



## Givinostat Development Update

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# Disclosures

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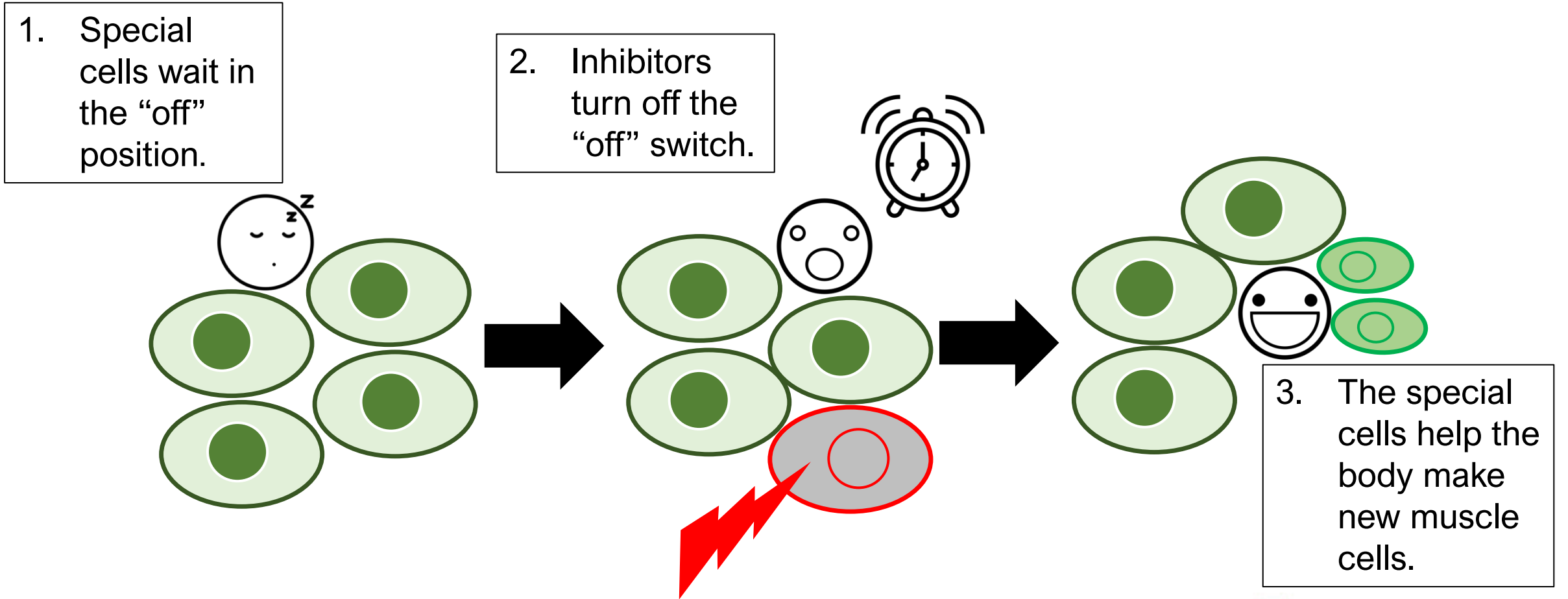
- Ana Christensen is an employee of TRiNDS, a contract research organization.
- Italfarmaco has contracted with TRiNDS to provide patient advocacy services.
- Givinostat is currently in development for the treatment of DMD and BMD. It is not approved for sale in any country.
- This presentation is intended to share scientific information with the DMD community.

# Take Home Messages

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- Your muscle cells are supposed to repair themselves after they're damaged. In DMD, this doesn't work properly.
- Givinostat is an investigational drug designed to make the muscle repair process work more normally.
- In a Phase 2 clinical trial, muscle tissue tests, functional tests, and pulmonary tests showed a delay of disease progression compared with natural history data.
- A Phase 3 trial is open now at sites around the world.

