharmacokinetics of EVRYSDI have been characterized in healthy adult subjects and in patients with SMA.

After administration of EVRYSDI as an oral solution, pharmacokinetics of risdiplam were approximately linear between 0.6 and 18 mg in a single-ascending-dose study in healthy adult subjects, and between 0.02 and 0.25 mg/kg once daily in a multiple-ascending-dose study in patients with SMA. Following once-daily oral administration of risdiplam in healthy subjects, approximately 3-fold accumulation of peak plasma concentrations ( $C_{max}$ ) and area under the plasma concentration-time curve ( $AUC_{0-24h}$ ) was observed. Risdiplam exposures reach steady state 7 to 14 days after once daily administration. EVRYSDI tablet (swallowed whole or dispersed in water) demonstrated comparable bioavailability to EVRYSDI for oral solution in adult healthy volunteers under fasted and fed states.

### Absorption

Following oral administration of risdiplam in fasted state, the median time to reach maximum plasma concentration ( $T_{max}$ ) was 3.26 to 4 hours. The  $T_{max}$  was delayed by up to 1 hour in fed state compared to that under fasted state.

### *Effect of Food*

Food (high-fat, high calorie breakfast) had no relevant effect on the exposure of risdiplam. In the clinical efficacy studies (Study 1 and Study 2), risdiplam was administered with a morning meal or after breastfeeding.

### Distribution

The apparent volume of distribution at steady state is 190.4 L for a 31.3 kg patient.

Risdiplam is predominantly bound to serum albumin, without any binding to alpha-1 acid glycoprotein, with a free fraction of 11%.

### Elimination

The apparent clearance (CL/F) of risdiplam is 2.45 L/h for a 31.3 kg patient. The terminal elimination half-life of risdiplam was approximately 50 hours in healthy adults.

### *Metabolism*

Risdiplam is primarily metabolized by flavin monooxygenase 1 and 3 (FMO1 and FMO3) and also by CYPs 1A1, 2J2, 3A4, and 3A7.

Parent drug was the major component found in plasma, accounting for 83% of drug-related material in circulation. The pharmacologically-inactive metabolite M1 was identified as the major circulating metabolite.



### *Excretion*

Following a dose of 18 mg, approximately 53% of the dose (14% unchanged risdiplam) was excreted in the feces and 28% in urine (8% unchanged risdiplam).

### Specific Populations

There were no clinically significant differences in the pharmacokinetics of EVRYSDI based on race or gender. Renal impairment is not expected to alter the exposures to risdiplam.

The impact of geriatric age on the pharmacokinetics of EVRYSDI has not been studied.

### *Hepatic Impairment*

The pharmacokinetics and safety of risdiplam have been studied in subjects with mild or moderate hepatic impairment (as defined by Child-Pugh class A and B, respectively, n = 8 each) compared to subjects with normal hepatic function (n = 10). Following the administration of 5 mg EVRYSDI, the AUC<sub>inf</sub> and C<sub>max</sub> of risdiplam were approximately 20% and 5% lower, respectively, in subjects with mild hepatic impairment and were approximately 8% and 20% higher, respectively, in subjects with moderate hepatic impairment, versus matched healthy control subjects. The magnitude of these changes is not considered to be clinically meaningful. The pharmacokinetics and safety in patients with severe hepatic impairment (Child-Pugh class C) have not been studied.

### *Pediatric Patients*

Body weight and age were found to have significant effect on the pharmacokinetics of risdiplam. The estimated exposure (mean AUC<sub>0-24h</sub>) in pre-symptomatic infants at the age of 1 to 2 months was 2090 ng.h/mL at the recommended dose of 0.15 mg/kg once daily. The estimated exposure for infantile-onset SMA patients (age 2 to 7 months at enrollment) at the recommended dose of 0.2 mg/kg once daily was 1930 ng.h/mL. The estimated exposure for later-onset SMA patients (2 to 25 years old at enrollment) at the recommended dose was 2070 ng.h/mL (0.25 mg/kg once daily for patients with a body weight < 20 kg and 5 mg once daily for patients with a body weight ≥ 20 kg).

No data on risdiplam pharmacokinetics are available in patients less than 16 days of age [*see Use in Specific Populations (8.4)*].

### Drug Interaction Studies

#### *Effect of Other Drugs on EVRYSDI*

Coadministration of 200 mg itraconazole (a strong CYP3A inhibitor) twice daily with a single 6 mg oral dose of risdiplam did not have a clinically relevant effect on the pharmacokinetics of risdiplam (11% increase in AUC and 9% decrease in C<sub>max</sub>).

