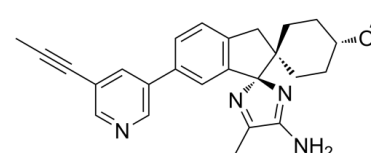


## Data Sheet

<b>Product Name:</b>	Lanabecestat
<b>Cat. No.:</b>	CS-7494
<b>CAS No.:</b>	1383982-64-6
<b>Molecular Formula:</b>	C <sub>26</sub> H <sub>28</sub> N <sub>4</sub> O
<b>Molecular Weight:</b>	412.53
<b>Target:</b>	Beta-secretase
<b>Pathway:</b>	Neuronal Signaling
<b>Solubility:</b>	DMSO : ≥ 100 mg/mL



### BIOLOGICAL ACTIVITY:

Lanabecestat (AZD3293) is a potent, orally active and blood-brain barrier penetrating **BACE1** inhibitor with a **K<sub>i</sub>** of 0.4 nM. Lanabecestat is used for the research of Alzheimer's disease<sup>[1]</sup>. IC<sub>50</sub> & Target: K<sub>i</sub>: 0.4 nM (BACE1)<sup>[1]</sup> *In Vitro*: Lanabecestat acts as a full inhibitor of BACE1 *in vitro*, with a competitive and reversible mechanism of action towards the hBACE1 active site. Lanabecestat displays a very high target affinity and a markedly slow target off-rate. The off-rate of lanabecestat has an estimated t<sub>1/2</sub> of approximately 9 h. Lanabecestat displays pM potency in primary neuron cultures from mice and guinea pigs and in SH-SY5Y cells over-expressing AβPP (IC<sub>50</sub>=610 pM, 310 pM, and 80 pM, respectively). The *in vitro* plasma protein binding of lanabecestat is determined by equilibrium dialysis using mouse, rat, guinea pig, dog, and human plasma. The compound is stable in the plasma of these species for at least the duration of the *in vitro* incubation period. The unbound fractions are 1.3% to 1.8% for mice, 4.2% to 5.9% for rats, 8.3% to 10.3% for guinea pigs, 9.4% to 10.3% for dogs, and 7.7% to 9.4% for human plasma. The mean blood:plasma ratio of 0.7 in human blood indicates no significant association with red blood cells. The free fraction in the brain tissue binding assay is 4.5%<sup>[1]</sup>. *In Vivo*: In mice, guinea pigs, and dogs, lanabecestat displays significant dose- and time-dependent reductions in plasma, cerebrospinal fluid, and brain concentrations of Aβ<sub>40</sub>, Aβ<sub>42</sub>, and sAβPPβ<sup>[1]</sup>.

### PROTOCOL (Extracted from published papers and Only for reference)

**Cell Assay:** <sup>[1]</sup>Cells are incubated with different lanabecestat concentrations for 5 to 16 h, and the release of sAβPPβ, Aβ<sub>1-40</sub>, Aβ<sub>1-42</sub>, or sAβPPα into the medium is analyzed using kits. Cytotoxic effect of lanabecestat is evaluated in the cell plates using cell proliferation/cytotoxicity kit<sup>[1]</sup>. **Animal Administration:** Lanabecestat is prepared in 5% dimethylacetamide in 0.3 M gluconic acid, pH 3.<sup>[1]</sup> Female 7- to 14-week-old C57BL/6 mice (n=6 per treatment group and timepoint) receive vehicle or lanabecestat solution at 50, 100, or 200 μmol/kg (20, 41, or 82 mg/kg) as a single dose via oral gavage. Mice and guinea pigs are anesthetized 1.5, 2, 3, 4, 6, 8, 16, 24, or 48 h after the (last) administration of vehicle or drug. Cerebrospinal fluid (CSF) is aspirated from the cisterna magna, and plasma is isolated from blood collected by cardiac puncture into EDTA tubes. The animals are then sacrificed by decapitation, and the brains are dissected into hemispheres<sup>[1]</sup>.

### References:

[1]. Eketjäll S, et al. AZD3293: A Novel, Orally Active BACE1 Inhibitor with High Potency and Permeability and Markedly Slow Off-Rate Kinetics. J Alzheimers Dis. 2016;50(4):1109-23.

**CAIndexNames:**

Dispiro[cyclohexane-1,2'-[2H]indene-1'(3'H),2''-[2H]imidazol]-4''-amine, 4-methoxy-5''-methyl-6'-[5-(1-propyn-1-yl)-3-pyridinyl]-, (1 $\alpha$ ,1'R,4 $\beta$ )-

**SMILES:**

CC#CC1=CC(C2=CC([C@@]34N=C(C)C(N)=N4)=C(C[C@@]53CC[C@@H](OC)CC5)C=C2)=CN=C1

**Caution: Product has not been fully validated for medical applications. For research use only.**

Tel: 610-426-3128

Fax: 888-484-5008

E-mail: [sales@ChemScene.com](mailto:sales@ChemScene.com)

Address: 1 Deer Park Dr, Suite F, Monmouth Junction, NJ 08852, USA