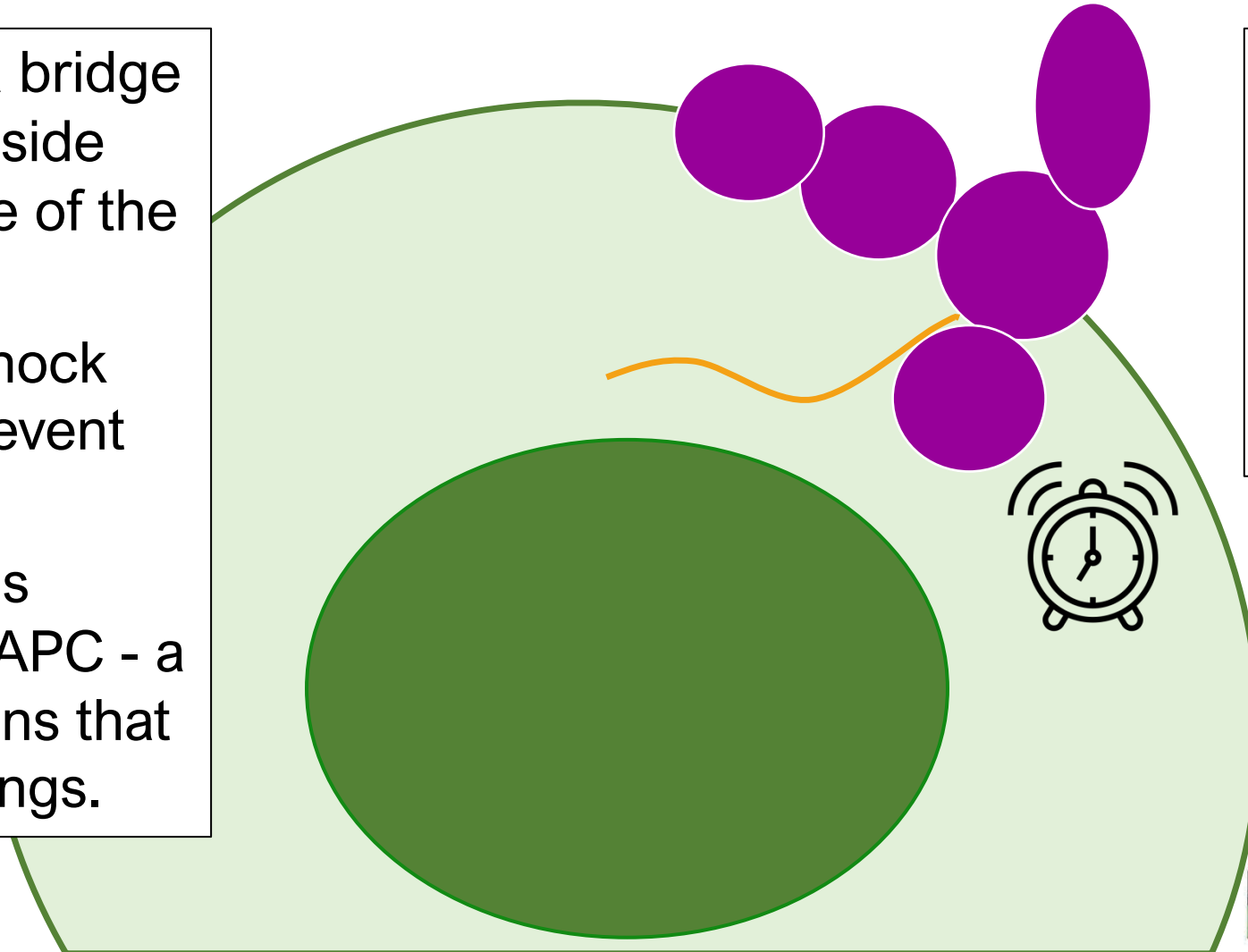
# How do Muscles Repair Themselves?



# What About Dystrophin?

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- Dystrophin is a bridge between the inside and the outside of the cell.
- It works as a shock absorber to prevent damage.
- But it also holds together the DAPC - a group of proteins that does lots of things.



- One of the things the DAPC does is to control muscle regeneration.



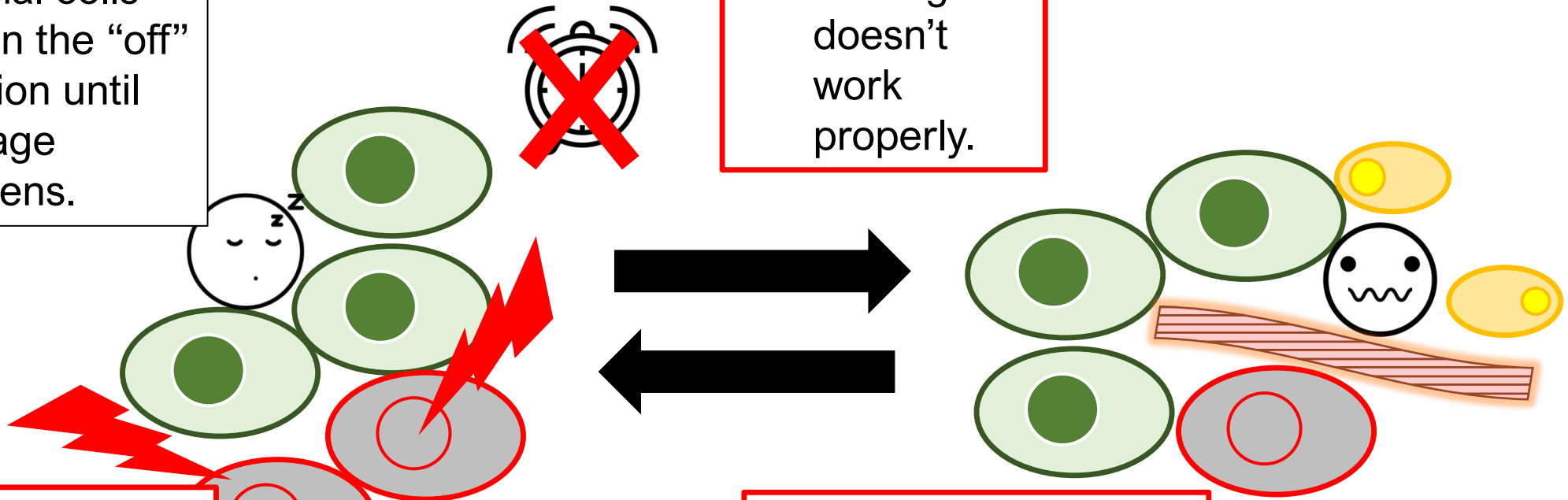
# What Happens in DMD?

