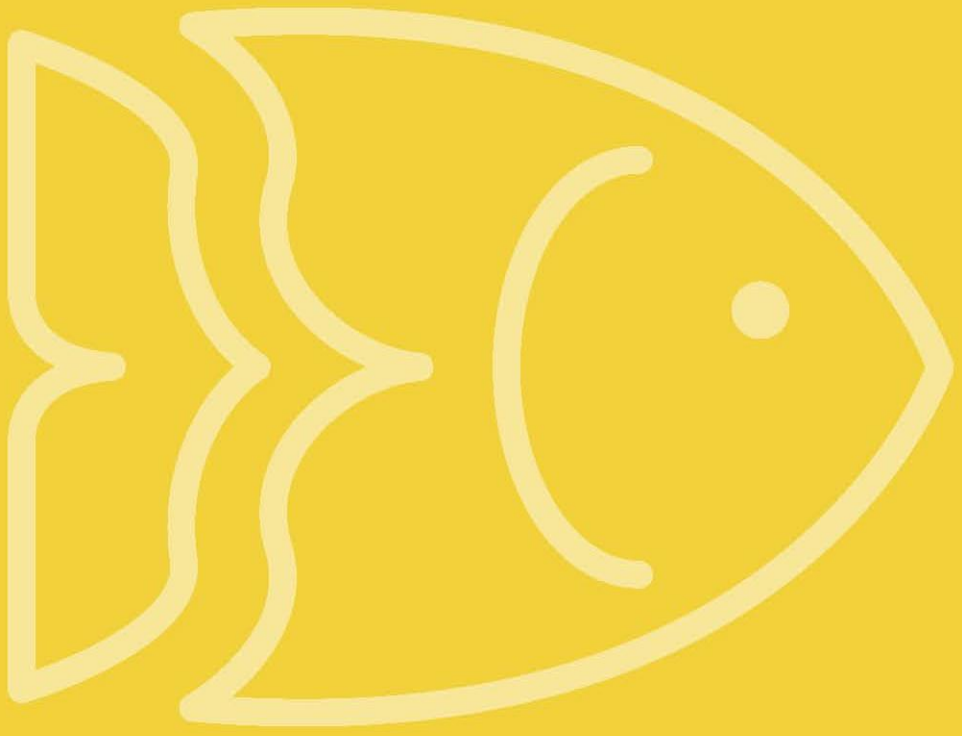
A summary of the final results of SUNFISH, a clinical trial to establish the efficacy and safety of risdiplam in children, adolescents and adults with Type 2 or 3 SMA



See the end of the document for the full title of the study

Date of preparation: September 2024 | M-XX-00017650

About this summary

This is a summary of the results of a clinical trial (called a 'study' in this document). It has been written for members of the public and for people who took part in the study.

The SUNFISH study started in October 2016 and finished in October 2023 when the last person to join the study completed 5 years on the study. This summary was written after the study had ended. The drug being investigated in this study was risdiplam.

SUNFISH met its main aims (endpoints) in September 2019, when the last participant in SUNFISH Part 2 had completed 1 year in the study.

This summary focusses on the long-term safety findings (side effects) following treatment with risdiplam for up to 5 years.

This summary includes the following information:

Previous documents were made that provided a summary of results of the SUNFISH study after patients had completed 1 and 2 years of treatment.

Please click here to view the Year 1 summary and here to view the Year 2 summary.

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What is SMA?

Spinal muscular atrophy (SMA) is a rare, genetic neuromuscular disease, which destroys muscle-controlling nerve cells called motor neurons.

SMA destroys muscle-controlling nerve cells in the spinal cord called motor neurons.

The loss of motor neurons causes muscle weakness and loss of movement due to muscle wasting (atrophy).

People living with SMA have difficulty performing the basic functions of life, including breathing and swallowing.

The severity of SMA varies between people and depends on a range of factors, including age at which symptoms begin. There are five types of SMA, based on the age that symptoms begin, and the highest physical milestone achieved (such as being able to sit or walk).

Types of SMA

SMA type	Age that symptoms start	Impact
0	Before birth	Infants have reduced movement in the womb and are born with severe muscle weakness
1	Birth to 6 months	Children with this form of SMA will never sit independently
2	6 to 18 months	Children are typically able to sit, and some may stand with assistance, but they are not able to walk
3	18 months onwards	Children can walk, but may lose the ability over time
4	18 years onwards	This form of SMA develops in adulthood. This is the least severe SMA type

SMA, spinal muscular atrophy.

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Why was this study done?

When this study started, there were no treatments for people with SMA.

The goal of new treatments is to treat the underlying cause of SMA, help people with SMA live longer, reduce overall symptoms, maintain a person's ability to move (motor function), and improve quality of life.

The SUNFISH study was carried out to understand the safety and efficacy (how well a treatment works) of risdiplam in people with Type 2 or Type 3 SMA, who were aged between 2 years and 25 years when they entered the study.

Other studies taking place at the same time looked at how risdiplam worked in people of different ages and with different types of SMA.

SMA, spinal muscular atrophy.

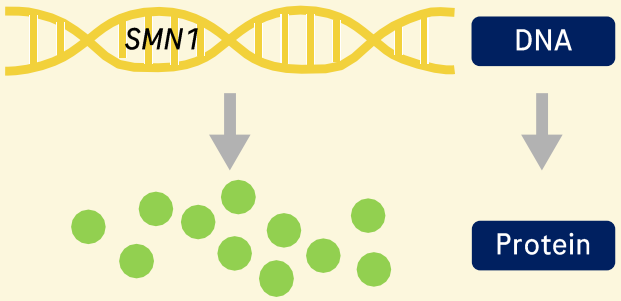
What causes SMA? (1/2)

SMA is caused by low levels of a protein called 'survival of motor neuron' (also known as SMN protein).