Risdiplam is a weak substrate of human MDR-1 and breast cancer resistant protein (BCRP) transporters in vitro. Human MDR-1 or BCRP inhibitors are not expected to result in a clinically significant increase of risdiplam concentrations.

#### *Effect of EVRYSDI on Other Drugs*

Risdiplam and its major circulating metabolite M1 did not induce CYP1A2, 2B6, 2C8, 2C9, 2C19, or 3A4 in vitro. Risdiplam and M1 did not inhibit (reversible or time-dependent inhibition) any of the CYP enzymes tested (CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6), with the exception of CYP3A in vitro.

EVRYSDI is a weak inhibitor of CYP3A. In healthy adult subjects, administration of EVRYSDI once daily for 2 weeks slightly increased the exposure of midazolam, a sensitive CYP3A substrate (AUC 11%; C<sub>max</sub> 16%); this increase is not considered clinically relevant. Based on



physiologically-based pharmacokinetic (PBPK) modeling, a similar increase is expected in children and infants as young as 2 months of age.

In vitro studies have shown that risdiplam and its major metabolite are not significant inhibitors of human MDR1, organic anion-transporting polypeptide (OATP) 1B1, OATP1B3, organic anion transporter 1 and 3 (OAT 1 and 3) transporters, and human organic cation transporter 2 (OCT2), at clinically relevant concentrations. Risdiplam and its metabolite are, however, in vitro inhibitors of the multidrug and toxin extrusion (MATE) 1 and MATE2-K transporters [*see Drug Interactions (7.1)*].

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

#### Carcinogenesis

Risdiplam was not carcinogenic in Tg.rasH2 mice when administered at oral doses of up to 9 mg/kg/day for 26 weeks.

In a 2-year carcinogenicity study in rats, oral administration of risdiplam (0, 0.3, 1, or 3 mg/kg/day) resulted in increased incidences of preputial gland squamous cell carcinomas in males and combined thyroid follicular cell adenomas and carcinomas in females at the highest dose tested. The higher dose not associated with an increase in tumors (1 mg/kg/day) was associated with plasma drug exposures (AUC) similar to that in humans at the maximum recommended human dose (MRHD) of 5 mg/day.

#### Mutagenesis

Risdiplam was negative in an in vitro Ames assay. In an in vivo combined bone marrow micronucleus and comet assay in rat, risdiplam was clastogenic, as evidenced by an increase in micronuclei in bone marrow, but was negative in the comet assay. A pronounced increase in bone marrow micronuclei was also observed in toxicity studies in adult and juvenile rats [*see Use in Specific Populations (8.4)*].

#### Impairment of Fertility

Oral administration of risdiplam to rats for 4 (0, 1, 3, or 9 mg/kg/day) or 26 (0, 1, 3, or 7.5 mg/kg/day) weeks resulted in histopathological effects in the testis (degenerated spermatocytes, degeneration/atrophy of the seminiferous tubules) and epididymis (degeneration/necrosis of ductular epithelium) at the mid and/or high doses. At the high dose in the 26-week study, the testicular lesions persisted to the end of the recovery period, which corresponds, in rat, to approximately one spermatogenic cycle. The no-effect dose for adverse reproductive system effects in adult male rats (1 mg/kg/day) was associated with plasma drug exposures (AUC) similar to that in humans at the maximum recommended human dose (MRHD) of 5 mg/day.

Adverse effects of risdiplam on the testis could not be fully evaluated in the monkey because the majority of monkeys tested were sexually immature. However, oral administration of risdiplam (0, 2, 4, or 6 mg/kg/day) for 2 weeks resulted in histopathological changes in the testis (increases in multinucleate cells, germ cell degeneration) at the highest dose. At the no-effect dose for testicular toxicity in monkeys, plasma exposures were approximately 3 times that in humans at the MRHD.

Oral administration of risdiplam to postweaning juvenile rats resulted in male reproductive toxicity (degeneration/necrosis of the testis seminiferous epithelium with associated oligo/azospermia in the epididymis and abnormal sperm parameters). The no-effect dose for adverse reproductive effects in postweaning male juvenile rats was associated with plasma



exposures approximately 4 times that in humans at the MRHD [see *Use in Specific Populations (8.4)*].

## **13.2 Animal Toxicology and/or Pharmacology**

### Retinal toxicity

Risdiplam-induced functional and structural retinal abnormalities were seen in animal studies. In a 39-week toxicity study in monkeys, oral administration of risdiplam (0, 1.5, 3, or 7.5/5 mg/kg/day; high dose lowered after 4 weeks) produced functional abnormalities on the electroretinogram (ERG) in all mid- and high-dose animals at the earliest examination time (Week 20). These findings were associated with retinal degeneration, detected by optical coherence tomography (OCT), on Week 22, the first examination time. The retinal degeneration, with peripheral photoreceptor loss, was irreversible. A no-effect dose for the retinal findings (1.5 mg/kg/day) was associated with plasma exposures (AUC) similar to that in humans at the maximum recommended human dose (MRHD) of 5 mg.