1. Special cells wait in the “off” position until damage happens.

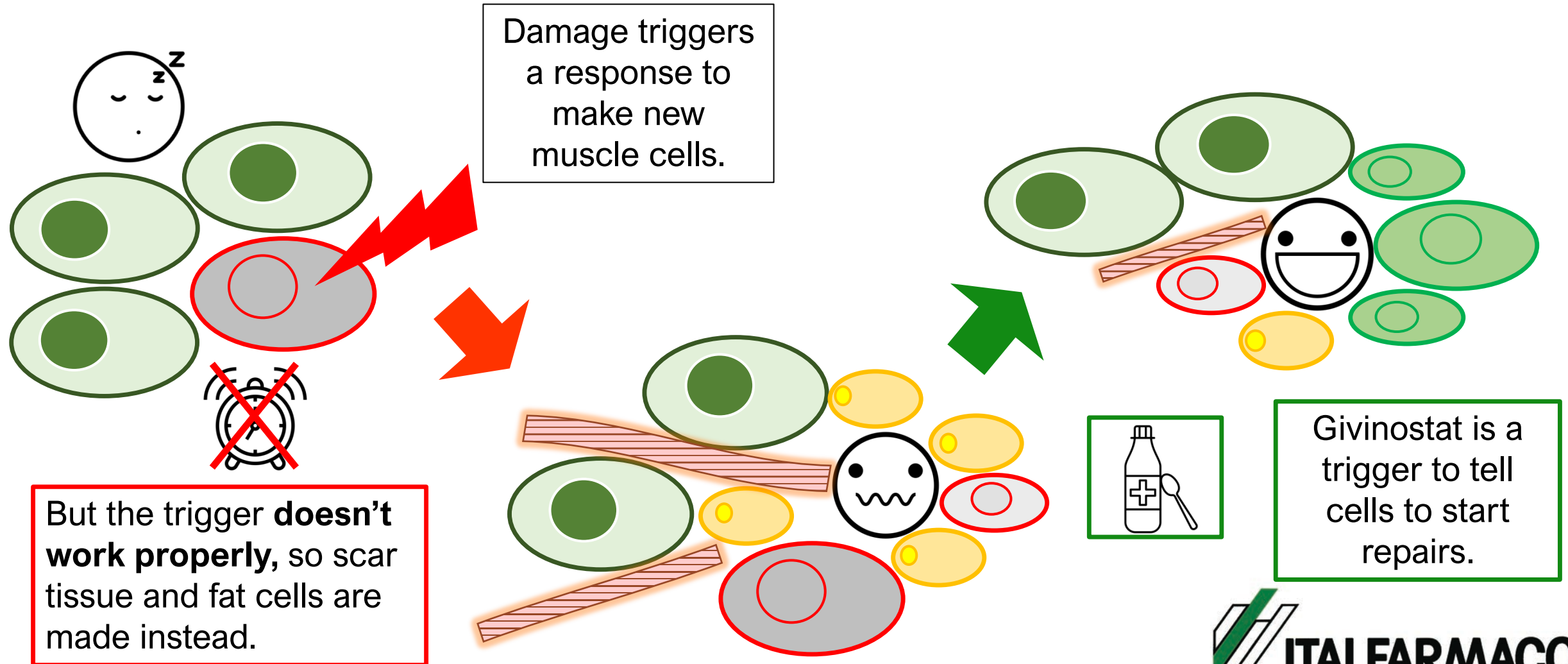
2. In DMD, more muscle cells are damaged due to lack of Dystrophin.