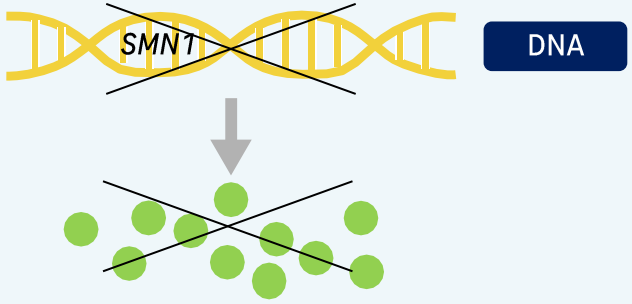
SMN protein is critical to the function of the nerves that control the muscles. Without high enough levels of SMN protein, these nerves stop working properly (degenerate) and eventually die, causing muscles to become weak and waste away.

SMN protein is mostly made by a gene called 'survival of motor neuron 1' (also known as *SMN1*).

In healthy people, *SMN1* produces SMN protein



People with SMA have a change (mutation) in the *SMN1* gene that stops it from making SMN protein



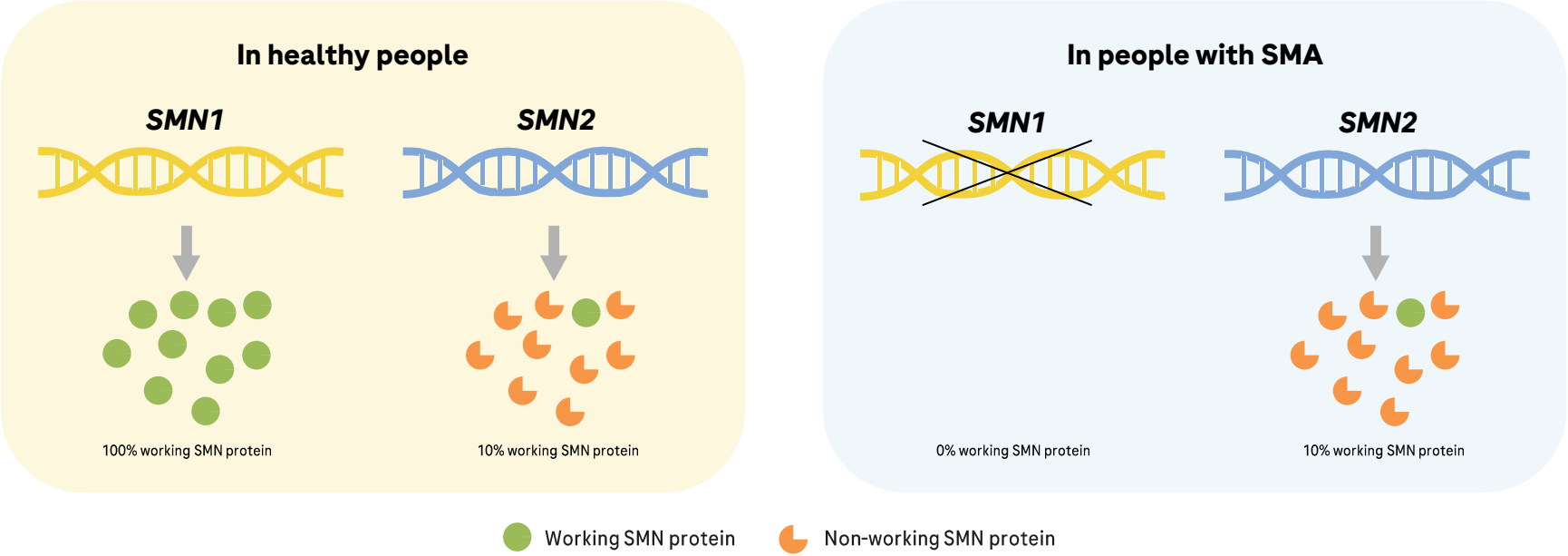
SMA, spinal muscular atrophy; SMN, survival of motor neuron.

What causes SMA? (2/2)

People have a similar gene called survival of motor neuron 2 (also known as *SMN2)* which can act as a 'back-up' gene to make SMN protein. People with SMA need to use *SMN2* to make SMN protein as they do not have *SMN1*.

However, only about 1 in 10 (10%) of the SMN protein produced by *SMN2* works properly. This is not enough protein to make up for the loss of the *SMN1* gene.

The more copies of the *SMN2* gene a person has, the more SMN protein they can produce, which makes the symptoms of SMA less severe.



SMA, spinal muscular atrophy; SMN, survival of motor neuron.

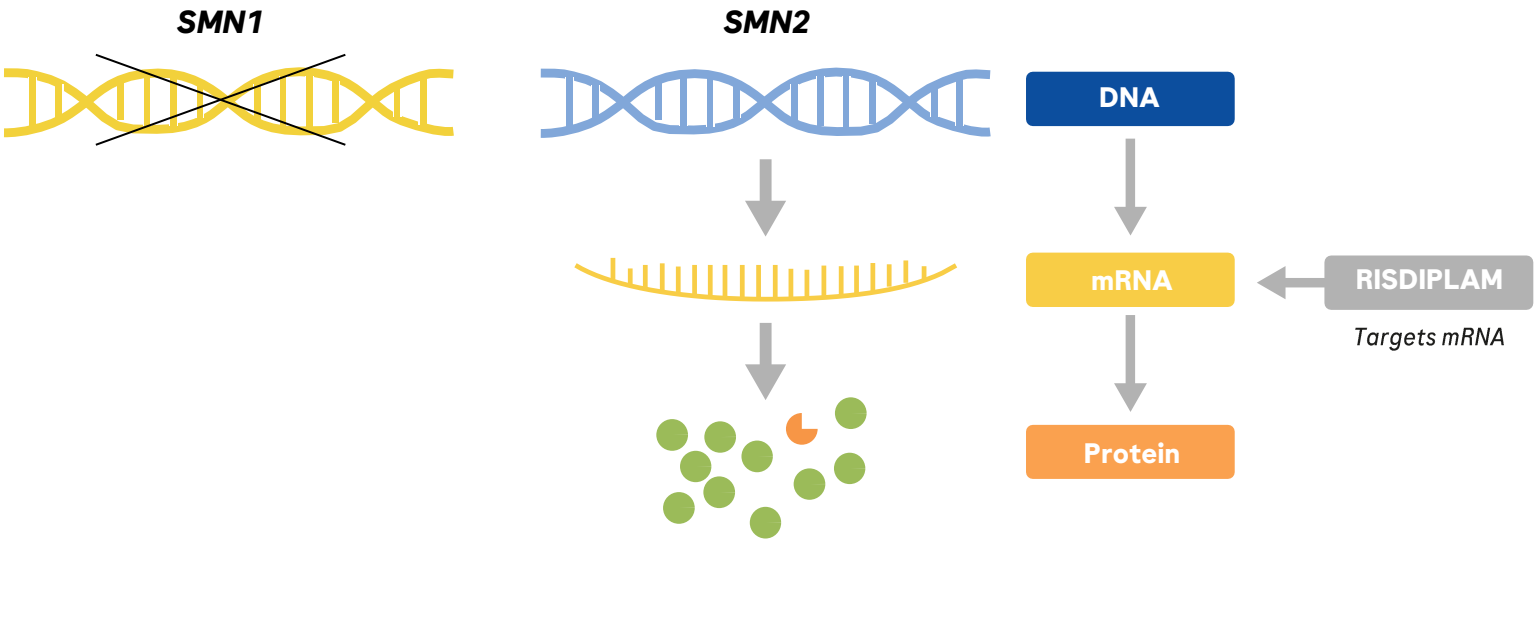
What is risdiplam, and how does it work?

