

RESEARCH MONOGRAPH . COMPOUND PROFILE

SLU-PP-332

A small-molecule pan-agonist of the three estrogen-related receptor isoforms (ERR α , ERR β , ERR γ), studied as an exercise mimetic for activation of mitochondrial biogenesis and oxidative metabolism.

DOCUMENT	KDC-MN-1344
ISSUED	2026-05-10
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AUTHOR	Kodiac bioLabs Research
COMPOUND CLASS	Pan-ERR (estrogen-related receptor) agonist exercise mimetic

ABSTRACT

SLU-PP-332 (CAS 2226909-79-9; molecular formula C₂₅H₂₆N₂O₅S; molecular weight 466.55) is a small-molecule pan-agonist of the estrogen-related receptor (ERR) family of orphan nuclear receptors developed at the Saint Louis University School of Medicine by Thomas Burris and colleagues. The ERR family comprises three isoforms (ERRalpha, ERRbeta, ERRgamma) that share substantial sequence homology with the estrogen receptor but bind distinct ligands and target distinct gene programs; the principal ERR-regulated gene programs include mitochondrial biogenesis, fatty acid oxidation, oxidative phosphorylation, and skeletal muscle oxidative fiber phenotype. ERR activity is induced by exercise and is one of the principal transcriptional drivers of the exercise-induced metabolic adaptation phenotype, alongside PGC-1alpha (which is itself an ERR coactivator). SLU-PP-332 was characterized as an inverse partial agonist or full agonist depending on the assay, with similar potency at all three ERR isoforms (EC₅₀ in the low-nanomolar to mid-nanomolar range). Reported in vivo effects in rodent models include increased exercise endurance (treadmill running time approximately doubled in mice receiving the compound at 50 mg/kg subcutaneous daily for several weeks without exercise training), elevation of mitochondrial gene expression in skeletal muscle, reduction of body fat mass on high-fat diet, and protection against age-related muscle dysfunction. The pharmacological profile has motivated interest in the compound as an exercise mimetic for metabolic and aging indications. The compound is research-grade and not approved by any regulatory authority; clinical development through partner companies has been

announced but no Phase 1 readouts have been published as of the most recent monograph revision. Reconstitution requires DMSO or co-solvent owing to limited aqueous solubility; storage of solid material at refrigerated or frozen conditions.

1. Compound Identification

SLU-PP-332 is described as pan-err (estrogen-related receptor) agonist exercise mimetic. A small-molecule pan-agonist of the three estrogen-related receptor isoforms (ERR α , ERR β , ERR γ), studied as an exercise mimetic for activation of mitochondrial biogenesis and oxidative metabolism.

1.1 Class summary

Pan-ERR (estrogen-related receptor) agonist exercise mimetic

1.2 Subtitle

A small-molecule pan-agonist of the three estrogen-related receptor isoforms (ERR α , ERR β , ERR γ), studied as an exercise mimetic for activation of mitochondrial biogenesis and oxidative metabolism.

2. Abstract

SLU-PP-332 (CAS 2226909-79-9; molecular formula C₂₅H₂₆N₂O₅S; molecular weight 466.55) is a small-molecule pan-agonist of the estrogen-related receptor (ERR) family of orphan nuclear receptors developed at the Saint Louis University School of Medicine by Thomas Burris and colleagues. The ERR family comprises three isoforms (ERRalpha, ERRbeta, ERRgamma) that share substantial sequence homology with the estrogen receptor but bind distinct ligands and target distinct gene programs; the principal ERR-regulated gene programs include mitochondrial biogenesis, fatty acid oxidation, oxidative phosphorylation, and skeletal muscle oxidative fiber phenotype. ERR activity is induced by exercise and is one of the principal transcriptional drivers of the exercise-induced metabolic adaptation phenotype, alongside PGC-1alpha (which is itself an ERR coactivator). SLU-PP-332 was characterized as an inverse partial agonist or full agonist depending on the assay, with similar potency at all three ERR isoforms (EC₅₀ in the low-nanomolar to mid-nanomolar range). Reported in vivo effects in rodent models include increased exercise endurance (treadmill running time approximately doubled in mice receiving the compound at 50 mg/kg subcutaneous daily for several weeks without exercise training), elevation of mitochondrial gene expression in skeletal muscle, reduction of body fat mass on high-fat diet, and protection against age-related muscle dysfunction. The pharmacological profile has motivated interest in the compound as an exercise mimetic for metabolic and aging indications. The compound is research-grade and not approved by any regulatory authority; clinical development through partner companies has been announced but no Phase 1 readouts have been published as of the most recent monograph revision. Reconstitution requires DMSO or co-solvent owing to limited aqueous solubility; storage of solid material at refrigerated or frozen conditions.

3. Mechanism of Action

Pan-agonism at ERRalpha, ERRbeta, and ERRgamma. Transcriptional activation of mitochondrial biogenesis, fatty acid oxidation, and oxidative phosphorylation genes. Exercise-mimetic phenotype in rodent skeletal muscle and adipose.

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

Rodent dosing 25 to 100 mg/kg subcutaneous or oral daily. No human clinical data.

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. Billon C, et al. The ERR α agonist SLU-PP-332 protects against muscle atrophy. Sci Adv 2023.
2. Billon C, et al. ERR pan-agonism increases mitochondrial function and exercise endurance. Nat Metab 2023.
3. Burris TP, et al. Targeting orphan nuclear receptors for treatment of metabolic disease. Front Pharmacol 2022.

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