3. The signal doesn't work properly.

4. The special cells make fat cells and scar tissue (fibrosis) instead of muscle cells.



# How Does Givinostat Work?



# Phase 2: Trial Design

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- 20 patients were enrolled in 2013, of whom 18 completed the 52 months of treatment.
- Boys were 7 to 11 years old and were ambulatory and on steroids at enrollment.
- Twice a day Givinostat was given at the dose found in first part of the study.
- Participants completed muscle biopsies and functional testing before and after 12 months of treatment. Functional tests were done every 3 months until the end of the study
- Primary endpoint: Changes in muscle biopsy



# Phase 2 Trial Results: Safety

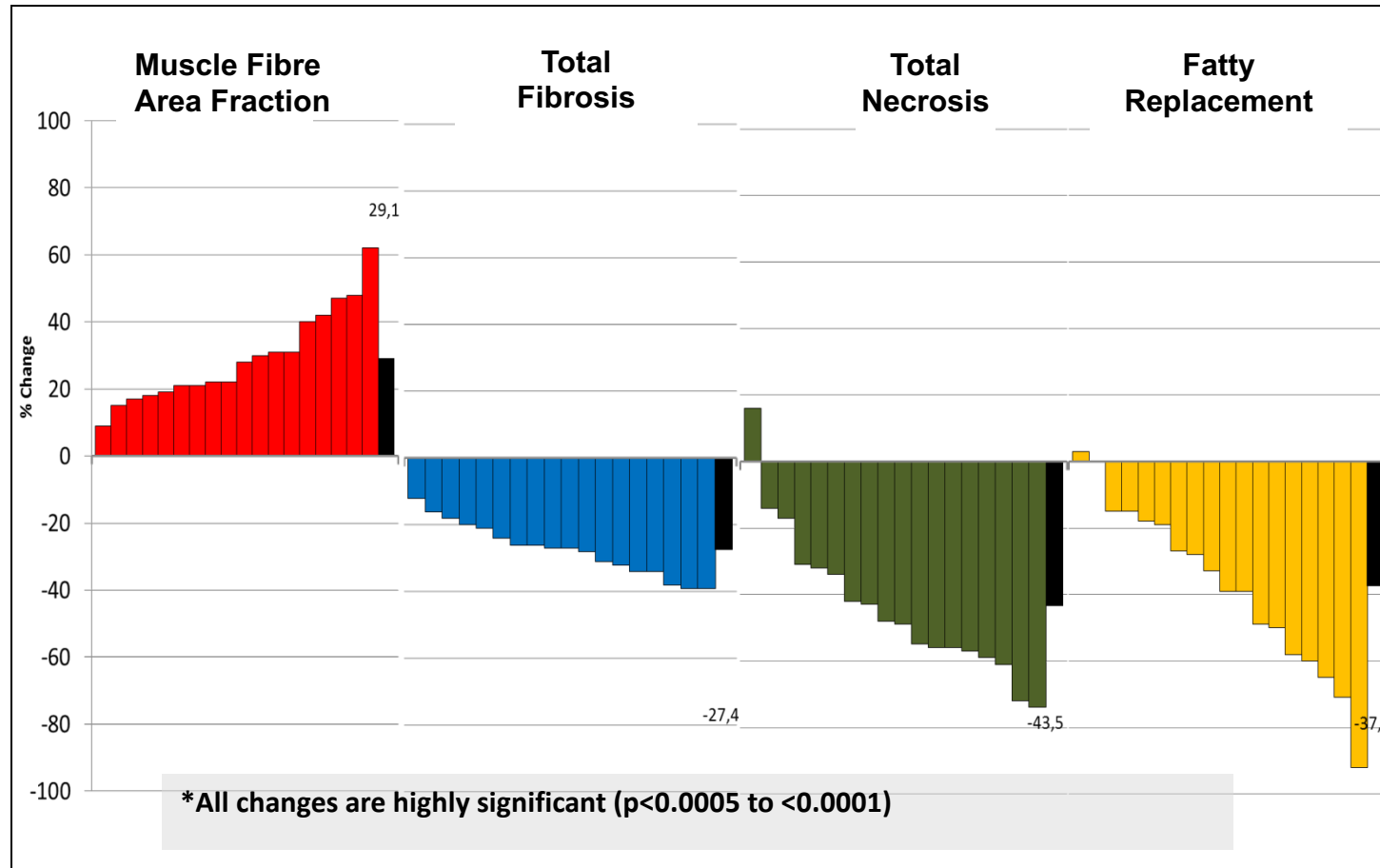
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## Common Adverse Events (4+ participants)

	All Events N (%)	Drug Related N (%)
Diarrhoea	15 (75)	15 (75)
Platelet count decreased	14 (70)	14 (70)
Abdominal pain	11 (55)	9 (45)
Decreased appetite	7 (35)	7 (35)
Vomiting	8 (40)	5 (25)
White blood cell count decreased	4 (20)	4 (20)

- 8 participants had at least one Serious Adverse Event.
  - 2 were related to treatment (decreased platelet count).
  - One resulted in leaving the study.
- All subjects had at least one adverse event.
- Most were mild or moderate (11 severe).

