

Initial Results from Single Subcutaneous Administration of ACE-031, a Form of the Soluble Activin Type IIB Receptor, in Healthy Postmenopausal Volunteers.

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Abstract:

ACE-031 is a fusion protein derived from the extracellular domain of the human activin receptor type IIB (ActRIIB) linked to the Fc portion of human IgG1. ACE-031 binds with high affinity to GDF-8 (myostatin) and other negative regulators of muscle mass.

In mice, treatment with ACE-031 results in dose dependent increases in lean body mass, skeletal muscle and strength. The increase in skeletal muscle mass is due hypertrophy of the muscle. The pharmacologic response to ACE-031 was extended to non-human primates. The pharmacology observed in normal animals has been extended to rodent disease models of Duchene's Muscular Dystrophy (MDX mice) and ALS (SOD mice). Treatment with ACE-031 in the disease models resulted in increase in skeletal muscle, strength and functional benefit.

In the first Phase 1 study the safety and tolerability of single, escalating doses of ACE-031 in healthy postmenopausal women were evaluated. Secondary outcomes included assessments of the pharmacokinetic and pharmacodynamic properties of ACE-031.

Subjects received a single subcutaneous dose of ACE-031 or placebo at dose levels ranging from 0.02 to 3 mg/kg. ACE-031 was safe and well tolerated at all dose levels, with a linear PK profile and a T1/2 ranging from 10-14 days. Increases in lean body mass (LBM), as measured by DXA, were observed as early as 15 days following ACE-031 administration and were maintained at 2 months post dose (2.6 % mean increase from baseline). Changes in several biomarkers of pharmacologic activity were observed including increases in serum adiponectin and decreases in serum leptin consistent with increased fat metabolism. Increases in bone formation biomarker (bone specific alkaline phosphatase) and decreases in the bone resorption biomarker (serum-CTX,) were also observed.

These data support the development of ACE-031 in neuromuscular diseases such as DMD, FSHD and ALS.