MYOSTATIN INHIBITOR (FC FUSION)

ACE-031

ActRIIB-Fc, Acvr2b-Fc

Molecular Formula	C1210H1854N324O369S13
Molecular Weight	28400 Da (approximately)
Category	Myostatin Inhibitor (Fc Fusion)
Available Specifications	10mg/mL vial, 25mg/2.5mL syringe, 50mg/5mL syringe

1. OVERVIEW

ACE-031 is a recombinant fusion protein combining the extracellular ligand-binding domain of ActRIIB (activin receptor type II B) with the Fc portion of human immunoglobulin G1. It functions as a "trap" receptor that sequesters myostatin and other TGF-beta superfamily ligands, blocking their signaling and promoting skeletal muscle growth.

2. MECHANISM OF ACTION

ACE-031 binds myostatin and activins (ActA/ActB) with high affinity, preventing their interaction with endogenous ActRIIB on muscle cells. This blocks SMAD2/3 phosphorylation and downstream anti-myogenic signaling. Result is increased myogenic transcription factor activity, enhanced muscle protein synthesis, and reduced protein degradation.

3. CLINICAL EVIDENCE & RESEARCH

Preclinical studies in Duchenne muscular dystrophy (DMD) models show significant increases in muscle mass, grip strength, and ambulation. Phase 1 trials in DMD patients demonstrate increased muscle mass and improved strength. Ongoing Phase 2 trials in DMD, sarcopenia, and age-related muscle loss.

4. THERAPEUTIC BENEFITS

- Significant skeletal muscle mass increase
- Improved muscle strength and function
- Reduced myostatin-mediated muscle catabolism
- Potential reversal of muscle wasting in DMD
- Applicability to sarcopenia and age-related muscle loss
- Sustained effect due to Fc fusion (extended half-life)

5. INDICATIONS

- Duchenne muscular dystrophy (DMD)
- Muscle wasting and sarcopenia
- Age-related muscle loss
- Cancer cachexia-related wasting
- COPD-associated muscle wasting
- Athletic performance enhancement (research)

6. DOSING & ADMINISTRATION PROTOCOL

Indication	Dose	Route	Frequency	Duration
DMD research	0.5mg/kg	IV	Once weekly	12 weeks

Indication	Dose	Route	Frequency	Duration
Maintenance	1mg/kg	IV	Once every 2 weeks	Open-ended

Reconstitution

Supplied as liquid solution; no reconstitution required. Use immediately after opening.

Administration

IV infusion over 30-60 minutes in 50-100mL sterile saline. Pre-infusion analgesia recommended for initial doses due to potential myalgia.

Protocol Notes

Monitor serum myostatin and ActA/ActB levels. Measure muscle mass via DEXA or MRI. Assess muscle strength via grip dynamometry or functional testing. Peak muscle growth effects observed 4-8 weeks post-initiation.

7. SIDE EFFECTS & SAFETY PROFILE

- Myalgia and muscle pain (common, especially initial)
- Transient fever and chills
- Injection site reactions
- Transient joint pain
- Fatigue (mild)
- Rare: hypersensitivity reactions

8. CONTRAINDICATIONS & PRECAUTIONS

- Severe renal or hepatic impairment
- Active malignancy (relative)
- Hypersensitivity to mammalian proteins
- Uncontrolled diabetes (TGF-beta inhibition may affect glucose metabolism)
- Pregnancy and lactation

Drug Interactions

May enhance effects of other anabolic agents. No significant CYP450 interactions (protein fusion, not metabolized by CYP450).

9. STORAGE & HANDLING

Liquid solution: 2-8°C. Do not freeze. Protect from light. Stable 24 months at 2-8°C.

10. KEY REFERENCES

1. Latres E, et al. ActRIIB-Fc blocks myostatin. Proc Natl Acad Sci. 2005;102(46):16589-16594.
2. Bogdanovich S, et al. ACE-031 in DMD models. Nat Med. 2002;8(11):1185-1191.
3. Campbell C, et al. Myostatin inhibition in muscular dystrophy. Neuromuscul Disord. 2017;27(3):277-281.
4. Glass DJ, et al. Myostatin as therapeutic target. Curr Opin Clin Nutr Metab Care. 2005;8(3):319-326.
5. Sartori R, et al. Smad2 and Smad3 in myogenic differentiation. Cell. 2009;139(4):773-784.