

RESEARCH MONOGRAPH . COMPOUND PROFILE

Cotadutide

A dual GLP-1 and glucagon receptor agonist; investigated for type 2 diabetes, NASH, and obesity.

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ABSTRACT

Cotadutide (MEDIO382; CAS 2125247-22-1; modified peptide with glucagon backbone and GLP-1 modifications; approximately 30 amino acid peptide with C16 fatty acid extension; molecular weight approximately 4140 Da) is a dual GLP-1/glucagon receptor agonist developed at AstraZeneca for type 2 diabetes, non-alcoholic steatohepatitis (NASH), and obesity. The compound is a balanced co-agonist (approximately 5:1 GLP-1:glucagon ratio at receptor). The GLP-1 component drives glucose-dependent insulin secretion, glucagon suppression, and appetite reduction; the glucagon component independently increases hepatic fatty acid oxidation, energy expenditure, and lipolysis. Phase 2 trials demonstrated superior weight loss and HbA1c reduction compared to GLP-1 monoagonists at matched dose, with hepatic fat reduction supporting the NASH indication. Plasma half-life supports once-daily subcutaneous dosing; phase 3 development is ongoing. Used as a reference dual GLP-1/glucagon agonist in metabolic research.

1. Compound Identification

Cotadutide is described as glp-1 / glucagon dual receptor agonist. A dual GLP-1 and glucagon receptor agonist; investigated for type 2 diabetes, NASH, and obesity.

1.1 Class summary

GLP-1 / glucagon dual receptor agonist

1.2 Subtitle

A dual GLP-1 and glucagon receptor agonist; investigated for type 2 diabetes, NASH, and obesity.

2. Abstract

Cotadutide (MEDI0382; CAS 2125247-22-1; modified peptide with glucagon backbone and GLP-1 modifications; approximately 30 amino acid peptide with C16 fatty acid extension; molecular weight approximately 4140 Da) is a dual GLP-1/glucagon receptor agonist developed at AstraZeneca for type 2 diabetes, non-alcoholic steatohepatitis (NASH), and obesity. The compound is a balanced co-agonist (approximately 5:1 GLP-1:glucagon ratio at receptor). The GLP-1 component drives glucose-dependent insulin secretion, glucagon suppression, and appetite reduction; the glucagon component independently increases hepatic fatty acid oxidation, energy expenditure, and lipolysis. Phase 2 trials demonstrated superior weight loss and HbA1c reduction compared to GLP-1 monoagonists at matched dose, with hepatic fat reduction supporting the NASH indication. Plasma half-life supports once-daily subcutaneous dosing; phase 3 development is ongoing. Used as a reference dual GLP-1/glucagon agonist in metabolic research.

3. Mechanism of Action

Dual GLP-1 and glucagon receptor agonism (~5:1 GLP-1:glucagon ratio). Combines GLP-1 glucoregulatory and appetite effects with glucagon-mediated lipolysis and energy expenditure.

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

Investigational; phase 2 doses 100 to 600 mcg subcutaneous daily.

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. Ambery P, et al. MEDI0382, a GLP-1/glucagon receptor dual agonist, in obese or overweight patients with type 2 diabetes. Lancet 2018.
2. Parker VER, et al. Cotadutide in NASH: glucagon co-agonism rationale. Hepatology 2020.
3. Robertson D, et al. Pharmacokinetics and pharmacodynamics of cotadutide. Clin Pharmacokinet 2019.

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