ACE-083 FSHD Trial
Myostatin Inhibitor

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2018 FSHD CONNECT
The FSH Society’s International Network Meeting
Acceleron Pharma’s Approach to Drugs Targeting Muscle

ACE-2494
Systemic Agent

ACE-083
Local Agent
Atrophy and weakness of specific muscles can have a devastating impact on activities of daily living and a patient’s overall quality of life.

**Weakness of the Tibialis Anterior (TA)**
- Causes foot drop
- Impairs mobility/walking
- Increases risk of falls

**Weakness of the biceps brachii (BB)**
- Impairs ability to feed oneself
- Reduces ability to maintain hygiene
- Limits ability to lift objects
ACE-083 – A Locally-Acting Muscle Therapeutic

- ACE-083 is a locally-acting drug based on follistatin, a naturally occurring stimulator of muscle (myostatin+ inhibitor)
- Designed to be locally injected in affected muscles, to increase muscle mass and strength
- Increased muscle first demonstrated in healthy volunteers

ACE-083 FSHD Phase 2 Study Design

**Treatment**
- ACE-083 is injected into tibialis anterior (TA) or biceps muscle(s)

**Part 1 – 3 mos open-label, N=36**
- **TA, Biceps**
  - 150 mg unilateral
  - N=6/muscle
- **TA, Biceps**
  - 200 mg unilateral
  - N=6/muscle
- **TA 200 mg bilateral**
- **Biceps 240 mg unilateral**
  - N=6/muscle

**Part 2 – 6 mos placebo-controlled → 6 mos open-label, N=56**
- Randomize 1:1
  - **ACE-083**
    - bilateral
    - N=14/muscle
  - **Placebo**
    - bilateral
    - N=14/muscle
  - **ACE-083**
    - bilateral
    - N=14/muscle

**Key Eligibility Criteria**
- Age ≥ 18 years
- FSHD1 or FSHD2
- Mild to moderate weakness in ankle dorsiflexion or elbow flexion
- No medications affecting muscle

**Objectives**
- Safety and tolerability
- Dose selection
- Muscle mass, fat fraction (MRI)
- Measures of strength, function, quality of life, gait
ACE-083 FSHD Study – Safety Summary
Part 1 Cohorts 1 and 2

- ACE-083 was safe and generally well tolerated in patients who were treated for up to 3 months
- No serious adverse events
- Most common adverse events were injection site reactions and muscle pain
- No clinically significant laboratory abnormalities on treatment
Increases in *muscle volume* were dose dependent

Decreases in *fat fraction* in the tibialis anterior indicate leaner muscle
ACE-083 Multi-National Phase 2 Trial – US Sites

- Placebo–controlled Part 2 of FSHD study now enrolling (NCT02927080)
- Participating sites in US, Canada, and Spain

ACE-083 is an investigational drug, not approved by the FDA
Thank you