Risdiplam is the drug that was studied in SUNFISH.

Risdiplam is a liquid taken once a day by mouth (orally) or by feeding tube for those with difficulty swallowing.

Risdiplam is designed to help the *SMN2* gene to produce more working SMN protein to maintain and improve muscle function.

The instructions from the *SMN2* gene are faulty, and most of the SMN protein produced doesn't work. Risdiplam targets the instructions (mRNA) from the *SMN2* gene to make more SMN protein that works.



SMA, spinal muscular atrophy; SMN, survival of motor neuron.

What were the aims of the study?

The SUNFISH study aimed to answer many different questions about risdiplam.

To understand the effects of risdiplam and help answer the researchers' different questions, the study included certain outcome measures (endpoints).

- **A primary endpoint** aims to answer the main research question. The study is considered successful if this outcome or event happens (the primary endpoint is met)
- **Secondary endpoints** provide more information to help understand the effects of the treatment that is being studied.
- **Exploratory endpoints** are outcomes that are included to help researchers explore new questions about the treatment.

The SUNFISH study was divided into two parts:

SUNFISH Part 1 tested different doses of risdiplam to identify potential side effects and to look at how well risdiplam worked within the body to increase SMN protein levels in children, adolescents and adults with Type 2 or Type 3 SMA.

The results from Part 1 were used to select the dose of risdiplam that was used to treat the people taking part in SUNFISH Part 2.

SUNFISH Part 2 tested the efficacy (how well the medicine worked) and safety of risdiplam in children, adolescents and adults with Type 2 or Type 3 SMA. People who received risdiplam in Part 2 were given the most effective dose based on the research in Part 1.

Both parts of the SUNFISH study are now complete.

SMA, spinal muscular atrophy; SMN, survival of motor neuron.

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What did the researchers want to find out in SUNFISH Part 1?

What were the main things (the primary endpoints) that researchers wanted to find out in SUNFISH Part 1?

SUNFISH Part 1 had two **primary endpoints**:

1. To evaluate the **safety**, **tolerability**, **pharmacokinetics** and **pharmacodynamics** of risdiplam in people with Type 2 and Type 3 SMA.

Safety and tolerability refers to the number and seriousness of the side effects associated with a particular medicine.

Pharmacokinetics (shortened to **PK**) looks at the levels of the medicine in blood.

Pharmacodynamics (shortened to **PD**) refers to how the medicine works in the body and the effects it has (for example the effects of risdiplam on SMN mRNA and SMN protein levels).

2. To select the dose for use in SUNFISH Part 2.

PD, pharmacodynamics; PK, pharmacokinetics; SMN, survival of motor neuron.

What did the researchers want to find out in SUNFISH Part 2?

What was the main question (the primary endpoint) that researchers wanted to answer in SUNFISH Part 2?

- The **primary endpoint** of SUNFISH Part 2 was to investigate the efficacy of risdiplam (i.e. how well risdiplam works).
- This was assessed by measuring how the physical abilities of the people taking part in the study changed over time. This was measured using the **32-item Motor Function Measure** assessment scale (also known as the **MFM32**).

What were other important questions (the secondary endpoints) that researchers wanted to answer in SUNFISH Part 2?

- What percentage of people taking part stabilised or improved in physical ability as measured by the MFM32?
- What was the change in physical ability over time as measured by the total score on the **Revised Upper Limb Module** assessment scale (also known as the **RULM**) ?
- What was the change in physical ability over time as measured by the total score on the **Hammersmith Functional Motor Scale – Expanded** assessment scale (also known as the **HFMSE**)?
- What was the change in the level of help required to perform daily activities over time as measured by the total score on the **SMA Independence Scale – Upper Limb Module** (also known as the **SMAIS-ULM**)?

See pages 13–16 for a description of the MFM32, RULM, HFMSE and SMAIS-ULM

SMA, spinal muscular atrophy.

How did the researchers assess physical ability in SUNFISH?

Researchers used three assessment scales to measure the physical abilities of the people who took part in SUNFISH.