### Effect on Epithelial Tissues

Oral administration of risdiplam to rats and monkeys resulted in histopathological changes in epithelium of the gastrointestinal (GI) tract (apoptosis/single cell necrosis), lamina propria (vacuolation), the exocrine pancreas (single cell necrosis), the skin, tongue, and larynx (parakeratosis/hyperplasia/degeneration) with associated inflammation. The skin and GI epithelial effects were reversible. The no-effect doses for effects on epithelial tissues in rats and monkeys were associated with plasma exposures (AUC) similar to that in humans at the MRHD.

## **14 CLINICAL STUDIES**

The efficacy of EVRYSDI for the treatment of patients with infantile-onset, later-onset, and pre-symptomatic SMA was evaluated in three clinical studies, Study 1 (NCT02913482) and Study 2 (NCT02908685), and Study 3 (NCT03779334), respectively.

The overall findings of these studies support the effectiveness of EVRYSDI in SMA pediatric and adult patients and appear to support the early initiation of treatment with EVRYSDI.

### **14.1 Infantile-Onset SMA**

Study 1 was an open-label, 2-part study to investigate the efficacy, safety, pharmacokinetics, and pharmacodynamics of EVRYSDI for oral solution in patients with Type 1 SMA (symptom onset between 28 days and 3 months of age). All patients had genetic confirmation of homozygous deletion or compound heterozygosity predictive of loss of function of the SMN1 gene, and two SMN2 gene copies.

Part 1 of Study 1 was designed as a dose-finding study. Part 2 of Study 1 assessed the safety and efficacy of EVRYSDI at 0.20 mg/kg, the recommended dose determined in Part 1 [see *Dosage and Administration (2.4)*]. Patients from Part 1 did not take part in Part 2.

A total of 62 patients with symptomatic Type 1 SMA were enrolled in FIREFISH Part 1 (n = 21) and Part 2 (n = 41), of which 58 patients received the recommended dosage [see *Dosage and Administration (2.1)*]. The median age of onset of clinical signs and symptoms was 1.5 months (range: 0.9 to 3.0 months). The median age at enrollment was 5.6 months (range: 2.2 to 6.9 months), and the median time between onset of symptoms and the first dose was 3.7 months (range 1.0 to 6.0 months). Of these patients, 60% were female, 57% were Caucasian, and 29% were Asian. The demographics and baseline disease characteristics were comparable between Part 1 and Part 2 of the study.

Effectiveness was established based on the ability to sit without support for at least 5 seconds (as measured by Item 22 of the Bayley Scales of Infant and Toddler Development – Third Edition



(BSID-III) gross motor scale) and on the basis of survival without permanent ventilation. Permanent ventilation was defined as requiring a tracheostomy or more than 21 consecutive days of either non-invasive ventilation ( $\geq 16$  hours per day) or intubation, in the absence of an acute reversible event.

The primary endpoint was the proportion of patients with the ability to sit without support for at least 5 seconds (BSID-III gross motor scale, Item 22) after 12 months of treatment in Part 2; 29% of patients (n = 12/41) achieved this milestone.

Other efficacy endpoints of EVRYSDI-treated patients in Study 1 (pooled Part 1 and Part 2) are shown in Table 3.

**Table 3 Key Efficacy Results at Month 12 and Month 24 (Study 1, Parts 1 and Part 2)**

<b>Efficacy Endpoints</b>	<b>Proportion of Patients Parts 1 &amp; 2 at Month 12</b>	<b>Proportion of Patients Parts 1 &amp; 2 at Month 24</b>
Motor Function and Development Milestones	N = 58 <sup>a</sup>	
BSID-III, Item 22: sitting without support for at least 5 seconds	32.8%	60.3%
Survival and Event-Free Survival	N = 62 <sup>b</sup>	
Alive without Permanent Ventilation	87.1%	83.8%

<sup>a</sup> Results were pooled from all patients who received the recommended dose of risdiplam (all patients in Part 2 and those in the high-dose cohort of Part 1; n = 58).

<sup>b</sup> Results were pooled from all patients who received any dose of risdiplam in Part 1 and Part 2 (n = 62).

At Month 24, 40% (23/58) of patients who received the recommended dose achieved sitting without support for 30 seconds (BSID-III, Item 26). In addition at Month 24, patients continued to achieve additional motor milestones; 28% (16/58) of patients achieved a standing measure (16% [9/58] supporting weight and 12% [7/58] standing with support), as measured by Section 2 of the Hammersmith Infant Neurological Examination (HINE-2) which assesses motor milestones.