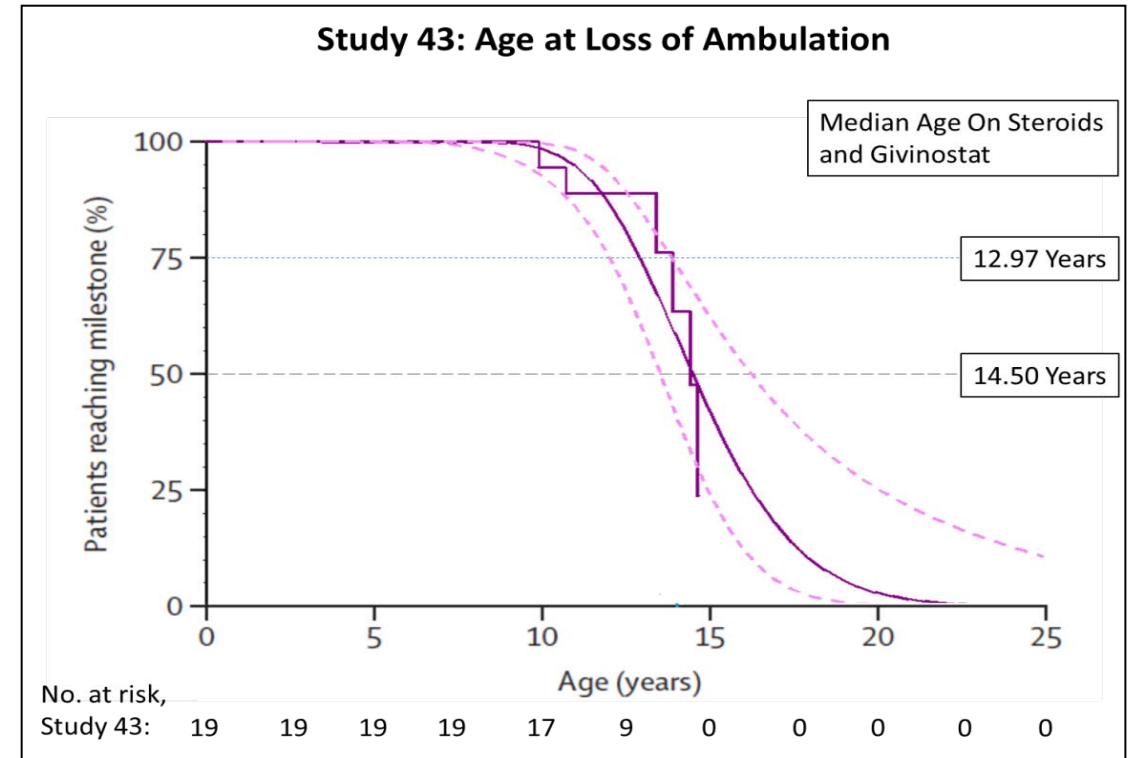
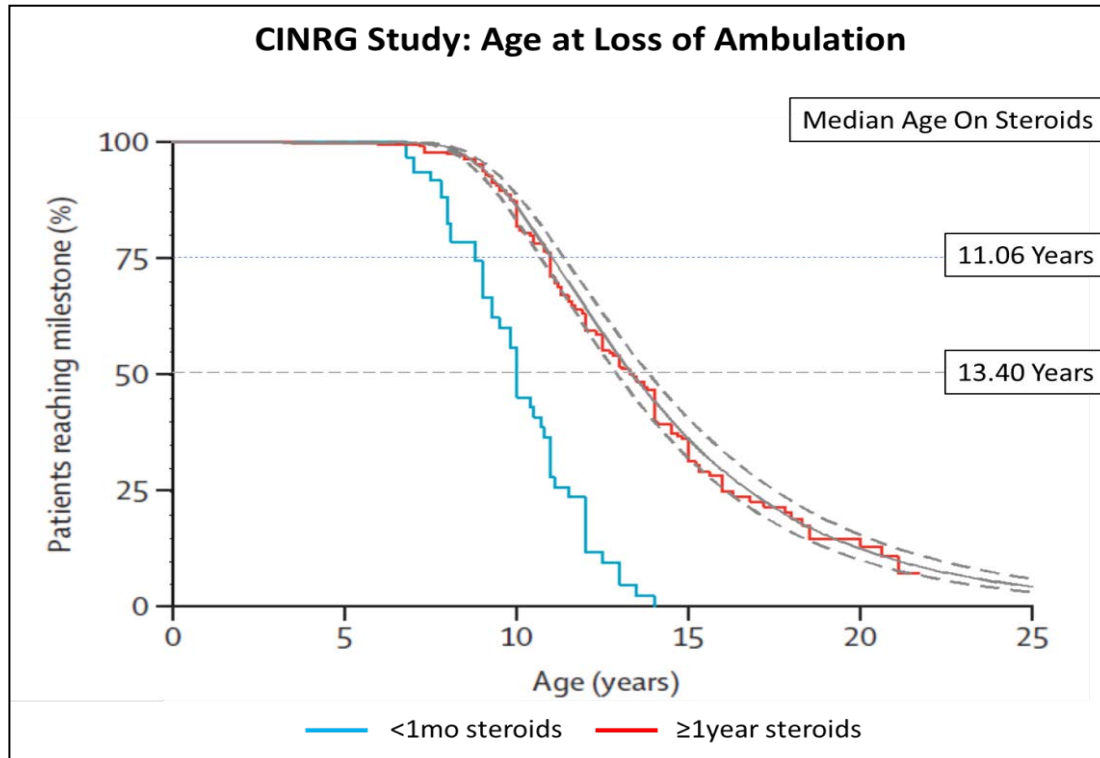
# Phase 2 Trial Results: Biopsy