The 32-item Motor Function Measure (MFM32)

- The MFM32 measures the movement of people with neuromuscular diseases, such as SMA.
- It helps assess people with a range of disease severities and ages.
- The MFM32 measures how well a person can move by measuring three functions:

Standing position and transfers (how well a person can do activities that involve standing)

Axial and proximal limb function (how well a person can do activities using the trunk and head [axial function], and the shoulders and upper arms [proximal function])

Distal limb motor function (how well a person can do activities using their forearms, hands, fingers and feet)

The Hammersmith Functional Motor Scale – Expanded (HFMSE)

- The HFMSE measures gross motor function.
- 'Gross' motor function looks at how well a person can move using large muscles in their arms, legs and torso. This could be measured by seeing if a person can move from their bed to their wheelchair or stand up from sitting.
- The HFMSE is an assessment scale that was developed specifically for SMA.
- The HFMSE helps measure gross motor skills in stronger people with SMA who can sit or walk.

The Revised Upper Limb Module (RULM)

- The RULM measures movement and coordination (motor function) of the arm, forearm and hand (upper limb).
- The RULM was designed to complement the HFMSE and was developed specifically for people with SMA.
- People who have very limited mobility may not be able to complete many items of the HFMSE that focusses on the legs (lower limbs).
- The RULM measures abilities or movements that are needed to perform daily activities, such as drinking from a cup.

SMA, spinal muscular atrophy.

For more information, please see the brochure 'Understanding the MFM and the SMAIS in the context of outcome measurements in SMA'.

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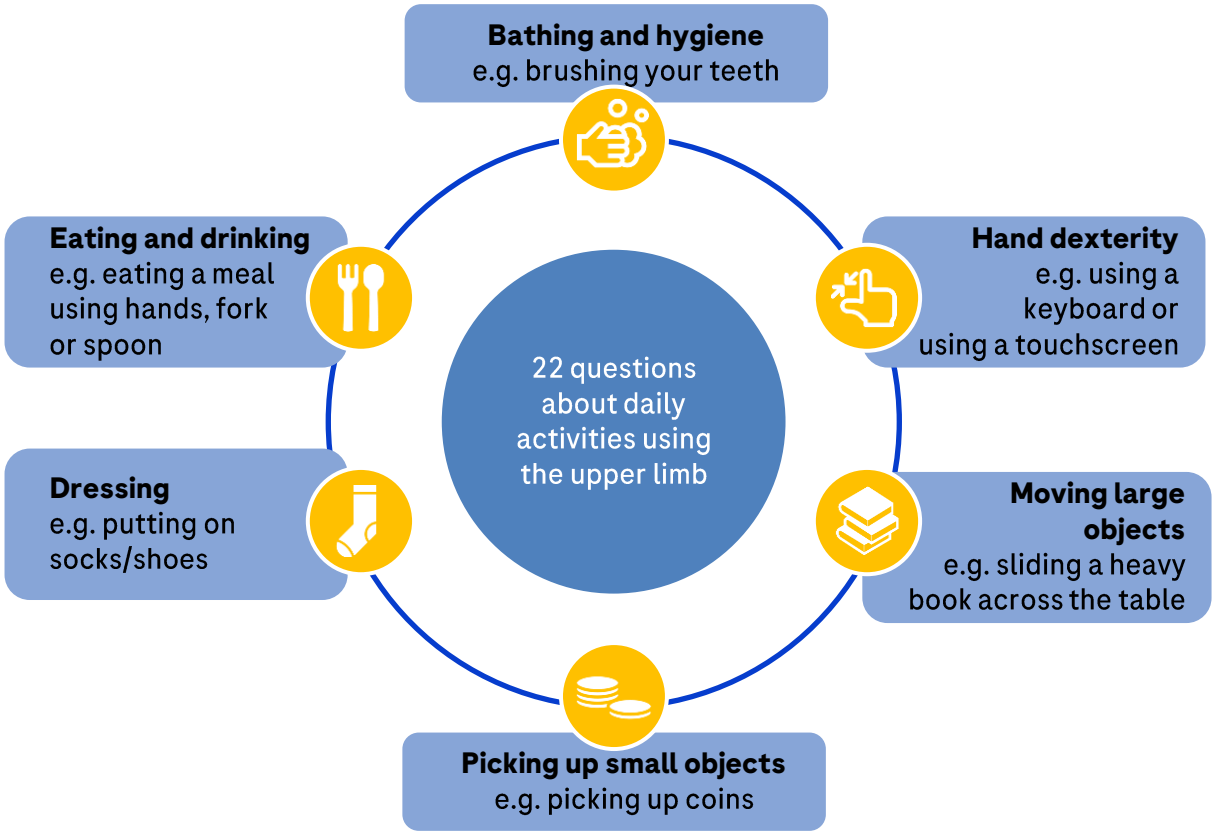
How did researchers assess independence in SUNFISH?

Researchers used the **SMA Independence Scale–Upper Limb Module (SMAIS-ULM)** to assess independence in SUNFISH.

- Independence can be measured by testing how much help a person needs to perform certain daily activities, such as brushing their teeth, getting dressed or drinking from a cup.
- The SMAIS-ULM includes 22 questions about daily activities that use the arm, forearm and hand (upper limb).

The SMAIS-ULM was completed by the people taking part in SUNFISH (if they were at least 12 years old) and by their caregivers.



For more information, please see the brochure 'Understanding the MFM and the SMAIS in the context of outcome measurements in SMA'.

SMA, spinal muscular atrophy.

How was the SUNFISH study designed?

The SUNFISH study was a '**double-blind**, **placebo-controlled** and **randomised**' study:

'Double-blind' means that neither the researchers nor the people taking part in the study knew which treatment each person was given.

'Placebo-controlled' means that people taking part were given either the study drug (risdiplam) or a 'placebo'. A placebo looks the same as the study drug but has no medicine inside.

'Randomised' means that the people taking part were assigned to the risdiplam or placebo group by chance (similar to flipping a coin). In SUNFISH, the individuals were randomly placed in a group using a computer program.

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When and where did the study take place?

The SUNFISH study started in October 2016 and finished in October 2023. This summary was written after the study had ended.

SUNFISH was a global clinical trial that took place in 43 hospitals across 15 countries. The map below shows where the study took place.

The countries that took part in the SUNFISH study were:

- Belgium
- Brazil
- Canada
- China
- Croatia
- France
- Germany
- Italy
- Japan
- Poland
- Russia
- Serbia
- Spain
- Turkey
- USA

Who could take part in the study?

