

Product Data Sheet

Product Name: Verubecestat (MK-8931)

Cat. No.: GC11098

Chemical Properties

Cas. No. 1286770-55-5

Chemical Name (R)-5-fluoro-N-(4-fluoro-3-(3-imino-2,5-dimethyl-1,1-dioxido-1,2,4-thiadiazinan-5-yl)phenyl)picolinamide 2,2,2-trifluoroacetate

SMILES O=C(C1=NC=C(F)C=C1)NC2=CC=C(F)C([C@@](C3)(C)NC(N(C)S3(=O)=O)=N)=C2.FC(F)(F)C(=O)O

Formula $C_{19}H_{18}F_5N_5O_5S$

M.Wt 523.43

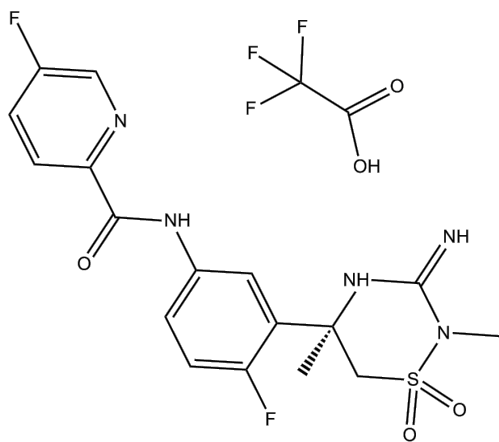
Solubility $\geq 40.9\text{mg/mL}$ in DMSO

Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Background

Ki: 2.2 and 3.4 nM for human and mouse Bace1, respectively

Verubecestat (MK-8931) is a BACE1 inhibitor.

β -Amyloid ($A\beta$) peptides are regarded to be involved in the etiology of AD. BACE1 is required for the

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Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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A β production, and BACE1 inhibition is therefore an promising target for the AD treatment.

In vitro: Verubecestat has been identified as a potent inhibitor of both human and mouse Bace1 and verubecestat could also inhibit the production of A β 40, A β 42, and sAPP β in human cells with similar potency. Verubecestat was also found to be a potent inhibitor of purified human BACE2. Moreover, verubecestat was essentially inactive with over 45,000-fold selectivity in the purified human aspartyl proteases cathepsin D, cathepsin E, and pepsin and had a very weak inhibitor of purified human renin with 15,000-fold selectivity. In addition, verubecestat was also found to have minimal or no activity against various tested receptors, ion channels, transporters, as well as enzymes [1].

In vivo: Verubecestat could reduce plasma, cerebrospinal fluid, and brain concentrations of A β 40, A β 42, and sAPP β after acute and chronic administration to both rats and monkeys. Moreover, the chronic treatment of rats and monkeys with verubecestat at exposures >40-fold higher than those tested in clinical trials did not cause many of the adverse effects previously reported to BACE inhibition. In rabbits and mice but not in monkeys, fur hypopigmentation was found [1].

Clinical trial: Single and multiple doses of verubecestat were generally well tolerated and produced reductions in A β 40, A β 42, and sAPP β in the CSF [1].

Reference:

[1] Kennedy ME et al. The BACE1 inhibitor verubecestat (MK-8931) reduces CNS β -amyloid in animal models and in Alzheimer's disease patients. Sci Transl Med.2016 Nov 2;8(363):363ra150.

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