Roche/Genentech Anti-Myostatin Adnectin RG6206 Development Program in Duchenne

Roxana Dreghici, MD
Clinical Science Leader, Associate Medical Director, Roche

This compound and its uses are investigational and have not been approved by the U.S. FDA.

GPT/053119/0036

Disclaimer

This session contains general information about our Duchenne Muscular Dystrophy program and is not intended as specific medical advice.

RG6206 is an investigational (not approved) medicine that is being studied for the treatment of people with Duchenne Muscular Dystrophy. RG6206 has not been approved by the US Food and Drug Administration (US FDA). The effectiveness and safety of RG6206 are currently being studied.

You should talk with your healthcare provider for information and advice about your condition, including any current or potential treatments.

Agenda

- Overview of our anti-myostatin development program:
  - What is RG6206?
  - Overview of RG6206 clinical studies
  - Status to date and next steps
- Q&A

This compound and its uses are investigational and have not been approved by the U.S. FDA.

What is RG6206?

Myostatin

- Myostatin is a naturally occurring protein that is produced primarily in skeletal muscle cells[1]
- Its function is usually to **stop muscles growing too large**[1,2]
- We are investigating if blocking myostatin could increase muscle growth and muscle strength in children with Duchenne

RG6206

- RG6206 is **an investigational molecule** being investigated for people with Duchenne
- RG6206 is designed to **bind myostatin** and to potentially limit its function
- Per study protocol, RG6206 is administered at home once weekly by **subcutaneous injection** (injection under the skin) **into the abdomen** (tummy), **thigh or back of upper arm** after initial training at the site

1. Parent Project MD [Internet; cited 2019 May 29). Available from: www.parentprojectmd.org
2. Sharma M, et al. IUBMB Life 2015; 67:589–600.
3. Schuelke M, et al. N Engl J Med 2004; 350: 2682–2688.

This compound and its uses are investigational and have not been approved by the U.S. FDA.

Clinical Studies of RG6206

Genentech
A Member of the Roche Group

Roche

Phase 1

Phase 1b/2

Phase 2/3

Study WN40225

Safety of RG6206 in 103 healthy adults[1,2]

Completed.

Study WN40226
Thunderjet

Safety and tolerability of RG6206 in 43 ambulatory boys with Duchenne[3]

Recruitment completed, Open Label Extension ongoing.

Study WN40227
SPITFIRE

Safety, tolerability and efficacy of RG6206 in 159 ambulatory boys with Duchenne[4]

Ongoing.

Clinicaltrials.gov/show/ **1**.NCT02145234 **2**. NCT03100630 **3**. NCT02515669 **4**. NCT03039686 (June 2019)

This compound and its uses are investigational and have not been approved by the U.S. FDA.

Phase 1b/2 Study of RG6206

Assessing the Safety and Tolerability of RG6206 in Ambulatory Boys With Duchenne

Genentech
A Member of the Roche Group

Roche

Phase 1b/2

Study WN40226

Thunderjet

Current status:

- **43 ambulatory boys with Duchenne** (5–10 yrs old) enrolled in the double blind part of the study[1]
- Over 24 weeks, each received a weekly subcutaneous dose of **either RG6206 or placebo**[1]
- Multiple Increasing Subcutaneous Dose Study
- 41 Study participants are **now all receiving RG6206** in an open-label 228-week extension[2]

1. Clinicaltrials.gov/show/NCT02515669 (Accessed June 2019);
2. K. Wagner et al., A Phase 1b/2 study of the anti-myostatin adnectin RG6206 (BMS- 986089) in ambulatory boys with Duchenne muscular dystrophy. Presented at Action Duchenne conference 2018, PPMD Conference 2018.

This compound and its uses are investigational and have not been approved by the U.S. FDA.

Phase 2/3 SPITFIRE Study of RG6206

Assessing the Safety, Tolerability and Efficacy of RG6206 in Ambulatory Boys with Duchenne

Genentech
A Member of the Roche Group

Roche

Phase 2/3

Study WN40227
SPITFIRE

Approximately 159 boys

All DMD mutations are eligible

Double-blind period
48 weeks

RG6206 Placebo

- Patients will be randomly allocated to a treatment
- Neither the patient, or the investigator will know if they are receiving RG6206 or placebo
- 2 doses of RG6206 are being studied
- 2:1 randomization means that twice as many people receive RG6206 versus placebo

Open label period
192 weeks

RG6206

RG6206 is given to all participants

All participants will also receive corticosteroids for the entire trial

Additional study inclusion and exclusion criteria can be found at ClinicalTrials.gov