The proportion of patients alive without permanent ventilation (event-free survival) was 84% for all patients at Month 24 (Table 3). Out of 62 patients, 6 infants died (4 within the first 3 months following study enrollment) and one additional patient withdrew from treatment and died 3.5 months later. Four patients required permanent ventilation by Month 24. These results indicate a clinically meaningful deviation from the natural history of untreated infantile-onset SMA. As described in the natural history of untreated infantile-onset SMA, patients would not be expected to attain the ability to sit independently, and no more than 25% of these patients would be expected to survive without permanent ventilation beyond 14 months of age.

## 14.2 Later-Onset SMA

Study 2 was a 2-part, multicenter trial to investigate the efficacy, safety, pharmacokinetics, and pharmacodynamics of EVRYSDI for oral solution in patients diagnosed with SMA Type 2 or Type 3. Part 1 of Study 2 was dose-finding and exploratory in 51 patients (14% ambulatory). Part 2 was randomized, double-blind, placebo-controlled, and is described below.

The primary endpoint in Study 2 Part 2 was the change from baseline to Month 12 in the Motor Function Measure 32 (MFM32) score. A key secondary endpoint was the proportion of patients



with a 3-point or greater change from baseline to Month 12 in the MFM32 total score. The MFM32 measures motor function abilities that relate to daily functions. The total MFM32 score is expressed as a percentage (range: 0 to 100) of the maximum possible score, with higher scores indicating greater motor function. Another key secondary endpoint was the Revised Upper Limb Module (RULM). The RULM is a tool used to assess motor performance of the upper limb in SMA patients. It tests proximal and distal motor functions of the arm. The total score ranges from 0 (all the items cannot be performed) to 37 (all the activities are achieved fully without any compensatory maneuvers).

Study 2 Part 2 enrolled 180 non-ambulatory patients with Type 2 (71%) or Type 3 (29%) SMA. Patients were randomized 2:1 to receive EVRYSDI at the recommended dosage [*see Dosage and Administration (2.1)*] or placebo. Randomization was stratified by age group (2 to 5, 6 to 11, 12 to 17, or 18 to 25 years of age).

The median age of patients at the start of treatment was 9.0 years (range: 2 to 25), and the median time between onset of initial SMA symptoms and first treatment was 102.6 months (range: 1 to 275). Of the 180 patients included in the trial, 51% were female, 67% were Caucasian, and 19% were Asian. At baseline, 67% of patients had scoliosis (32% of them with severe scoliosis). Patients had a mean baseline MFM32 score of 46.1, and RULM score of 20.1. Overall baseline demographic characteristics were reasonably balanced between the treatment groups (EVRYSDI and placebo), with the exception of scoliosis (63% in the EVRYSDI arm vs. 73% in the placebo group).

The primary analysis on the change from baseline in MFM32 total score at Month 12 showed a clinically meaningful and statistically significant difference between patients treated with EVRYSDI and placebo. The results of the primary analysis and key secondary endpoints are shown in Table 4 and Figure 1.



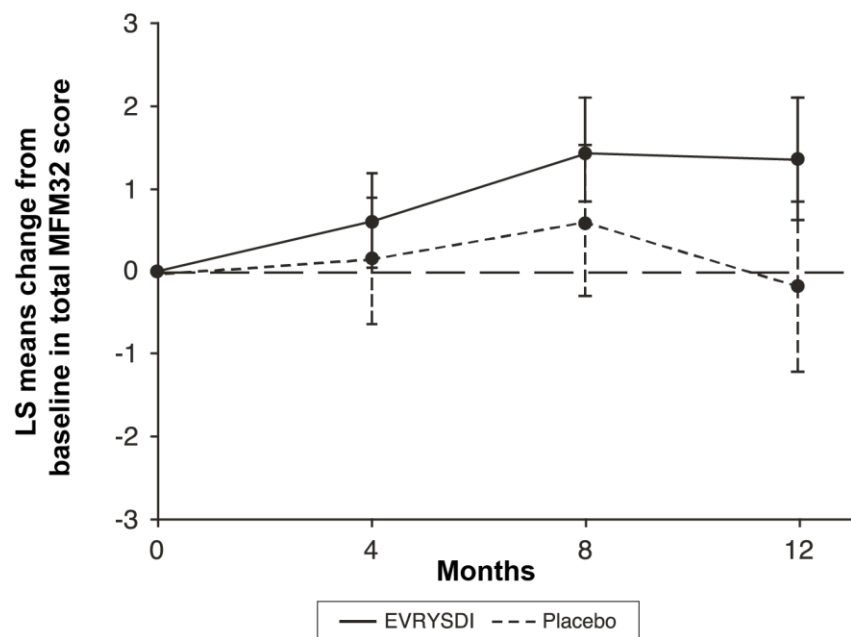
**Table 4 Summary of Efficacy in Patients with Later-Onset SMA at Month 12 of Treatment (Study 2 Part 2)**