The SUNFISH study included children, adolescents and adults with Type 2 or Type 3 SMA, aged between 2 and 25 years at the time they entered the study.

The following were the main requirements for people to take part in the study:

Main inclusion criteria	Main exclusion criteria
People could take part in Part 1 if they: • Had Type 2 or 3 SMA **People could take part in Part 2 if they:** • Had Type 2 or non-ambulant Type 3 SMA *(non-ambulant means unable to walk 10 m without help)* • Scored at least 2 on the RULM entry Item A (can raise 1 hand or 2 hands to mouth but cannot raise a cup with a 200 g weight in it to mouth) • Were able to sit independently	**People could not take part in either Part 1 or Part 2 if they:** • Had taken part in another clinical trial within the past 3 months • Had previously received gene or cell therapy • Had experienced any recent emergencies needing an overnight stay in hospital or major illnesses from which they had not fully recovered • Had recently developed eye disease

Full details of the inclusion/exclusion criteria can be found at:
https://clinicaltrials.gov/ct2/show/NCT02908685.

RULM, Revised Upper Limb Module; SMA, spinal muscular atrophy.

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What happened during SUNFISH Part 1?

Different groups of people were randomised to receive either different doses of risdiplam or placebo.

The study drug (either risdiplam or placebo) was taken once every day for 12 weeks.

After the first 12 weeks, the people who were on placebo started to receive risdiplam.

When the dose was decided on for use in Part 2, everyone then received risdiplam at the selected dose until the study finished. This was the **open-label** phase of the study.

'Open label' means that both the researchers and people taking part knew which medicine was being given.

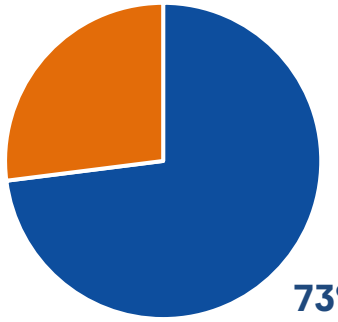
SUNFISH Part 1 enrolled 51 people

47% (24 out of 51 people) were male

53% (27 out of 51 people) were female

People were aged between 2 and 24 years

7 The average age at enrolment was 7 years



27% (14 out of 51 people) Type 3 SMA

73% (37 out of 51 people) had Type 2 SMA

57% (29 out of 51) had scoliosis (a curvature of the spine) at the start of the study

SMA, spinal muscular atrophy.

What were the main results of SUNFISH Part 1?

The main aim (primary endpoint) of SUNFISH Part 1 was to decide on the recommended dose of risdiplam for the treatment of people with Type 2 or Type 3 SMA

People taking part in Part 1 received different doses of risdiplam. The recommended dose was decided on once everyone taking part had completed at least 12 weeks of treatment with risdiplam.

Researchers looked at the results for the different doses of risdiplam used in Part 1.

The most suitable dose was chosen, and this was used in SUNFISH Part 2.

Once the dose was chosen for Part 2, everyone taking part in SUNFISH Part 1 was switched to receive that same dose of risdiplam until the study finished.

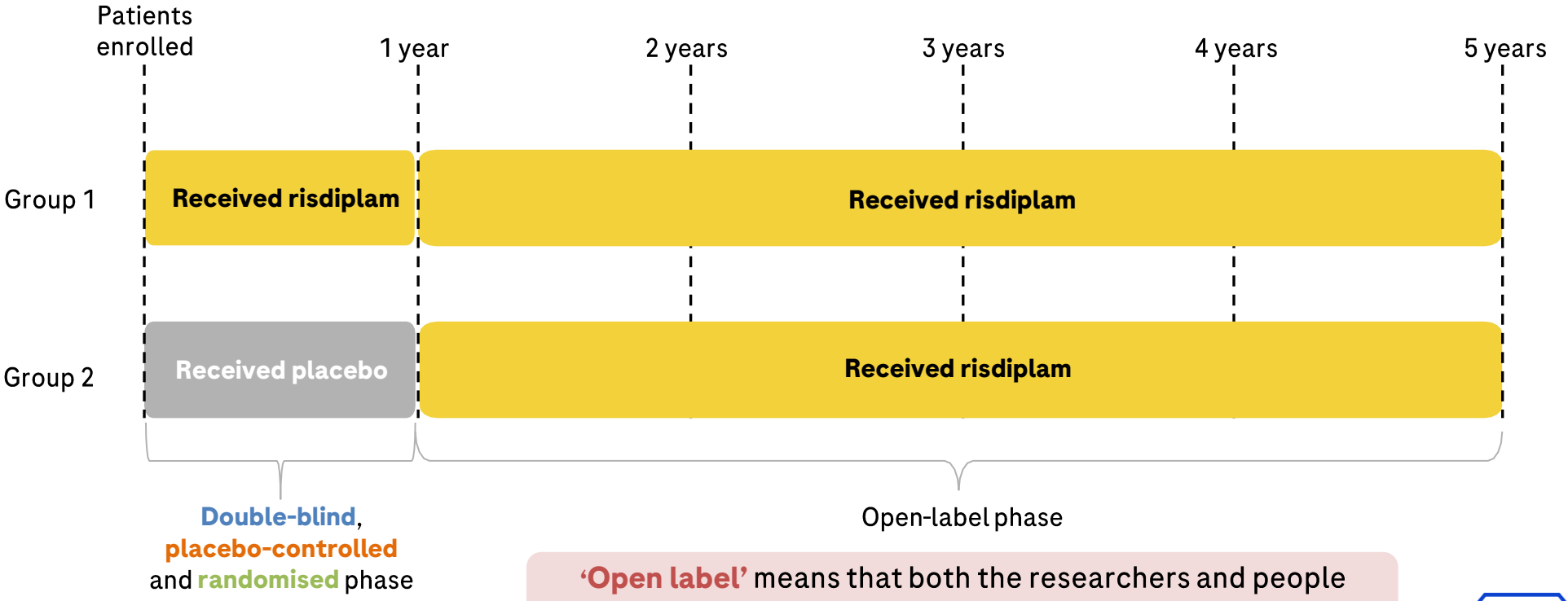
SMA, spinal muscular atrophy.

