

RESEARCH MONOGRAPH . COMPOUND PROFILE

Romosozumab

A humanized monoclonal antibody against sclerostin; a dual-action bone agent that increases formation and decreases resorption.

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ABSTRACT

Romosozumab (CAS 909395-70-6; humanized IgG2 monoclonal antibody against sclerostin; molecular weight approximately 145 kDa) is a humanized monoclonal antibody developed by Amgen and UCB and approved by the FDA in 2019 (Evenity). The compound binds sclerostin (a glycoprotein produced by osteocytes that inhibits Wnt signaling on osteoblasts), neutralizing its inhibitory effect on bone formation. Mechanism is dual-action: increased bone formation (Wnt pathway de-inhibition on osteoblasts) plus decreased bone resorption (reduced osteoclast differentiation), an unusual combination producing more rapid BMD gains than any other osteoporosis agent. Approved for postmenopausal osteoporosis at high fracture risk. The ARCH trial demonstrated superior fracture reduction versus alendronate. Cardiovascular safety signal (increased cardiovascular events versus alendronate in ARCH) led to a black-box warning; the compound is contraindicated in patients with recent myocardial infarction or stroke. Treatment duration is 12 months (loss of effect with longer treatment). Used as the canonical anti-sclerostin agent.

1. Compound Identification

Romosozumab is described as anti-sclerostin monoclonal antibody. A humanized monoclonal antibody against sclerostin; a dual-action bone agent that increases formation and decreases resorption.

1.1 Class summary

Anti-sclerostin monoclonal antibody

1.2 Subtitle

A humanized monoclonal antibody against sclerostin; a dual-action bone agent that increases formation and decreases resorption.

2. Abstract

Romosozumab (CAS 909395-70-6; humanized IgG2 monoclonal antibody against sclerostin; molecular weight approximately 145 kDa) is a humanized monoclonal antibody developed by Amgen and UCB and approved by the FDA in 2019 (Evenity). The compound binds sclerostin (a glycoprotein produced by osteocytes that inhibits Wnt signaling on osteoblasts), neutralizing its inhibitory effect on bone formation. Mechanism is dual-action: increased bone formation (Wnt pathway de-inhibition on osteoblasts) plus decreased bone resorption (reduced osteoclast differentiation), an unusual combination producing more rapid BMD gains than any other osteoporosis agent. Approved for postmenopausal osteoporosis at high fracture risk. The ARCH trial demonstrated superior fracture reduction versus alendronate. Cardiovascular safety signal (increased cardiovascular events versus alendronate in ARCH) led to a black-box warning; the compound is contraindicated in patients with recent myocardial infarction or stroke. Treatment duration is 12 months (loss of effect with longer treatment). Used as the canonical anti-sclerostin agent.

3. Mechanism of Action

Anti-sclerostin monoclonal antibody; blocks osteocyte-derived Wnt inhibitor sclerostin. Dual-action: increased bone formation plus decreased resorption.

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

Clinical 210 mg subcutaneous monthly for 12 months.

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. Cosman F, et al. Romosozumab treatment in postmenopausal women with osteoporosis. N Engl J Med 2016.
2. Saag KG, et al. Romosozumab or alendronate for fracture prevention in women with osteoporosis (ARCH). N Engl J Med 2017.
3. Padhi D, et al. Single-dose, placebo-controlled, randomized study of AMG 785, a sclerostin monoclonal antibody. J Bone Miner Res 2011.

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