Endpoint	EVRYSDI (N = 120)	Placebo (N = 60)
<b>Primary Endpoint:</b>		
Change from baseline in total MFM32 score at Month 12, LS means (95% CI) <sup>1,2,3</sup>	1.36 (0.61, 2.11)	-0.19 (-1.22, 0.84)
Difference from Placebo, Estimate (95% CI) <sup>1</sup> p-value	1.55 (0.30, 2.81) 0.0156	
<b>Secondary Endpoints:</b>		
Proportion of patients with a change from baseline MFM32 total score of 3 or more at Month 12 (95% CI) <sup>2,3</sup>	38.3% (28.9, 47.6)	23.7% (12.0, 35.4)
Odds ratio for overall response (95% CI) adjusted <sup>4</sup> (unadjusted) p-value <sup>5</sup>	2.35 (1.01, 5.44) 0.0469 (0.0469)	
Change from baseline in total score of RULM at Month 12, LS means (95% CI) <sup>1, 6</sup>	1.61 (1.00, 2.22)	0.02 (-0.83, 0.87)
Difference from Placebo, Estimate (95% CI) adjusted <sup>4</sup> (unadjusted) p-value <sup>1</sup>	1.59 (0.55, 2.62) 0.0469 (0.0028)	

- <sup>1</sup>. The Mixed Model Repeated Measure (MMRM) analysis included the change from baseline total score as the dependent variable and as independent variables the baseline total score, treatment group, time, treatment-by-time interaction, and the randomization stratification variable of age group (2 to 5, 6 to 11, 12 to 17, 18 to 25).
- <sup>2</sup>. The MFM total score was calculated according to the user manual, expressed as a percentage of the maximum score possible for the scale (i.e., sum of the 32 item scores divided by 96 and multiplied by 100).
- <sup>3</sup>. Based on the missing data rule for MFM32, 6 patients were excluded from the analysis (EVRYSDI n = 115; placebo control n = 59).
- <sup>4</sup>. The adjusted p-value was obtained for the endpoints included in the hierarchical testing and was derived based on all the p-values from endpoints in order of the hierarchy up to the current endpoint.
- <sup>5</sup>. The logistic regression analysis included the baseline total score, treatment and age group as independent variables.
- <sup>6</sup>. Based on the missing data rule for RULM, 3 patients were excluded from the analysis (EVRYSDI n = 119; placebo control n = 58).



**Figure 1 Mean Change from Baseline in Total MFM32 Score Over 12 Months (Study 2 Part 2)<sup>1,2</sup>**



<sup>1</sup> Error bars denote the 95% confidence interval.

<sup>2</sup> The MFM total score was calculated according to the user manual, expressed as a percentage of the maximum score possible for the scale (i.e., sum of the 32 item scores divided by 96 and multiplied by 100).

### 14.3 Pre-Symptomatic SMA

Study 3 was an open-label, single-arm, multicenter clinical study to investigate the efficacy, safety, pharmacokinetics, and pharmacodynamics of EVRYSDI in infants up to 6 weeks of age (at first dose) who have been genetically diagnosed with SMA but do not yet present with symptoms.

The efficacy in pre-symptomatic SMA patients was evaluated at Month 12 in 26 patients treated with EVRYSDI in Study 3: 8 patients had 2 copies of the *SMN2* gene, 13 patients had 3 copies, and 5 patients had 4 or more copies. The median age of these patients at first dose was 25 days (range: 16 to 41), 62% were female, and 85% were Caucasian. The primary efficacy population (N = 5) included patients with 2 *SMN2* copies and a baseline CMAP amplitude  $\geq 1.5$  mV.

The primary efficacy endpoint was the proportion of patients with the ability to sit without support for at least 5 seconds (BSID-III gross motor scale, Item 22) at Month 12. This milestone was achieved by 80% (4/5) of patients in the primary efficacy population. This milestone was also achieved by 87.5% (7/8) of all patients with 2 copies of *SMN2* and 96.2% (25/26) of patients in the full treated population.

