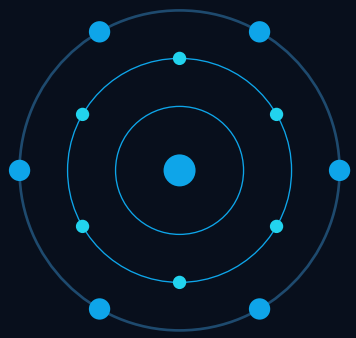
TESOFENSINE

Triple Monoamine Reuptake Inhibitor

NS2330 | Investigational Compound | Obesity & Metabolic Research

PHASE II CLINICAL DATA
NeuroSearch / Saniona



~10%	6.5%	32 wk	203
Mean Body Weight Loss	vs Placebo Difference	Trial Duration	Participants Phase IIb

COMPOUND OVERVIEW

What Is Tesofensine?

Tesofensine (NS2330) is an investigational small-molecule compound originally developed by NeuroSearch (later Saniona) that inhibits the presynaptic reuptake of serotonin, dopamine, and norepinephrine. Initially investigated for neurodegenerative indications including Alzheimer's and Parkinson's disease, tesofensine demonstrated significant weight-reducing effects in early clinical trials, redirecting research focus toward obesity pharmacotherapy.

By simultaneously modulating three major monoaminergic pathways, tesofensine produces potent appetite suppression and enhanced energy expenditure — a dual mechanism that distinguishes it from single-pathway agents such as selective serotonin reuptake inhibitors (SSRIs) or norepinephrine-dopamine reuptake inhibitors (NDRIs) used in other contexts.

MECHANISM OF ACTION

Triple-Pathway Neurotransmitter Modulation

5-HT — Serotonin Reuptake Inhibition

Blocks SERT transporter, elevating synaptic serotonin. Contributes to satiety signaling via hypothalamic 5-HT2C receptors and reduces hedonic food intake.

DA — Dopamine Reuptake Inhibition

Inhibits DAT transporter, increasing mesolimbic dopamine. Modulates reward-driven eating behavior and reduces motivational drive for calorie-dense foods.

NE — Norepinephrine Reuptake Inhibition

Blocks NET transporter, amplifying sympathomimetic signaling. Increases resting metabolic rate and promotes thermogenesis via adrenergic activation.

"Tesofensine 0.5 mg produced the largest weight loss seen in a Phase II obesity trial at the time of publication."

ADDITIONAL FINDINGS & SAFETY PROFILE

Secondary Efficacy Endpoints

- Significant waist circumference reduction (–7.6 cm at 0.5 mg)
- Improvements in fasting glucose and insulin sensitivity
- Favorable effects on triglycerides and HDL cholesterol
- Reduced hunger scores on validated appetite questionnaires
- Enhanced satiety and reduced cravings for high-fat foods
- Sustained weight loss trajectory through 24-week endpoint

Safety & Tolerability Profile

- Most common AEs: dry mouth, nausea, constipation, insomnia
- Mild, transient increase in heart rate (~8 bpm at 0.5 mg)
- Small, dose-dependent increase in systolic BP (~1–3 mmHg)
- No serious cardiac events reported in Phase II program
- No clinically relevant liver enzyme elevations observed
- Discontinuation rate similar to other obesity agents

RESEARCH APPLICATIONS

Areas of Scientific Interest

Obesity Pharmacotherapy

Dose-response modeling and long-term efficacy investigation in various obesity phenotypes including metabolic syndrome.

Neuroscience Research

Investigating monoamine pathway interactions, reward circuitry modulation, and appetite regulatory neuroscience.

Cardiometabolic Health

Exploring effects on metabolic syndrome components: insulin resistance, dyslipidemia, and visceral adiposity.

CNS Drug Development

Platform for triple reuptake inhibitor (TRI) pharmacology research and structure-activity relationship studies.

IMPORTANT: This document is intended exclusively for qualified researchers and scientific professionals. Tesofensine (NS2330) is an investigational compound that has not been approved by the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), or any other regulatory authority for human therapeutic use. This material does not constitute medical advice and must not be used to guide clinical treatment decisions. All research must comply with applicable institutional, national, and international regulations governing investigational compounds.