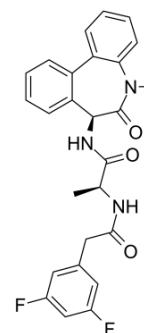


## YO-01027

<b>Cat. No.:</b>	HY-13526		
<b>CAS No.:</b>	209984-56-5		
<b>Molecular Formula:</b>	C <sub>26</sub> H <sub>23</sub> F <sub>2</sub> N <sub>3</sub> O <sub>3</sub>		
<b>Molecular Weight:</b>	463.48		
<b>Target:</b>	Notch; $\gamma$ -secretase		
<b>Pathway:</b>	Neuronal Signaling; Stem Cell/Wnt		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO :  $\geq$  33 mg/mL (71.20 mM)  
 H<sub>2</sub>O : < 0.1 mg/mL (insoluble)  
 \* " $\geq$ " means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.1576 mL	10.7880 mL	21.5759 mL
	5 mM	0.4315 mL	2.1576 mL	4.3152 mL
	10 mM	0.2158 mL	1.0788 mL	2.1576 mL

Please refer to the solubility information to select the appropriate solvent.

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
 Solubility: 2.5 mg/mL (5.39 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE- $\beta$ -CD in saline)  
 Solubility: 2.5 mg/mL (5.39 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
 Solubility:  $\geq$  2.5 mg/mL (5.39 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

YO-01027 (Dibenzazepine;DBZ) is a potent  $\gamma$ -secretase inhibitor with IC<sub>50</sub> values of 2.92 and 2.64 nM for Notch and APPL cleavage, respectively.

#### IC<sub>50</sub> & Target

IC<sub>50</sub>: 2.92 $\pm$ 0.22 (Notch), 2.64 $\pm$ 0.30 (APPL) nM<sup>[1]</sup>

<b>In Vitro</b>	<p>Increasing concentrations of DBZ administered to APPL- or Notch-expressing cells leads to the progressive accumulation of APPL CTF fragments and a decrease in NICD production in a strictly dose-dependent manner<sup>[1]</sup>. The molecular targets of CE and DBZ are the N-terminal fragment of presenilin 1 within the <math>\gamma</math>-secretase complex<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>In Vivo</b>	<p>DBZ blocks activated Notch1 signaling in abdominal aortic aneurysm (AAA) tissue from both Ang II-infused Apo E<sup>-/-</sup> mice and human undergoing AAA repair. DBZ markedly prevents Ang II-stimulated accumulation of macrophages and CD4+ T cells, and ERK-mediated angiogenesis, simultaneously reverses Th2 response, in vivo<sup>[3]</sup>. Administration of DBZ markedly attenuates renal fibrosis and expression of fibrotic markers, including collagen 1<math>\alpha</math>1/3<math>\alpha</math>1, fibronectin, and <math>\alpha</math>-smoothmuscle actin. DBZ significantly inhibits ureteral obstruction -induced expression of transforming growth factor (TGF)- <math>\beta</math>, phosphorylated Smad 2, and Smad 3<sup>[4]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## PROTOCOL

<b>Cell Assay</b> <sup>[1]</sup>	<p>DBZ (0.1, 1, 2.5, 5, 7.5, 10, 25, 50, 100, 250 nM) are added to the S2 cell medium upon induction of Notch or APPL expression, 6 h before protein harvesting. For each sample, the same inhibitor is also included at the corresponding concentration in the lysis buffer for protein extraction and immunoblot analysis<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>Animal Administration</b> <sup>[3]</sup>	<p>Mice: Male wild-type (WT) C57BL/6J and Apo E<sup>-/-</sup> mice are used in the study. Ang II-treated mice are received an intraperitoneal injection of either saline vehicle or <math>\gamma</math>-secretase inhibitor, dibenzazepine (DBZ) (1 mg/kg/d, dissolved in saline) 1 day before mini-pump implantation, and the treatment continued daily for 4 weeks. The blood pressure is measured in conscious mice using a computerized tail-cuff system. All mice are anesthetized. The aortic tissues are removed and prepared for further histological and molecular analysis<sup>[3]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## REFERENCES

- [1]. Groth C, et al. Pharmacological analysis of Drosophila melanogaster gamma-secretase with respect to differential proteolysis of Notch and APP. *Mol Pharmacol*. 2010 Apr;77(4):567-74.
- [2]. Fuwa H, et al. Divergent synthesis of multifunctional molecular probes to elucidate the enzyme specificity of dipeptidic gamma-secretase inhibitors. *ACS Chem Biol*. 2007 Jun 15;2(6):408-18.
- [3]. Zheng YH, et al. Notch  $\gamma$ -secretase inhibitor dibenzazepine attenuates angiotensin II-induced abdominal aortic aneurysm in ApoE knockout mice by multiple mechanisms. *PLoS One*. 2013 Dec 16;8(12):e83310.
- [4]. Xiao Z, et al. The Notch  $\gamma$ -secretase inhibitor ameliorates kidney fibrosis via inhibition of TGF- $\beta$ /Smad2/3 signaling pathway activation. *Int J Biochem Cell Biol*. 2014 Oct;55:65-71.

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

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