At Month 12, 80.8% (21/26) of patients in the full treated population achieved sitting without support for 30 seconds (BSID-III, Item 26). Of the 26 patients treated with EVRYSDI, 25 patients had motor milestones measured by the HINE-2 at Month 12. Of these, 24 (96%) achieved sitting (23 patients could pivot/rotate and 1 achieved stable sit); 21 (84%) could stand (13 patients could stand unaided and 8 could stand with support); and 12 (48%) could walk independently. Seven patients were not tested for walking at Month 12. All 26 patients were alive at 12 months without permanent ventilation.



## 16 HOW SUPPLIED/STORAGE AND HANDLING

### 16.1 EVRYSDI for Oral Solution

#### How Supplied

Each amber glass bottle of EVRYSDI for oral solution is packaged with a bottle adapter, two 1 mL reusable oral syringes, two 6 mL reusable oral syringes, and one 12 mL reusable oral syringe. EVRYSDI for oral solution is a light yellow, pale yellow, yellow, greyish yellow, greenish yellow, or light green powder. Each bottle contains 60 mg of risdiplam (NDC 50242-175-07).

#### Storage and Handling

Store the dry powder at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C to 30°C (59°F to 86°F) [*see USP controlled room temperature*]. Keep in the original carton.

Keep the constituted oral solution of EVRYSDI in the original amber bottle to protect from light. Store in a refrigerator at 2°C to 8°C (36°F to 46°F) [*see Dosage and Administration (2.4)*].

### 16.2 EVRYSDI Tablets

#### How Supplied

Pale yellow film-coated tablet, round and curved, with EVR debossed on one side; available in HDPE bottles of 30 tablets with a child-resistant cap (NDC 50242-202-01).

#### Storage and Handling

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [*see USP Controlled Room Temperature*]. Keep the bottle tightly closed in order to protect from moisture.

## 17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

#### Pregnancy and Fetal Risk

Inform pregnant women and women of reproductive potential that, based on animal studies, EVRYSDI may cause fetal harm [*see Use in Specific Populations (8.1)*].

Discuss with women of childbearing age whether they are pregnant, might be pregnant, or are trying to become pregnant.

Advise women of childbearing potential to use effective contraception during treatment with EVRYSDI and for at least 1 month after stopping EVRYSDI.

Advise a female patient to immediately inform the prescriber if she is pregnant or planning to become pregnant [*see Use in Specific Populations (8.3)*].

#### Pregnancy Registry

Encourage patients to enroll in the EVRYSDI Pregnancy Registry if they become pregnant while taking EVRYSDI [*see Use in Specific Populations (8.1)*].

#### Potential Effects on Male Fertility

Advise male patients that their fertility may be compromised while on treatment with EVRYSDI [*see Use in Specific Populations (8.3)*].

#### Instructions for Preparation of Oral Solution



Advise patients/caregivers to ensure that EVRYSDI oral solution is in liquid form when received from the pharmacy.

Instruct patients/caregivers to take EVRYSDI oral solution with or without food or before or after breastfeeding at approximately the same time each day. However, instruct caregivers not to mix EVRYSDI with formula or milk.

Instruct patients/caregivers to take EVRYSDI oral solution immediately after it is drawn up into the reusable oral syringe [see *Dosage and Administration (2.1)*].

#### Instructions for EVRYSDI Tablets

Advise patients/caregivers to swallow EVRYSDI tablets whole with water. Do not chew, cut, or crush the tablets.

Alternatively, the tablet can be dispersed in one teaspoon (5 mL) of room temperature non-chlorinated drinking water (e.g., filtered water) and taken immediately. EVRYSDI tablets must not be dispersed in any liquid other than non-chlorinated drinking water. Instruct the patient/caregivers that the dispersion must be administered within 10 minutes of adding non-chlorinated drinking water, or it must be discarded.

Advise patients/caregivers that the EVRYSDI tablet dispersion is for oral administration only. If administration through a nasogastric/gastrostomy tube is required, EVRYSDI for oral solution should be used.

Advise patients/caregivers to wash their hands before and after preparing or taking EVRYSDI tablets.

Advise patients/caregivers to avoid getting the dispersed tablet on their skin or in their eyes. Advise patients/caregivers to wash the area with soap and water if the dispersed tablet gets on the skin. Advise patients/caregivers to rinse their eyes with water if the dispersed tablet gets in the eyes.

Advise patients/caregivers to use a dry paper towel to dry the area if the dispersion is spilled and then clean with soap and water. Advise patients/caregivers to throw the paper towel away in the trash and wash their hands with soap and water.

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EVRYSDI® [risdiplam]

Distributed by:

**Genentech, Inc.**

A Member of the Roche Group

1 DNA Way

South San Francisco, CA 94080-4990

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## Patient Information

**EVERYSDI® [ev-RIZ-dee]  
(risdiplam)  
for oral solution**

**EVERYSDI® [ev-RIZ-dee]  
(risdiplam)  
tablets**

### What is EVERYSDI?

- EVERYSDI is a prescription medicine used to treat spinal muscular atrophy (SMA) in children and adults.