What happened during SUNFISH Part 2?

During SUNFISH Part 2, people were randomly selected to receive either risdiplam or placebo. For every two people who received risdiplam, one person received placebo. This was the **double-blind**, **placebo-controlled** and **randomised** phase.

Risdiplam or placebo was taken once every day for 1 year.

After 1 year, people receiving placebo were switched to risdiplam. Everyone then received risdiplam until the end of the study. This was the **open-label** phase of the study.



'Open label' means that both the researchers and people taking part knew which study medicine was being given.

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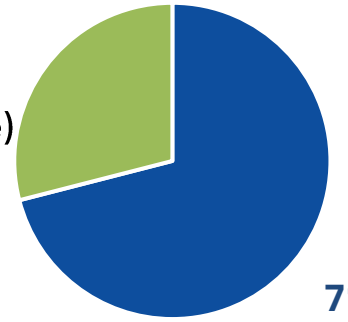
SUNFISH Part 2 enrolled 180 people

49% (89 out of 180 people) were male

51% (91 out of 180 people) were female

People were aged between 2 and 25 years

9 The average age at enrolment was 9 years



29% (128 out of 180 people) had non-ambulant Type 3 SMA

71% (128 out of 180 people) had Type 2 SMA

67% (120 out of 180 people) had scoliosis at the start of the study

32% (57 out of 180 people) had a curvature greater than an angle of 40 degrees

SMA, spinal muscular atrophy.

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What were the main results of SUNFISH Part 2?

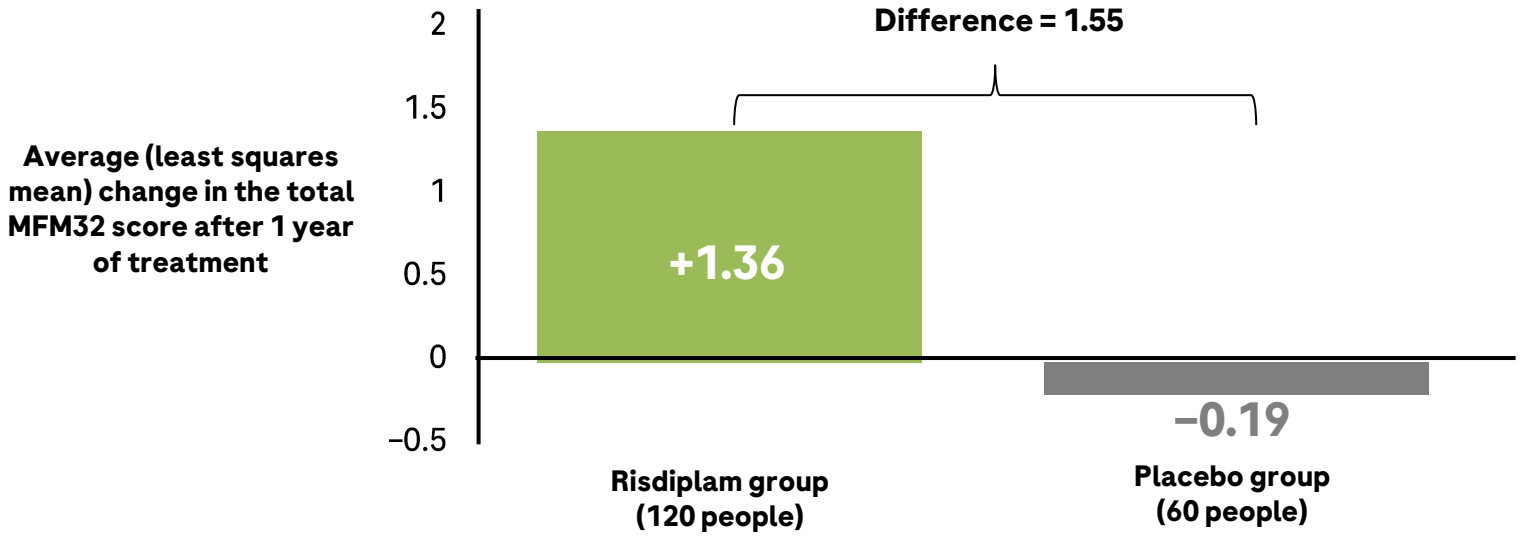
The main aim (primary endpoint) of SUNFISH Part 2 was to investigate the efficacy of risdiplam (how well risdiplam works).

Researchers looked at the results once all people taking part in the study had completed 1 year of treatment.

Each person taking part had their functional ability measured using the MFM32 assessment scale at the start of the study and after 1 year of treatment with risdiplam or placebo.

After 1 year, the average (least squares mean: a standard method for fitting a curve to a set of points) change in the total MFM32 score from the start of the study was **+1.36 points in people who received risdiplam** and **–0.19 points in people who received placebo**.

The difference between the risdiplam and placebo groups was 1.55 points.



People treated with risdiplam had significantly improved functional ability measured by the MFM32 compared with those not taking risdiplam

MFM32, 32-item Motor Function Measure.

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Summaries have previously been produced that show the full SUNFISH results after 1 year and 2 years of treatment

For the full results after 1 year of treatment, please click here.

For the full results after 2 years of treatment, please click here.

Information about side effects is now available for people in SUNFISH treated with risdiplam for up to 5 years

The study is now complete as the last person taking part in SUNFISH has completed 5 years on the study.

Safety data are available from 51 people in SUNFISH Part 1 and from 179 people in SUNFISH Part 2. These people have received treatment with risdiplam for up to 5 years.

The side effects reported during the SUNFISH study are listed on the next pages.

Side effects are medical problems (such as feeling dizzy or feeling sick) that happen during the study.

Not all side effects are related to the study medication, some occur by chance. Doctors report all medical problems that people have during the study to Roche so that they can look for patterns across every person taking part.

