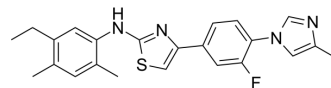


## NGP555

<b>Cat. No.:</b>	HY-108714		
<b>CAS No.:</b>	1304630-27-0		
<b>Molecular Formula:</b>	C <sub>23</sub> H <sub>23</sub> FN <sub>4</sub> S		
<b>Molecular Weight:</b>	406.52		
<b>Target:</b>	γ-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	2 years
		-20°C	1 year



### SOLVENT & SOLUBILITY

<b>In Vitro</b>	DMSO : 25 mg/mL (61.50 mM; Need ultrasonic)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	<b>Preparing Stock Solutions</b>	1 mM	2.4599 mL	12.2995 mL	24.5990 mL
		5 mM	0.4920 mL	2.4599 mL	4.9198 mL
10 mM		0.2460 mL	1.2300 mL	2.4599 mL	
Please refer to the solubility information to select the appropriate solvent.					
<b>In Vivo</b>	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: 2.5 mg/mL (6.15 mM); Suspended solution; Need ultrasonic  2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (6.15 mM); Clear solution				

### BIOLOGICAL ACTIVITY

<b>Description</b>	NGP555 is a γ-secretase modulator. NGP555 Lowers the Amyloid Biomarker Aβ <sub>42</sub> <sup>[1]</sup> .
<b>IC<sub>50</sub> &amp; Target</b>	γ-secretase <sup>[1]</sup>
<b>In Vitro</b>	NGP555 potently lowers Aβ <sub>42</sub> in cell cultures (9 nM) while increasing shorter forms of Aβ <sup>[1]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
<b>In Vivo</b>	NGP555 significantly lowers Aβ <sub>42</sub> in the cerebrospinal fluid (CSF) at time points from 8 to 10 hours post dose, panel B shows that reduction of Aβ cerebrospinal fluid (CSF) levels is significant at 3.75 mg/kg of NGP555 and above, and panel C shows an increase in Aβ <sub>38</sub> levels at 15 mg/kg of NGP555 and above. When combining the reduction of Aβ <sub>42</sub> with an increase in Aβ <sub>38</sub> ,

NGP555 is effective at raising CSF A $\beta$ <sub>38/42</sub> ratio at 1.87 mg/kg and above (panel D). NGP555-treated Tg mice show a significant protection from decline in performance with >65% less decline (P<0.005) when comparing the differential of Tg to non-Tg vehicle-treated mice. NGP555 also shows good oral bioavailability and is brain-penetrant with a brain:plasma ratio of ~0.93 in mice<sup>[1]</sup>.

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## PROTOCOL

### Cell Assay <sup>[1]</sup>

SH-SY5Y-APP cells, Tg2576 mixed brain cultures, or C57 mixed brain cultures are treated with various concentrations of NGP555 in triplicate wells, for 18 hours. Media is collected and analyzed for A $\beta$  peptides using triplex ELISA (A $\beta$ <sub>38</sub> and A $\beta$ <sub>42</sub>) <sup>[1]</sup>.

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### Animal Administration <sup>[1]</sup>

For CSF studies, Normal Sprague-Dawley male rats (250 to 300 g) are administered NGP555 in 80% PEG orally or vehicle only, n=10/group. Rats are dosed once-daily for a single-dose or 14 days of dosing. After the final dose, cerebrospinal fluid (CSF) samples are either collected at varying time points or a single time point post-last dose. Rats are deeply anesthetized with isoflurane, and CSF is collected from the cisterna magna. Samples are tested for A $\beta$  level. For Y-maze study, transgenic mice (Tg2576 line expressing the APP-Swe mutation) and non-transgenic age-matched littermates (n=a minimum of 12/group) are treated with vehicle, NGP555 (25 mg/kg) once-daily for 30 consecutive days (starting at 5 months of age). At 6 months, mice are assessed on the Y-maze behavior test<sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## REFERENCES

[1]. Kounnas MZ, et al. NGP 555, a  $\gamma$ -Secretase Modulator, Lowers the Amyloid Biomarker, A $\beta$ <sub>42</sub>, in Cerebrospinal Fluid while Preventing Alzheimer's Disease Cognitive Decline in Rodents. *Alzheimers Dement* (N Y). 2017 Jan;3(1):65-73.

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

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