### Before taking EVERYSDI, tell your healthcare provider about all of your medical conditions, including if you:

- are pregnant or plan to become pregnant. If you are pregnant, or are planning to become pregnant, ask your healthcare provider for advice before taking this medicine. EVERYSDI may harm your unborn baby.
- are a woman who can become pregnant:
  - Before you start your treatment with EVERYSDI, your healthcare provider may test you for pregnancy. Because EVERYSDI may harm your unborn baby, you and your healthcare provider will decide if taking EVERYSDI is right for you during this time.
  - Talk to your healthcare provider about birth control methods that may be right for you. Use birth control while on treatment and for at least 1 month after stopping EVERYSDI.
  - **Pregnancy Registry.** There is a pregnancy registry for women who take EVERYSDI during pregnancy. The purpose of this registry is to collect information about the health of the pregnant woman and her baby. If you are pregnant or become pregnant while receiving EVERYSDI, tell your healthcare provider right away. Talk to your healthcare provider about registering with the EVERYSDI Pregnancy Registry. Your healthcare provider can enroll you in this registry or you can enroll by calling 1-833-760-1098 or visiting <https://www.evrysdipregnancyregistry.com>.
- are an adult male planning to have children: EVERYSDI may affect a man's ability to have children (fertility). If this is of concern to you, make sure to ask a healthcare provider for advice.
- are breastfeeding or plan to breastfeed. It is not known if EVERYSDI passes into breast milk and may harm your baby. If you plan to breastfeed, discuss with your healthcare provider about the best way to feed your baby while on treatment with EVERYSDI.

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Keep a list of them to show your healthcare provider, including your pharmacist, when you get a new medicine.

### How should I take EVERYSDI?

- For infants and children, your healthcare provider will determine the daily dose of EVERYSDI needed based on your child's age and weight. For adults, take 5 mg of EVERYSDI daily.
- Your healthcare provider will either prescribe:  
EVERYSDI for oral solution  
**Or**  
EVERYSDI tablet
- Your healthcare provider will tell you how long you or your child needs to take EVERYSDI. Do not stop treatment with EVERYSDI unless your healthcare provider tells you to.
  - Take EVERYSDI exactly as your healthcare provider tells you to take it. Do not change the dose without talking to your healthcare provider.
- Avoid getting EVERYSDI on your skin or in your eyes. If it gets on your skin, wash the area with soap and water. If it gets in your eyes, rinse your eyes with water.

### If you are taking EVERYSDI for oral solution:

- **see the detailed Instructions for Use that comes with it for information on how to take or give EVERYSDI for oral solution**
- You should receive EVERYSDI from the pharmacy as a liquid that can be given by mouth or through a feeding tube. The liquid solution is prepared by your pharmacist or other healthcare provider. If the medicine in the bottle is a powder, **do not use it**. Contact your pharmacist for a replacement.
- Take EVERYSDI one time daily with or without a meal at about the same time each day. Drink water afterwards to make sure EVERYSDI has been completely swallowed.
- In infants who are breastfed, EVERYSDI can be given before or after breastfeeding.
- Do not mix EVERYSDI with formula or milk.
- If you are unable to swallow and have a nasogastric (NG-tube) or gastrostomy tube (G-tube), EVERYSDI for oral solution can be given through the tube.



### Reusable Oral Syringes for EVRYSDI for Oral Solution

- Your pharmacist will provide you with the reusable oral syringes that are needed for taking your medicine and explain how to use them. You should receive 1 or 2 identical oral syringes depending on your prescribed daily dose.
- From the bottle, draw up (measure) the dose of EVRYSDI with these syringes, as they are made to protect the medicine from light.
- Take EVRYSDI right away after it has been drawn into the syringe. Do not store the EVRYSDI solution in the syringe. If EVRYSDI is not taken within 5 minutes of when it is drawn up, throw away the solution by pressing the plunger and prepare a new dose with the same syringe.
- Do not throw the syringes away because they are reusable.
- Wash the syringes per instructions after use.
- Contact your healthcare provider or pharmacist if your oral syringes are lost or damaged.

### If you are taking EVRYSDI Tablets:

- Take EVRYSDI one time daily with or without a meal at about the same time each day.
- Do not chew, cut, or crush the tablet.
- Swallow the EVRYSDI tablet whole with some water.

### Or

- You can take an EVRYSDI tablet by mouth after it is mixed with a teaspoon (5 mL) of room temperature non-chlorinated drinking water (e.g., filtered water). See the instructions below for taking EVRYSDI this way.