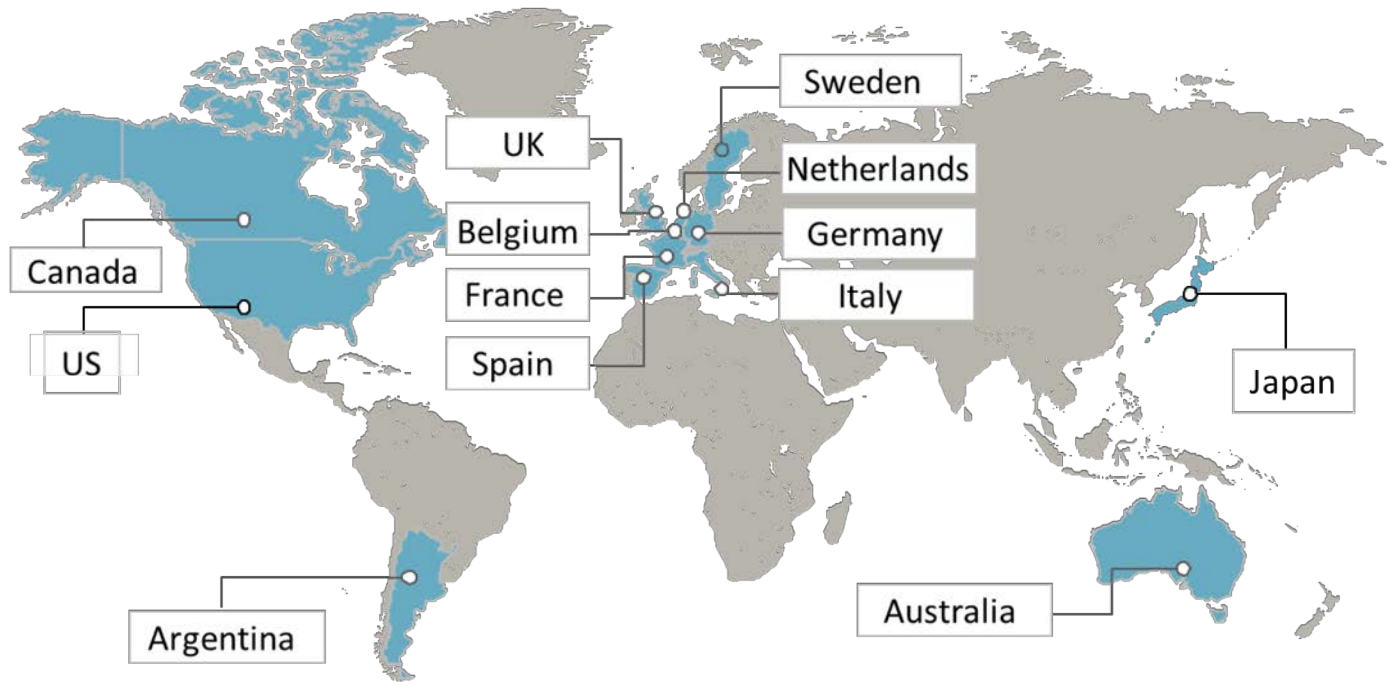
Clinicaltrials.gov/show/NCT03039686 (Accessed June 2019)

This compound and its uses are investigational and have not been approved by the U.S. FDA.

Phase 2/3 SPITFIRE Study of RG6206

Countries

Actual as of June 20



48 sites worldwide
18 US sites
3 Canada sites

SPITFIRE Study update

Screening is complete and we anticipate last patient to be enrolled in SPITFIRE study by the end of June 2019

Clinicaltrials.gov/show/NCT03039686 (Accessed June 2019)

This compound and its uses are investigational and have not been approved by the U.S. FDA.

Phase 2/3 SPITFIRE Study Investigating RG6206 in Ambulatory Boys with Duchenne

Study Rationale & Objectives

A Randomized, Double Blind, Placebo-Controlled, Study to Assess the Efficacy, Safety, and Tolerability of RG6206 in Ambulatory Boys with Duchenne Muscular Dystrophy

Primary Objective

Compare the change from baseline in NSAA total score at week 48 in RG6206 vs placebo treated participants

Secondary Objectives

Compare the change from baseline at week 48 in RG6206 vs placebo treated participants in:

- 4-Staired Climb (4SC) velocity
- Stand from supine velocity (time to stand from a lying down position)
- 10 meter walk/run velocity
- PODCI (pediatric outcomes instrument) transfers & basic mobility subscale score
- Proximal lower extremity flexor strength measured using manual myometry
- 6 Minute Walk Distance
- Clinical Global Impression of Change (CGI-C) rating.
- Stride velocity 95th centile (SV95C) measured at the ankle with ActiMyo

Clinicaltrials.gov/show/NCT03039686 (Accessed June 2019)

This compound and its uses are investigational and have not been approved by the U.S. FDA.

Stride Velocity 95th percentile measured with ActiMyo

Secondary Endpoint in Phase 2/3 SPITFIRE Study

- Roche/Genentech is working with other companies to investigate various ambulatory parameters and assessments in Duchenne
- ActiMyo is a wearable sensor (ankle) that is being investigated to record real-world ambulatory parameters
  - Stride (i.e. step) Velocity
  - Stride Length
  - Distance walked/ hour
- ActiMyo is being studied to detect different gait parameters and ambulatory capacity in a continuous manner
  - Parameters may be measured in a real world setting
  - Parameters may be collected independent from motivation or other confounding factors
- Stride Velocity 95th percentile is a secondary endpoint being measured in a subset of ambulatory boys with Duchenne in the Phase 2/3 Spitfire Study.

