

RESEARCH MONOGRAPH . COMPOUND PROFILE

ACE-031

A soluble activin receptor type IIB Fc fusion protein that traps myostatin and related ligands; investigated for muscular dystrophy.

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COMPOUND CLASS	Activin receptor type IIB ligand trap (myostatin pathway)

ABSTRACT

ACE-031 (sotatercept-related molecule; recombinant Fc fusion of the extracellular domain of human activin receptor type IIB; molecular weight approximately 100 kDa) is a soluble activin receptor type IIB ligand trap developed at Acceleron Pharma. The compound binds and sequesters myostatin (GDF-8), activin A, GDF-11, and other TGF-beta superfamily ligands in plasma, preventing receptor engagement at muscle and other tissues. Mechanism: myostatin pathway inhibition increases muscle mass and strength in preclinical models; the broader ligand trap mechanism distinguishes ACE-031 from antibody-based pure myostatin inhibitors (which target only myostatin). Phase 2 trials in Duchenne muscular dystrophy were halted in 2011 owing to epistaxis and gum bleeding (consistent with broader TGF-beta family disruption affecting vascular biology). The related compound sotatercept (luspatercept's predecessor) was approved for pulmonary arterial hypertension in 2024 with the same scaffold but different ligand binding profile. Used as a research probe for myostatin and broader TGF-beta family pharmacology.

1. Compound Identification

ACE-031 is described as activin receptor type iib ligand trap (myostatin pathway). A soluble activin receptor type IIB Fc fusion protein that traps myostatin and related ligands; investigated for muscular dystrophy.

1.1 Class summary

Activin receptor type IIB ligand trap (myostatin pathway)

1.2 Subtitle

A soluble activin receptor type IIB Fc fusion protein that traps myostatin and related ligands; investigated for muscular dystrophy.

2. Abstract

ACE-031 (sotatercept-related molecule; recombinant Fc fusion of the extracellular domain of human activin receptor type IIB; molecular weight approximately 100 kDa) is a soluble activin receptor type IIB ligand trap developed at Acceleron Pharma. The compound binds and sequesters myostatin (GDF-8), activin A, GDF-11, and other TGF-beta superfamily ligands in plasma, preventing receptor engagement at muscle and other tissues. Mechanism: myostatin pathway inhibition increases muscle mass and strength in preclinical models; the broader ligand trap mechanism distinguishes ACE-031 from antibody-based pure myostatin inhibitors (which target only myostatin). Phase 2 trials in Duchenne muscular dystrophy were halted in 2011 owing to epistaxis and gum bleeding (consistent with broader TGF-beta family disruption affecting vascular biology). The related compound sotatercept (luspatercept's predecessor) was approved for pulmonary arterial hypertension in 2024 with the same scaffold but different ligand binding profile. Used as a research probe for myostatin and broader TGF-beta family pharmacology.

3. Mechanism of Action

Soluble activin receptor type IIB Fc fusion ligand trap; binds and sequesters myostatin, activin A, GDF-11. Increases muscle mass via myostatin inhibition.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

Trial doses 0.5 to 3 mg/kg subcutaneous every 2 to 4 weeks.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Cadena SM, et al. Administration of a soluble activin type IIB receptor promotes skeletal muscle growth independent of fiber type. J Appl Physiol 2010.
2. Campbell C, et al. Myostatin inhibitors for Duchenne muscular dystrophy: phase 2 trial results. Muscle Nerve 2017.
3. Souza TA, et al. Proteomic identification and functional validation of activins and bone morphogenetic protein 11 as candidate novel muscle mass regulators. Mol Endocrinol 2008.

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