

# Bitopertin (R enantiomer)

Catalog No: **tcsc1261**



## Available Sizes

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**Size:** 1mg



## Specifications

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**CAS No:**

845614-12-2

**Formula:**

$C_{21}H_{20}F_7N_3O_4S$

**Pathway:**

Neuronal Signaling;Membrane Transporter/Ion Channel

**Target:**

GlyT;GlyT

**Purity / Grade:**

>98%

**Solubility:**

10 mM in DMSO

**Alternative Names:**

RG1678 (R enantiomer);RO4917838 (R enantiomer)

**Observed Molecular Weight:**

543.46

## Product Description

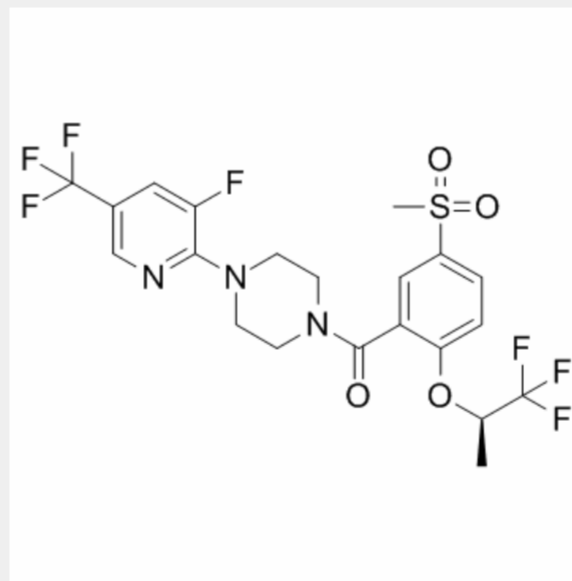
Bitopertin is a potent, noncompetitive **glycine reuptake** inhibitor, inhibits glycine uptake at human **GlyT1** with a concentration exhibiting **IC50** of 25 nM.

IC50 & Target: IC50: 25 nM (GlyT1)<sup>[1]</sup>

**In Vitro:**

Bitopertin (RG1678) competitively blocks [<sup>3</sup>H]ORG24598 binding sites at human GlyT1b in membranes from Chinese hamster ovary cells. Bitopertin potently inhibits [<sup>3</sup>H]glycine uptake in cells stably expressing hGlyT1b and mGlyT1b, with IC<sub>50</sub> values of 25±2 nM and 22±5 nM, respectively (n=6). Conversely, Bitopertin has no effect on hGlyT2-mediated glycine uptake up to 30 μM concentration. Bitopertin has high affinity for the recombinant hGlyT1b transporter. Under equilibrium conditions (1 h at room temperature), Bitopertin displaces [<sup>3</sup>H]ORG24598 binding with a K<sub>i</sub> of 8.1 nM. In hippocampal CA1 pyramidal cells, Bitopertin enhances NMDA-dependent long-term potentiation at 100 nM but not at 300 nM<sup>[1]</sup>. Additional profiling revealed that Bitopertin (RG1678) has an excellent selectivity profile against the GlyT2 isoform (IC<sub>50</sub>>30 μM) and toward a panel of 86 targets including transmembrane and soluble receptors, enzymes, ion channels, and monoamine transporters ([2]).

**In Vivo:** Bitopertin (RG1678) dose-dependently increases cerebrospinal fluid and striatal levels of glycine measured by microdialysis in rats. Additionally Bitopertin attenuates hyperlocomotion induced by the psychostimulant D-amphetamine or the NMDA receptor glycine site antagonist L-687,414 in mice. Bitopertin also prevents the hyper-response to D-amphetamine challenge in rats treated chronically with phencyclidine, an NMDA receptor open-channel blocker. Administration of vehicle has no effect on extracellular levels of striatal glycine, which remained constant throughout the experiment. In contrast, p.o. administration of Bitopertin (1-30 mg/kg) produced a dose-dependent increase in extracellular glycine levels. Bitopertin 30 mg/kg produces glycine levels 2.5 times higher than pretreatment levels. A similar dose-dependent increase in glycine concentration is observed in the CSF of rats treated p.o. with Bitopertin (1-10 mg/kg) compared with vehicle-treated animals, 3 h after drug administration. Interestingly, the level of CSF glycine increase 3 h after Bitopertin dosing is very similar to the increase in the microdialysis experiment at the same time point<sup>[1]</sup>. In vivo pharmacokinetic studies in rat and monkey reveals that Bitopertin (RG1678) has, in both species, a low plasma clearance, an intermediate volume of distribution, a good oral bioavailability (78% for rat, 56% for monkey), and a favorable terminal half-life (5.8 h for rat, 6.4 h for monkey). The plasma protein binding is high in the two preclinical species (97%) and in human (98%). The CNS penetration of Bitopertin in rat (brain/plasma=0.7) is better than that in mouse (brain/plasma=0.5)<sup>[2]</sup>.



All products are for RESEARCH USE ONLY. Not for diagnostic & therapeutic purposes!