

RESEARCH MONOGRAPH . COMPOUND PROFILE

Abaloparatide

A modified parathyroid hormone-related protein (PTHrP) 1-34 analog with PTH1R receptor selectivity for the RG conformation; an anabolic bone agent.

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RESEARCH USE ONLY

ABSTRACT

Abaloparatide (BA058; modified PTHrP 1-34 analog with substitutions at positions 12, 19, 22, 23, 25, 26, 28, 29, 33; molecular weight approximately 3961 Da) is a synthetic analog of parathyroid hormone-related protein 1-34 developed at Radius Health and approved by the FDA in 2017 (Tymlos). The compound binds the PTH1 receptor (PTH1R) with selectivity for the transient RG (G-protein coupled) conformation over the prolonged R0 conformation favored by teriparatide; this RG selectivity is hypothesized to produce shorter-lived but more anabolic-favoring receptor signaling. Approved for severe osteoporosis with high fracture risk. The ACTIVE trial demonstrated comparable fracture reduction to teriparatide with possibly faster onset and reduced hypercalcemia incidence. Plasma half-life is approximately 1 hour. The 18-month treatment course mirrors teriparatide's cumulative-dose limitation. Used as a reference RG-selective PTH1R agonist.

1. Compound Identification

Abaloparatide is described as synthetic pthrp 1-34 analog. A modified parathyroid hormone-related protein (PTHrP) 1-34 analog with PTH1R receptor selectivity for the RG conformation; an anabolic bone agent.

1.1 Class summary

Synthetic PTHrP 1-34 analog

1.2 Subtitle

A modified parathyroid hormone-related protein (PTHrP) 1-34 analog with PTH1R receptor selectivity for the RG conformation; an anabolic bone agent.

2. Abstract

Abaloparatide (BA058; modified PTHrP 1-34 analog with substitutions at positions 12, 19, 22, 23, 25, 26, 28, 29, 33; molecular weight approximately 3961 Da) is a synthetic analog of parathyroid hormone-related protein 1-34 developed at Radius Health and approved by the FDA in 2017 (Tymlos). The compound binds the PTH1 receptor (PTH1R) with selectivity for the transient RG (G-protein coupled) conformation over the prolonged R0 conformation favored by teriparatide; this RG selectivity is hypothesized to produce shorter-lived but more anabolic-favoring receptor signaling. Approved for severe osteoporosis with high fracture risk. The ACTIVE trial demonstrated comparable fracture reduction to teriparatide with possibly faster onset and reduced hypercalcemia incidence. Plasma half-life is approximately 1 hour. The 18-month treatment course mirrors teriparatide's cumulative-dose limitation. Used as a reference RG-selective PTH1R agonist.

3. Mechanism of Action

Modified PTHrP 1-34 analog; PTH1R RG-conformation selective; transient receptor signaling favoring anabolic over catabolic effects.

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 80 mcg subcutaneous daily for up to 18 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. Miller PD, et al. Effect of abaloparatide vs placebo on new vertebral fractures in postmenopausal women with osteoporosis (ACTIVE). JAMA 2016.
2. Hattersley G, et al. Binding selectivity of abaloparatide for PTH-Type-1-Receptor conformations and effects on downstream signaling. Endocrinology 2016.
3. Cosman F, et al. Anabolic agents for postmenopausal osteoporosis. Endocrinol Metab Clin North Am 2017.

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