It is important to know that:

- Not all the people in this study had all the side effects listed.
- Side effects may be mild to very serious, and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflet.

Serious and common side effects are listed in the following sections.

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What were the serious side effects in SUNFISH Part 1 over 5 years of treatment?

A side effect is considered 'serious' if it is life-threatening, needs hospital care or causes lasting problems.

Not all serious side effects reported are related to the study medicine.

In SUNFISH Part 1, no serious side effects were reported that were thought to be related to taking risdiplam by the study doctors.

However, other serious side effects were reported by 17 people in SUNFISH Part 1.

The most common serious side effects that were not related to risdiplam are reported here.

Each of these was reported in at least two people.

Most common serious side effects not related to risdiplam *Reported in at least two people*	**What percentage of people reported this side effect?**
Infection of the air sacs in the lungs *(pneumonia)*	**10%** (5 out of 51 people)
Broken leg *(femur fracture)*	**4%** (2 out of 51 people)

If a participant reported the same side effect more than one time during the study, it is only counted once.

What were the non-serious side effects in SUNFISH Part 1 over 5 years of treatment?

Non-serious side effects are any medical problems (such as feeling dizzy or feeling sick) that happen during the study. They are not all related to the study medicine.

The most common non-serious side effects in SUNFISH Part 1 are reported here.

Each of these side effects was reported in at least 10 people.

These non-serious side effects were not all thought to be related to risdiplam by the study doctors.

Most common non-serious side effects *Reported in at least 10 people*	**What percentage of people reported this side effect?**
Fever (pyrexia)	**65%** (33 out of 51 people)
Being sick (vomiting)	**39%** (20 out of 51 people)
Cough	**37%** (19 out of 51 people)
Infection in the nose, throat and airways (upper respiratory tract infection)	**35%** (18 out of 51 people)
Infection of the nose and throat (nasopharyngitis)	**31%** (16 out of 51 people)
COVID-19 **Infection or inflammation of the stomach and intestines** (gastroenteritis)	**27%** (14 out of 51 people)
Pain in the mouth or throat (oropharyngeal pain)	**25%** (13 out of 51 people)
Flu (influenza)	**24%** (12 out of 51 people)
Headache	**20%** (10 out of 51 people)

If a participant reported the same side effect more than one time during the study, it is only counted once.

What were the non-serious side effects in SUNFISH Part 1 that were related to risdiplam over 5 years of treatment?

In SUNFISH Part 1, 25% (13 out of 51) of people had reported non-serious side effects. Their doctors reported these side effects as related to risdiplam treatment.

The most common non-serious side effects related to taking risdiplam are listed here.

Each of these side effects was reported in at least two people.

Most common non-serious side effects related to taking risdiplam *Reported in at least two people*	**What percentage of people reported this side effect?**
Rash	**6%** (3 out of 51 people)
Belly pain *(abdominal pain)*	**4%** (2 out of 51 people)

If a participant reported the same side effect more than one time during the study, it is only counted once.

What were the serious side effects in SUNFISH Part 2 over 5 years of treatment?

Serious side effects were reported in 38% (68 out of 179) of people in SUNFISH Part 2.

The most common serious side effects are listed here.

Each of these side effects was reported in at least two people.

These side effects were not all thought to be related to risdiplam by the study doctors.

Most common serious side effects *Reported in at least two people*	**What percentage of people reported this side effect?**
Infection of the air sacs in the lungs (pneumonia)	**11%** (19 out of 179 people)
Infection in the nose, throat and airways (upper respiratory tract infection) **Fever** (pyrexia)	**3%** (5 out of 179 people)
Infection or inflammation of the stomach and intestines (gastroenteritis) **Flu** (influenza) **Broken leg** (femur fracture)	**2%** (4 out of 179 people)
Back pain	**2%** (3 out of 179 people)
Collapse of a lung (atelectasis) **Difficulty breathing** (respiratory disorder) **Dehydration** **Kidney stones** (nephrolithiasis) **Constipation** **Infection of the stomach** (gastritis) **Being sick** (vomiting) **Bacteria in the blood** (bacteraemia) **Infection of the airways in the lungs** (bronchitis) **COVID-19** **Chest infections** (lower respiratory tract infection) **Viral chest infection** (lower respiratory tract infection caused by a virus) **Infection of the air sacs in the lungs caused by breathing in food or fluids** (aspiration pneumonia) **Infection in the nose, throat and airways** (respiratory tract infection) **Viral infection in the nose, throat and airways** (viral upper respiratory tract infection)	**1%** (2 out of 179 people)

If a participant reported the same side effect more than one time during the study, it is only counted once.

What were the serious side effects in SUNFISH Part 2 that were related to risdiplam over 5 years of treatment?

In SUNFISH Part 2, 13 serious side effects that doctors thought were related to risdiplam were reported in two people from the same study site.

These side effects were reported in one person each:

- **Infection of the air sacs in the lungs** (pneumonia)
- **Low blood sugar levels** (hypoglycaemia)
- **Infection of the stomach and intestines** (gastroenteritis)
- **Infection of the nose, throat or sinuses** (upper respiratory tract infection)
- **Infection of the airways in the lungs** (bronchitis)
- **Swelling and narrowing of the airways** (asthma)
- **Bleeding in the digestive tract** (gastrointestinal haemorrhage)
- **Infection of the stomach** (gastritis)
- **Too much acid is produced in the body** (metabolic acidosis)

If a participant reported the same side effect more than one time during the study, it is only listed once.

What were the non-serious side effects in SUNFISH Part 2 over 5 years of treatment?

Non-serious side effects were reported in 99% (177 out of 179) of people.

The most common non-serious side effects are listed here.

Each of these side effects were reported in at least 15 people.

These side effects were not all thought to be related to risdiplam by the study doctors.