- **Biopsy results show:**

- Increase in muscle fiber area fraction
- Reduction in fibrosis
- Reduction in necrosis
- Reduction in fatty replacement

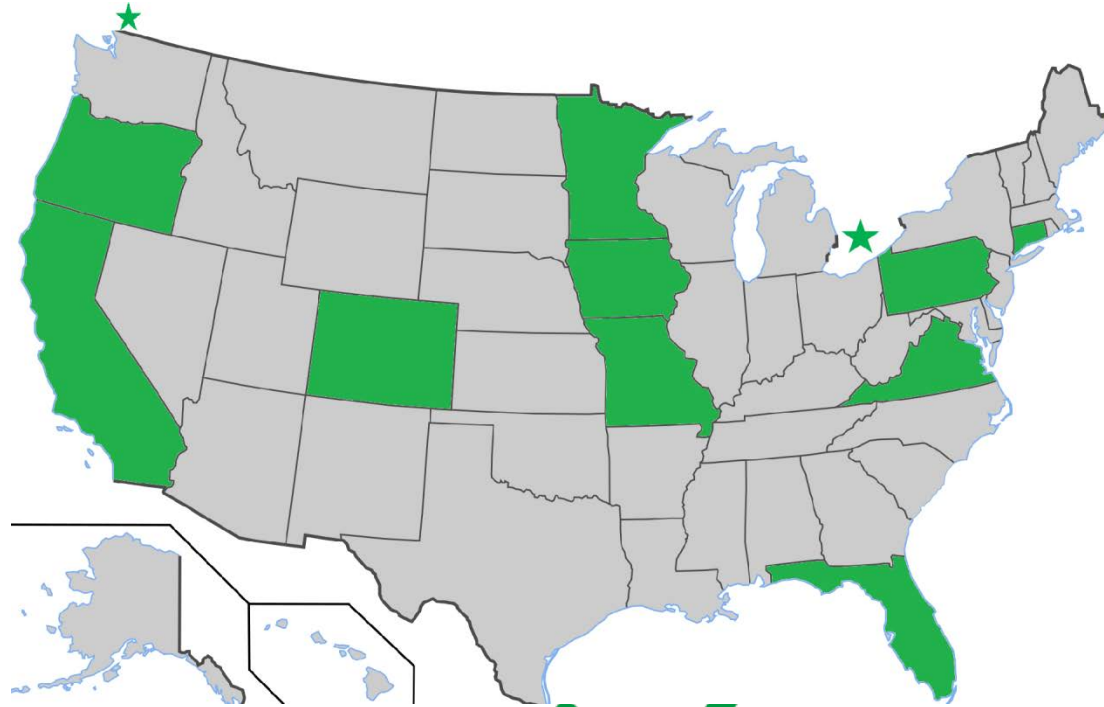
# Phase 2 Trial Results: Function



- Compared with natural history study results, participants showed delayed disease progression in Time to Rise, Loss of Ambulation, and pulmonary function testing.

# Phase 3 Trial: Now Open!

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- Randomized, double blind, placebo controlled study
- Enrolling 242 ambulatory boys worldwide
- Primary outcome measure is the 4 Stair Climb.
- Other outcome measures are 6MWT, Time to Rise from Floor, NSAA, MRI.
- North American sites in 10 states and 2 Canadian provinces.



