

RESEARCH MONOGRAPH . COMPOUND PROFILE

Mazdutide

A long-acting dual GLP-1 and glucagon receptor agonist; under development for obesity and type 2 diabetes.

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COMPOUND CLASS	GLP-1 / glucagon dual receptor agonist

ABSTRACT

Mazdutide (IBI362, LY3305677; modified peptide with glucagon backbone and GLP-1 modifications; molecular weight approximately 4500 Da) is a dual GLP-1/glucagon receptor agonist developed by Eli Lilly and out-licensed to Innovent Biologics for development in China. The compound is structurally and mechanistically similar to cotadutide and oxyntomodulin, with C18 fatty acid extension for once-weekly dosing. Phase 2 trials in type 2 diabetes and obesity demonstrated dose-dependent HbA1c reduction and weight loss comparable to or exceeding semaglutide at higher dose tiers. Phase 3 trials are ongoing in China (DREAMS program) and US. The dual mechanism produces increased energy expenditure (glucagon effect) on top of the GLP-1 appetite suppression. Used as a reference long-acting dual GLP-1/glucagon agonist.

1. Compound Identification

Mazdutide is described as glp-1 / glucagon dual receptor agonist. A long-acting dual GLP-1 and glucagon receptor agonist; under development for obesity and type 2 diabetes.

1.1 Class summary

GLP-1 / glucagon dual receptor agonist

1.2 Subtitle

A long-acting dual GLP-1 and glucagon receptor agonist; under development for obesity and type 2 diabetes.

2. Abstract

Mazdutide (IBI362, LY3305677; modified peptide with glucagon backbone and GLP-1 modifications; molecular weight approximately 4500 Da) is a dual GLP-1/glucagon receptor agonist developed by Eli Lilly and out-licensed to Innovent Biologics for development in China. The compound is structurally and mechanistically similar to cotadutide and oxyntomodulin, with C18 fatty acid extension for once-weekly dosing. Phase 2 trials in type 2 diabetes and obesity demonstrated dose-dependent HbA1c reduction and weight loss comparable to or exceeding semaglutide at higher dose tiers. Phase 3 trials are ongoing in China (DREAMS program) and US. The dual mechanism produces increased energy expenditure (glucagon effect) on top of the GLP-1 appetite suppression. Used as a reference long-acting dual GLP-1/glucagon agonist.

3. Mechanism of Action

Long-acting dual GLP-1 and glucagon receptor agonism with C18 fatty acid extension supporting once-weekly dosing.

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 1 to 9 mg subcutaneous weekly.

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. Ji L, et al. Efficacy and safety of mazdutide once weekly in Chinese adults with obesity. Lancet Diabetes Endocrinol 2024.
2. Coskun T, et al. LY3305677 (mazdutide), a balanced GLP-1/glucagon receptor co-agonist. Diabetes 2021.
3. Liu C, et al. Mazdutide in obesity and metabolic disease. Expert Opin Investig Drugs 2024.

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