Most common non-serious side effects *Reported in at least 15 people*	**What percentage of people reported this side effect?**
Infection in the nose, throat and airways (upper respiratory tract infection)	**42%** (75 out of 179 people)
Infection of the nose and throat (nasopharyngitis)	**41%** (73 out of 179 people)
Fever (pyrexia)	**34%** (61 out of 179 people)
COVID-19	**33%** (59 out of 179 people)
Headache	**26%** (47 out of 179 of people)
Being sick (vomiting)	**26%** (46 out of 179 people)
Diarrhoea	**25%** (45 out of 179 people)
Cough	**20%** (36 out of 179 people)
Stomach flu (gastroenteritis) Infection of the air sacs in the lungs (pneumonia)	**16%** (29 out of 179 people)

If a participant reported the same side effect more than one time during the study, it is only counted once.

What were the non-serious side effects in SUNFISH Part 2 that were related to risdiplam over 5 years of treatment?

Non-serious side effects that were related to taking risdiplam were reported in 21% (37 out of 179) of people.

The most common non-serious side effects that were related to risdiplam are listed here.

These side effects were each reported in at least two people.

Non-serious side effects *Reported in at least two people*	**What percentage of people reported this side effect?**
Blood in urine (haematuria)	**6%** (10 out of 179 people)
Infection in the nose, throat and airways (upper respiratory tract infection)	**5%** (9 out of 179 people)
Diarrhoea	**3%** (6 out of 179 people)
The blood takes longer to clot than usual (activated partial thromboplastin time prolonged)	**2%** (4 out of 179 people)
Feeling sick (nausea) **Mouth ulceration** **Headache**	**2%** (3 out of 179 people)
Upper belly pain (abdominal pain upper) **Infection of the air sacs in the lungs** (pneumonia) **Blister** **Rash** **A rash with a flat, red area on the skin that is covered with small bumps** (maculopapular rash) **Abnormal liver function test** **A bleeding disorder** (coagulopathy) **Extra fat in the liver** (hepatic steatosis) **Fever** (pyrexia)	**1%** (2 out of 179 people)

If a participant reported the same side effect more than one time during the study, it is only counted once.

How has this study helped individuals living with SMA and researchers?

For a health condition like SMA for which there are remaining medical gaps and unmet medical needs, the study of possible new drugs and different modes of administration (such as risdiplam as the only approved oral treatment for SMA) is important to advance patient outcomes and care.

Building on previous research, the study results from SUNFISH have given researchers and those living with SMA a better understanding of the effects of risdiplam in people with Type 2 and Type 3 SMA.

Studies with risdiplam are still ongoing and further studies are planned.

The results enabled the sponsoring company (Roche) to submit risdiplam for regulatory approval by health authorities to make this treatment available to people with Type 2 or Type 3 SMA around the world.

Risdiplam is approved by the US Food & Drug Administration for the treatment of SMA in adults and children.

Risdiplam is approved by the European Commission for the treatment of SMA in people with a clinical diagnosis of Type 1, Type 2 or Type 3 SMA or with one to four copies of the *SMN2* gene.

This summary included safety results from the whole of the SUNFISH study. Individuals have been treated with risdiplam for up to 5 years.

These results are important to confirm the safety profile of risdiplam for up to 5 years.

No single study can tell us everything about the risks and benefits of a medicine. Always speak to your doctor before making any decisions about your treatment.

SMA, spinal muscular atrophy; SMN, survival of motor neuron; US, United States.

Additional information

How is the SUNFISH study different from the FIREFISH study?

FIREFISH was carried out to understand the safety and efficacy of risdiplam in infants with Type 1 SMA, aged between 1 and 7 months at the time they entered the study.

SUNFISH was carried out to understand the safety and efficacy of risdiplam in children, teenagers and adults with Type 2 or Type 3 SMA, aged between 2 and 25 years at the time they entered the study.

The FIREFISH study was designed differently to the SUNFISH study

- The whole of the FIREFISH study was 'open label', meaning that all infants taking part in the study were given risdiplam, and all participants (or caregivers) and researchers knew what treatment they were receiving.
- The first year of the SUNFISH study compared risdiplam with a placebo ('placebo-controlled'). The next 4 years of the SUNFISH study was 'open label'.

Without treatment, most infants with Type 1 SMA would not live longer than 2 years or would need permanent breathing support. Therefore, it would have been unethical to give a placebo to infants participating in FIREFISH.

The data from FIREFISH and SUNFISH are presented differently

In FIREFISH, most of the infants from Part 1 and Part 2 received risdiplam at the same dose and for the same length of time. Therefore, the results from these infants can be combined and presented together.

In SUNFISH, the results from Part 1 and Part 2 cannot be combined because the study populations were different. People who could walk were allowed to participate in Part 1, whilst Part 2 only included people who were unable to walk.

SMA, spinal muscular atrophy.

Additional information

Where can I find more information?

You can find more information about this study on the websites listed below:

- https://clinicaltrials.gov/ct2/show/study/NCT02908685
- https://forpatients.roche.com/en/trials/muscle-and-peripheral-nerve-disease/sma/a-study-to-investigate-the-safety--tolerability--pharmacokinetic1.html

The protocol number for this study is: BP39055

The ClinicalTrials.gov identifier for this study is: NCT02908685

The EudraCT number for this study is: 2016-000750-35

Previous documents were made that provide a summary of results of Parts 1 and 2 of the SUNFISH study after participants had completed 1 and 2 years of treatment:

- For the results at 1 year, please click here to view the 2020 summary.
- For the results at 2 years, please click here to view the 2022 summary.

If you or your child have taken part in this study and have any questions about the results, please speak with your doctor or other medical staff at your study site.

If you have any further questions, please contact a representative at your local Roche office.

The full title of this study is: A Two Part Seamless, Multi-Center Randomized, Placebo-Controlled, Double-Blind Study to Investigate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Efficacy of RO7034067 in Type 2 and 3 Spinal Muscular Atrophy Patients.

The study is known as ‘SUNFISH’.

Address for the sponsor of this trial:

F. Hoffmann-La Roche Grenzacherstrasse 124 CH-4070 Basel, Switzerland

Roche