

RESEARCH MONOGRAPH . COMPOUND PROFILE

Cutamesine (SA-4503)

*A selective sigma-1 receptor agonist
developed for ischemic stroke recovery
and major depressive disorder.*

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ABSTRACT

Cutamesine (SA-4503; CAS 165377-44-6; molecular formula $C_{19}H_{30}N_2O_2$; molecular weight 318.45) is a selective sigma-1 receptor agonist developed at Santen Pharmaceutical and licensed to M's Science. The compound has high sigma-1 affinity (K_i approximately 17 nM) with greater than 100-fold selectivity over sigma-2 and minimal off-target binding. Sigma-1 is a chaperone protein at the mitochondria-associated ER membrane that modulates ion channels, calcium signaling, and stress response. Phase 2 trials in ischemic stroke recovery (60 mg, 28 days starting within 72 hours of stroke) showed modest improvement; phase 2 in MDD showed mixed efficacy. Plasma half-life is approximately 5 hours. The compound is the cleanest available research probe for sigma-1 pharmacology. Used as the canonical selective sigma-1 agonist in academic research.

1. Compound Identification

Cutamesine (SA-4503) is described as selective sigma-1 receptor agonist. A selective sigma-1 receptor agonist developed for ischemic stroke recovery and major depressive disorder.

1.1 Class summary

Selective sigma-1 receptor agonist

1.2 Subtitle

A selective sigma-1 receptor agonist developed for ischemic stroke recovery and major depressive disorder.

2. Abstract

Cutamesine (SA-4503; CAS 165377-44-6; molecular formula C₁₉H₃₀N₂O₂; molecular weight 318.45) is a selective sigma-1 receptor agonist developed at Santen Pharmaceutical and licensed to M's Science. The compound has high sigma-1 affinity (K_i approximately 17 nM) with greater than 100-fold selectivity over sigma-2 and minimal off-target binding. Sigma-1 is a chaperone protein at the mitochondria-associated ER membrane that modulates ion channels, calcium signaling, and stress response. Phase 2 trials in ischemic stroke recovery (60 mg, 28 days starting within 72 hours of stroke) showed modest improvement; phase 2 in MDD showed mixed efficacy. Plasma half-life is approximately 5 hours. The compound is the cleanest available research probe for sigma-1 pharmacology. Used as the canonical selective sigma-1 agonist in academic research.

3. Mechanism of Action

Selective sigma-1 receptor agonist (greater than 100-fold over sigma-2); chaperone protein modulator at mitochondria-associated ER membrane.

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

Trial doses 1 to 60 mg per oral administration 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. Hayashi T, Su TP. Sigma-1 receptor chaperones at the ER-mitochondrion interface regulate Ca(2+) signaling and cell survival. Cell 2007.
2. Urfer R, et al. Phase II trial of the sigma-1 receptor agonist cutamesine (SA4503) for recovery enhancement after acute ischemic stroke. Stroke 2014.
3. Ishikawa M, et al. The sigma-1 receptor agonist SA4503 in major depressive disorder. J Clin Psychopharmacol 2007.

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