Clinicaltrials.gov/show/NCT03039686 (Accessed June 2019)

This compound and its uses are investigational and have not been approved by the U.S. FDA.

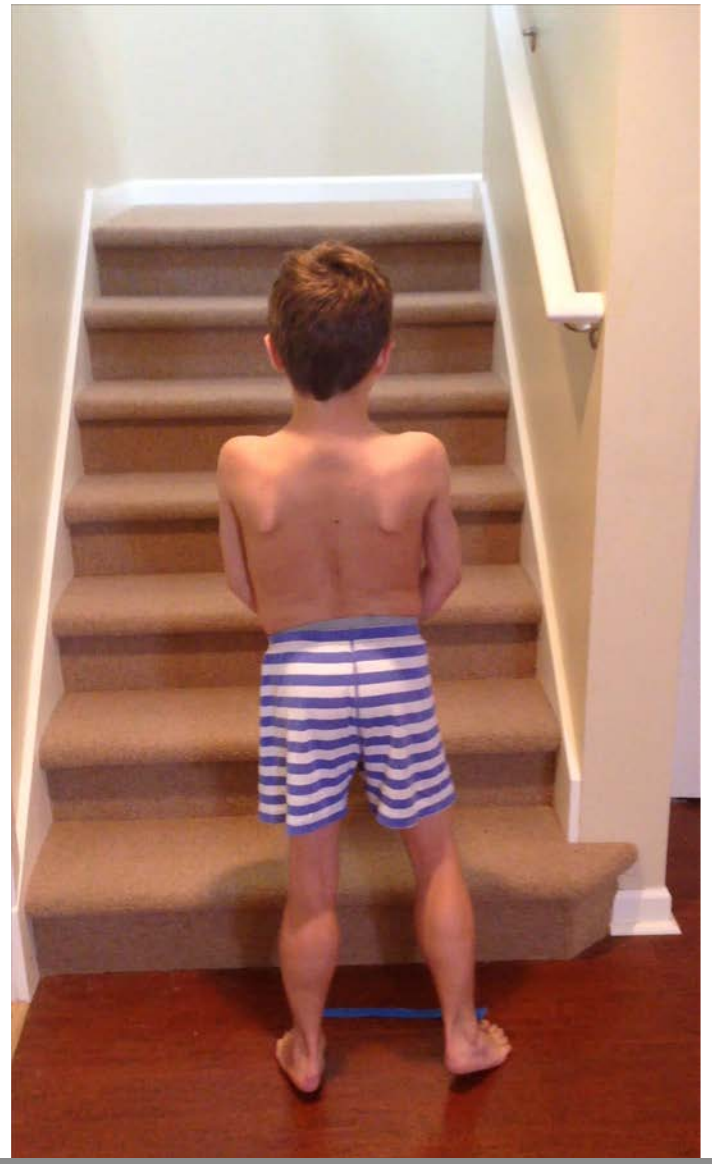
Caregiver video assessments

- Recorded through an application installed on the caregiver's smartphone
- Caregiver to film:
  - 5 pre-specified tasks[1] (sit up, stand up, walk, run, stairs), 1 caregiver choice task and new abilities
- Allows recording of the individual changes and functional abilities of the child in a familiar environment
- Videos reviewed and scored by independent/blinded physical therapists for changes in quality of movement

1. Leffler, M et al., "Home-Based Video Assessment of the Quality of Movement of Patients with Duchenne: Interviews with Physical Therapists to Inform Task Selection" . Presented at MDA Conference 2019, poster #161

This compound and its uses are investigational and have not been approved by the U.S. FDA.

Caregiver video assessments



Courtesy of M. Leffler, with a permission to use

		Number of Points
A. Inability to perform task; Cannot climb 5 stairs at all.	☐	9 points
B. Stepping pattern		
0. Typical stepping pattern	☐	0 points
1. Alternating legs (step over step), but with external hip rotation on both legs every step	☐	1 point
2. Step to pattern on 2 consecutive steps (leading with the same leg at least once)	☐	2 points
3. Step to pattern on 4 or more consecutive steps	☐	3 points
C. Use of upper body assistance for 1 or more steps (thighs, wall, handrail, or floor)		
0. No use of upper body assistance	☐	0 points
1. Using one arm on thighs, wall, handrail, or floor	☐	1 point
2. Using two arms on thighs, wall, handrail, or floor	☐	2 points
D. Body positioning		
0. Typical body positioning	☐	0 points
1. Wide base of support (equal to or greater than shoulder-width)	☐	1 point
2. Turning torso to face wall or railing to side step	☐	2 points
3. Uses the rail to bear weight	☐	3 points
Enter total number of points	X / 9	
Calculate percentage	Y %	

Genentech
A Member of the Roche Group

Roche

We would like to thank the patients and their families who take part in clinical trials as well as patient advocacy groups and caregivers who provide valuable input into the design of clinical trials and ongoing research.

For more information about the ongoing RG6206 trial
Visit ForPatients.roche.com or Clinicaltrials.gov

Genentech
A Member of the Roche Group

Roche

Q & A

Genentech
A Member of the Roche Group

Roche

Doing now what patients need next