### EVRYSDI Tablets Mixed with Non-chlorinated Drinking Water (e.g., Filtered Water)

- Wash your hands before and after preparing or taking EVRYSDI tablets.
- Put EVRYSDI tablets in a small cup with a teaspoon (5 mL) of room temperature non-chlorinated drinking water (e.g., filtered water).
- Do not mix EVRYSDI tablets with any liquids other than non-chlorinated drinking water.
- Do not expose the EVRYSDI tablet mixture to sunlight.
- Swirl the cup gently until the tablet and non-chlorinated drinking water are fully mixed (though some particles may remain). This may take up to 3 minutes.
- Take EVRYSDI tablet mixture right away after mixing with non-chlorinated drinking water. If you do not take it within 10 minutes of adding non-chlorinated drinking water, throw the mixture away and make a new dose.
- After taking EVRYSDI tablet mixture, to make sure there is no medicine left, refill the small cup with at least a tablespoon (15 mL) of non-chlorinated drinking water, swirl, and take right away.
- If the EVRYSDI tablet mixture is spilled, use a dry paper towel to dry the area and then clean with soap and water. Throw the paper towel away in the trash and wash your hands with soap and water.
- Do not give the EVRYSDI tablet mixture via a nasogastric (NG-tube) or gastrostomy tube (G-tube).

### If you miss a dose of EVRYSDI:

- If you remember the missed dose within 6 hours of when you normally take EVRYSDI, then take the dose. Continue taking EVRYSDI at your usual time the next day.
- If you remember the missed dose more than 6 hours after you normally take EVRYSDI, skip the missed dose. Take your next dose at your usual time the next day.
- If you do not fully swallow the dose, or you vomit after taking a dose, **do not take** another dose of EVRYSDI to make up for that dose. Wait until the next day to take the next dose at your usual time.

### What are the possible side effects of EVRYSDI?

#### The most common side effects of EVRYSDI include:

- **For later-onset SMA:**
  - fever
  - diarrhea
  - rash
- **For infantile-onset SMA:**
  - fever
  - runny nose, sneezing, and sore throat (upper respiratory infection)
  - constipation
  - diarrhea
  - lung infection (lower respiratory infection)
  - vomiting
  - rash
  - cough



These are not all of the possible side effects of EVRYSDI. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

### **How should I store EVRYSDI?**

#### **EVRYSDI for Oral Solution:**

- Store EVRYSDI in the refrigerator between 36°F to 46°F (2°C to 8°C). Do not freeze.
- If necessary, EVRYSDI can be kept at room temperature up to 104°F (up to 40°C) for a combined total of 5 days. EVRYSDI can be removed from, and returned to, a refrigerator. The total combined time out of refrigeration should not be more than 5 days.
- Keep EVRYSDI in an upright position in the original amber bottle to protect from light.
- Throw away (discard) any unused portion of EVRYSDI 64 days after it is mixed by the pharmacist (constitution) or if EVRYSDI has been kept at room temperature (below 104°F [40°C]) for more than a total combined time of 5 days. Discard EVRYSDI if it has been kept above 104°F (40°C). Please see the Discard After date written on the bottle label. (See the **Instructions for Use** that comes with EVRYSDI for oral solution).

#### **EVRYSDI Tablets:**

- Store at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep the bottle tightly closed in order to protect from moisture.

**Keep EVRYSDI, all medicines and syringes out of the reach of children.**

### **General information about the safe and effective use of EVRYSDI.**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use EVRYSDI for a condition for which it was not prescribed. Do not give EVRYSDI to other people, even if they have the same symptoms you have. It may harm them. You can ask your pharmacist or healthcare provider for information about EVRYSDI that is written for health professionals.

### **What are the ingredients in EVRYSDI?**

**Active ingredient:** risdiplam

**Inactive ingredients:**

**EVRYSDI for Oral Solution:** ascorbic acid, disodium edetate dihydrate, isomalt, mannitol, polyethylene glycol 6000, sodium benzoate, strawberry flavor, sucralose, and tartaric acid.

**EVRYSDI Tablets:** colloidal silicon dioxide, crospovidone, mannitol, microcrystalline cellulose, polyethylene glycol 3350, polyvinyl alcohol, sodium stearyl fumarate, strawberry flavor, talc, tartaric acid, titanium dioxide, and yellow iron oxide.

Distributed by: **Genentech, Inc.**, A Member of the Roche Group, 1 DNA Way, South San Francisco, CA 94080-4990

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For more information, go to [www.EVRYSDI.com](http://www.EVRYSDI.com) or call 1-833-387-9734.