# Who Can Do the Study?

**Now  
Updated!**

## Key Inclusion Criteria:

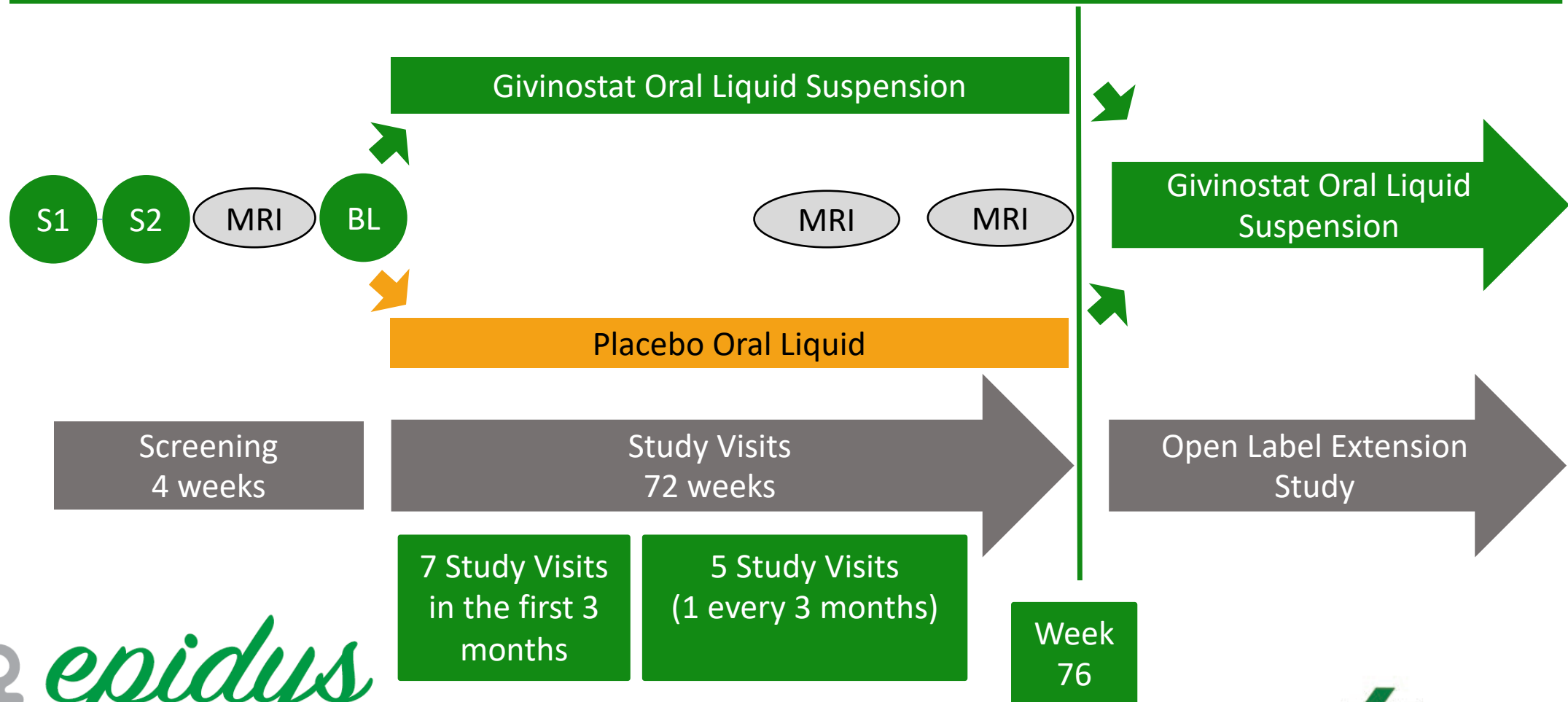
- Can walk
- Be age 6 or older
- Have DMD
- Can climb stairs and get up off the floor
- Are taking steroids
- Can do an MRI
- Can do stair test consistently

## Key Exclusion Criteria:

- Take other investigational drugs, idebenone, exon skipping, or premature stop codon readthrough drugs.
- Take other drugs that affect strength or muscle function.
- Have ankle contractures
- Will have surgery soon
- Are not healthy enough for the study



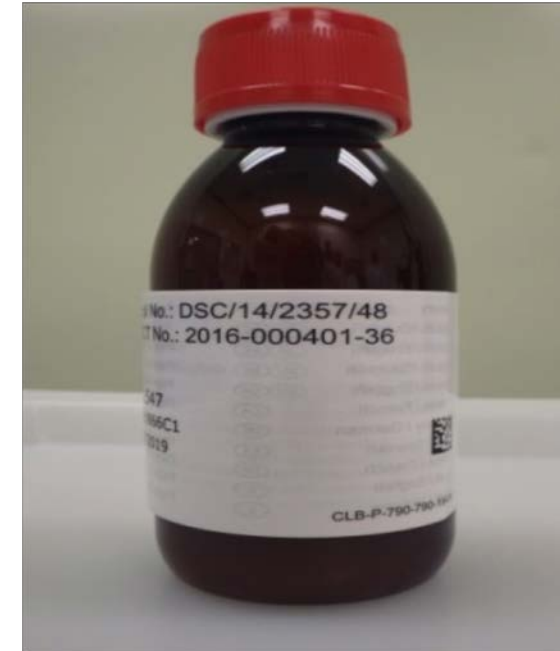
# Phase 3 Randomized Controlled Trial



# What Happens at Study Visits?

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- Informed Consent Paperwork
- Physical Exams
- Height, Weight, Vital Signs
- Heart Tests (ECG and Echo)
- Lung Tests (PFT)
- Blood and Urine Tests
- Surveys and Diaries
- Physical Therapy Tests (6MWT, NSAA, 4SC, QMT)
- 3 MRI tests



