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Characteristics of the Enrolled Population in the Phase 3 REACH Trial in Facioscapulohumeral Muscular Dystrophy (FSHD)

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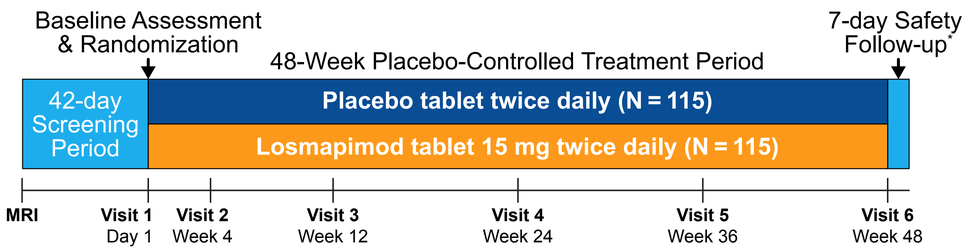
Introduction

- Facioscapulohumeral muscular dystrophy (FSHD) is one of the most common forms of muscular dystrophy. The disease is caused by toxic gain of function of the double homeobox 4 (DUX4) gene in skeletal muscle.[1]
- Currently, there are no treatment options for people living with FSHD that prevent and/or slow muscle wasting and weakness.
- Losmapimod is an investigational small molecule inhibitor of p38α/β Mitogen Activated Protein Kinase (MAPK) under development for the treatment of FSHD.
  - Preclinical research in FSHD muscle cells provided evidence that losmapimod:[2-4]
    - Reduced DUX4 expression
    - Normalized DUX4-regulated gene expression
    - Reduced muscle cell death
    - Did not impact myogenic differentiation
- Losmapimod was well tolerated in FSHD in two Phase 2 studies, FIS-001-2019 and FIS-002-2019 (ReDUX4) as well as several other adult indications.
  - The open-label extension periods of the Phase 2 studies are ongoing.
- Analysis of the ReDUX4 placebo-controlled trial data (N=80) provided evidence that treatment with losmapimod appears to slow disease progression and improve results of functional and structural outcome assessments that are relevant to FSHD.
- Study 1821-FSH-301 (REACH), the Phase 3 trial, is designed to assess efficacy and safety of losmapimod in a larger population of people with FSHD (including FSHD1 and FSHD2).
- Here, we report preliminary baseline characteristics for participants in REACH.

REACH Study Design

REACH: Phase 3 Randomized, Double-Blind, Placebo-Controlled, 48-Week Study of the Efficacy and Safety of Losmapimod in FSHD



*Upon completion of Part A, the placebo-controlled period, patients will have the option to roll over into Part B, the open-label extension.

Primary Objective

To evaluate the efficacy of losmapimod on FSHD disease progression assessed by reachable workspace (RWS) quantification of relative surface area (RSA) Q1–Q5 with 500 g wrist weight, averaged over right and left arms.

Main Inclusion Criteria

- Age 18–65 years
- Genetically confirmed diagnosis of FSHD1 or FSHD2
- Ricci score 2–4 (range 0–5). Patients who are wheelchair-dependent or dependent on walker or wheelchair for activities are not permitted to enroll in the study
- Screening total RSA (Q1–Q4) without weight in the dominant arm assessed by RWS ≥0.2 and ≤0.7

Reachable Workspace (RWS)

- RWS assesses an individual's reachability defined as a spherical envelope encompassing the set of farthest points relative to the shoulder that an individual can reach naturally by moving their arm in full extension
- Relative Surface Area (RSA) is the area of the spherical surface envelope that an individual's hand can reach in space with the arm extended, normalized to the participant's arm length.
  - Encompasses five quadrants (Q1–Q5) representing frontal and posterior inferior reachable area, each with a possible maximum score of 0.25
  - Scale: 0 (no reachable workspace) to 1.25 (theoretical maximum reachable workspace)

Study Demographics and Baseline Characteristics

Demographics and baseline characteristics of REACH study participants are summarized; corresponding ReDUX4 data are included for comparison.

- FSHD disease characteristics assessed by:
  - Age at first symptom
  - FSHD type
  - For FSHD1, number of repeat units in the contracted D4Z4 repeat array
- Disease severity at baseline assessed by:
  - Clinical severity using Ricci score (range 0–5)
  - RWS quantification of RSA Q1–Q5 with 500 g wrist weight, averaged over both arms

Study Demographics

	ReDUX4 (N=80)	REACH (N=260)
Sex, n (%)		
Male	54 (67.5)	145 (55.8)
Female	26 (32.5)	115 (44.2)
Race, n (%)		
White / Caucasian	70 (87.5)	231 (88.8)
Black / African American	0	3 (1.2)
American Indian / Alaska Native / Other Indigenous	0	0
Native Hawaiian or Other Pacific Islander	0	0
Asian	5 (6.3)	6 (2.3)
Other	1 (1.3)	9 (3.5)
Not Applicable / Not Reported	4 (5.0)	11 (4.2)
Age, mean (SD) years	45.7 (12.49)	43.9 (12.2)
Region, n (%)		
Europe	11 (13.8)	155 (59.6)
North America	69 (86.3)	105 (40.4)
BMI, mean (SD) kg/m^2	25.95 (5.16)	25.44 (4.63)

FSHD Disease Characteristics

	ReDUX4 (N=80)	REACH (N=260)
Age at First Symptom, years		
Mean (SD)	21.4 (13.2)	22.7 (11.5)
Median (min, max)	19.0 (1, 61)	21.0 (0, 54)
FSHD Type, n (%)		
Type 1	80 (100)*	242 (93.1)
Type 2	N/A	18 (6.9)
FSHD Repeats (Type 1 patients)		N=242
FSHD Repeats, mean (SD)	5.1 (1.5)	5.2 (1.6)
FSHD Repeat Category, n (%)		
1–3 repeats	13 (16.3)	34 (14.0)
4–9 repeats	67 (83.8)	208 (86.0)

*The ReDUX4 inclusion criteria specified FSHD Type 1 only.

Baseline Severity

	ReDUX4 (N=80)	REACH (N=260)
Ricci Score		
Mean (SD)	3.20 (0.47)	3.19 (0.59)
Category, n (%)		
2–3	49 (61.3)	148 (56.9)
3.5–4	31 (38.8)	112 (43.1)
RWS: Total RSA (Q1–Q5), average of both arms with weight		
Mean (SD)	0.536 (0.233)	0.521 (0.165)
Median	0.547	0.517

Conclusions

- Baseline characteristics of the REACH study population are similar to those of the ReDUX4 study population.
- Data are subject to updates upon database lock. Top-line efficacy and safety data from REACH are anticipated in Q4 2024.

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References: 1) Lemmers *Science* 2010;329:1650–53. **2)** Oliva *J Pharmacol Exp Ther* 2019; 370(2): 219–30. **3)** Rojas *J Pharmacol Exp Ther* 2020; 374(3): 489–98. **4)** Wilson MDA 2024 (Poster T347). **REACH:** NCT05397470; EudraCT Number: 2022-000389-16. **ReDUX4:** NCT04003974: EudraCT Number: 2019-001181-15.