

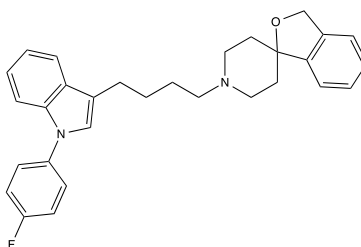
**Catalog # 10-4202**

**Siramesine**

CAS# 147817-50-3

1'-[4-[1-(4-Fluorophenyl)indol-3-yl]butyl]spiro[1H-2-benzofuran-3,4'-piperidine; Lu 28-179

Lot # FBS1060



Siramesine (Lu 28-179) is a  $\sigma_2$  selective agonist ( $IC_{50}$ 's:  $\sigma_1 = 17nM$ ,  $\sigma_2 = 0.2nM$ ).<sup>1</sup> It produced non-sedating potent and long-last anxiolytic effects in rodents.<sup>2</sup> Siramesine induced caspase-independent programmed cell death in various cancer cell lines *via* increased levels of ROS and lysosomal leakage.<sup>3,4,5</sup> Mitochondrial destabilization *via* loss of membrane potential and increased ROS has also been offered as a mechanism of action for the triggering of cell death by Siramesine.<sup>6</sup>

- 1) Perregaard *et al.* (1995), *Sigma ligands with subnanomolar affinity and preference for the sigma 2 binding site. 1. 3-(omega-aminoalkyl)-1H-indoles*; J.Med.Chem. **38** 1998
- 2) Sanchez *et al.* (1997), *The selective sigma2-ligand Lu 280179 has potent anxiolytic effects in rodents*; J.Pharmacol.Exp.Ther. **283** 1323
- 3) Ostenfeld *et al.* (2005), *Effective tumor cell death by sigma-2 receptor ligand siramesine involves lysosomal leakage and oxidative stress*; Cancer Res. **65** 8975
- 4) Ostenfeld *et al.* (2008), *Anti-cancer agent siramesine is a lysosomotropic detergent that induces cytoprotective autophagosome accumulation*; Autophagy **4** 487
- 5) Dielschneider *et al.* (2016), *Lysosomotropic agents selectively target chronic lymphocytic leukemia cells due to altered sphingolipid metabolism*; Leukemia **30** 1290
- 6) Cesen *et al.* (2013), *Siramesine triggers cell death through destabilization of mitochondria, but not lysosomes*; Cell Death Dis. **4** e818

**PHYSICAL DATA**

Molecular Weight: 454.59

Molecular Formula: C<sub>30</sub>H<sub>31</sub>FN<sub>2</sub>O

Purity: >98% by HPLC

NMR: Conforms

Solubility: DMSO (>25 mg/mL)

Physical Description: White solid

Storage and Stability: Store as supplied desiccated at -20°C for up to 1 year from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 3 months.

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