## Givinostat or Placebo

Liquid Oral Suspension  
*Twice a day after food*

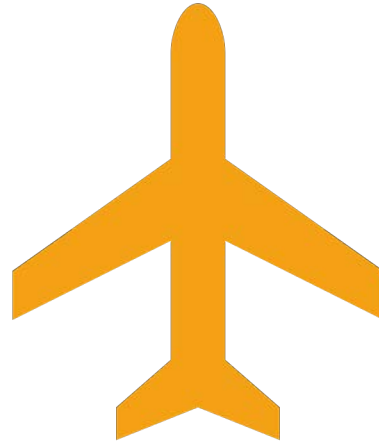


# Trial Support Programs

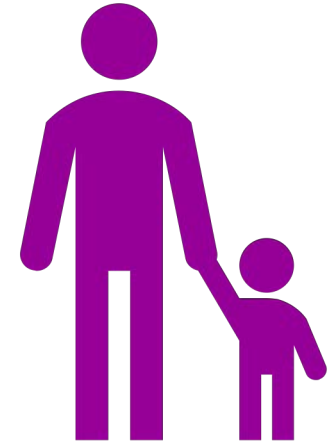
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- Home nursing visits available at Week 2, 3, 8 and any unscheduled visits



- Central travel and reimbursement support available

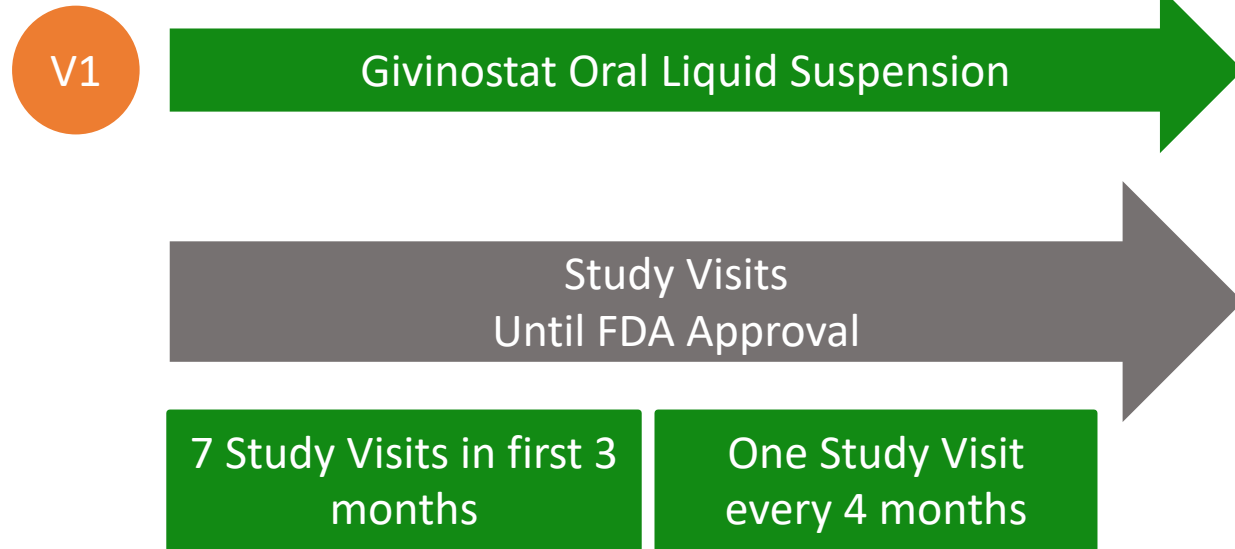


- Open label extension study open to everyone who finishes the trial.





# Open Label Extension Study



## Primary Objective:

- To learn the effects of long – term Givinostat use on:
  - Function and Strength
  - Respiratory Function
  - Daily Activity and Quality of Life

# How Can I Learn More?

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- Visit [clinicaltrials.gov](https://clinicaltrials.gov) (#NCT02851797) and learn all the details.
- Watch a presentation: <https://youtu.be/GZPkgyVWHow>
- Email [patientadvocacy@italfarmaco.com](mailto:patientadvocacy@italfarmaco.com) or call 412-593-4389



# THANK YOU!



FONDAZIONE



Italfarmaco would like to thank the **families** who participated in our trials, the **trial sites**, and all the **patient groups** for your hard work and support.

**THANK YOU!**

**DUCHENNE**  
DATA FOUNDATION

