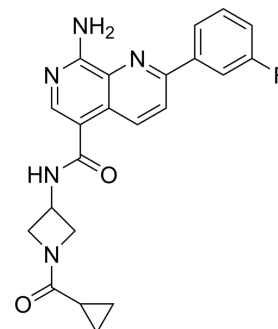


## GNE-495

<b>Cat. No.:</b>	HY-100343		
<b>CAS No.:</b>	1449277-10-4		
<b>Molecular Formula:</b>	C <sub>22</sub> H <sub>20</sub> FN <sub>5</sub> O <sub>2</sub>		
<b>Molecular Weight:</b>	405		
<b>Target:</b>	MAP4K		
<b>Pathway:</b>	MAPK/ERK Pathway		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	1 year
		-20°C	6 months



## SOLVENT & SOLUBILITY

### In Vitro

DMSO : 2.17 mg/mL (5.36 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.4691 mL	12.3457 mL	24.6914 mL
	5 mM	0.4938 mL	2.4691 mL	4.9383 mL
	10 mM	---	---	---

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

### In Vivo

- Add each solvent one by one: 2% DMSO >> 40% PEG300 >> 5% Tween-80 >> 53% PBS  
Solubility: 1 mg/mL (2.47 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 0.22 mg/mL (0.54 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 0.22 mg/mL (0.54 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 0.22 mg/mL (0.54 mM); Clear solution

## BIOLOGICAL ACTIVITY

### Description

GNE-495 is a potent and selective MAP4K4 inhibitor with an IC<sub>50</sub> of 3.7 nM.

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

MAP4K4  
3.7 nM (IC<sub>50</sub>)

## In Vitro

GNE-495 is a potent and selective MAP4K4 inhibitor with efficacy in retinal angiogenesis. GNE-495 shows the best balance of MAP4K4 inhibition, permeability, microsomal stability, and cellular potency<sup>[1]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## In Vivo

GNE-495 is administered intraperitoneally to neonatal mouse pups at high doses: 25 and 50 mg/kg. GNE-495 shows good in vivo profile in all species tested, with low clearances, moderate terminal half-lives, and reasonable oral exposure levels (F=37-47%)<sup>[1]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

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

Rats, Mice and Pups <sup>[1]</sup>

For the brain cassette study, three male Sprague-Dawley (SD) rats are dosed with intravenous (IV) bolus of six test compounds (e.g., GNE-495; 0.5 mg/kg). For the mouse PK study, female CD-1 mice are administered IV bolus doses of GNE-495 (1 mg/kg). In addition, female CD-1 mice are administered GNE-495 (5 mg/kg) via oral (PO) gavage. A dosing volume of 2 mL/kg is used for the rat brain cassette PK and 5 mL/kg is used for all other dosing. Animals are not fasted prior to dose administration, and water and food are available ad libitum. Following administration of the compound of interest, three blood samples (~60 µL) are collected at each time point from individual mice up to either 9 or 24 hours post-dose using a serial sampling approach. Immediately upon collection, the blood is mixed with K2EDTA and stored on ice or in a chilled Kryorack prior to centrifugation to obtain plasma. Within 1 hr of collection, blood samples are centrifuged at approximately 1000-2000× g for 10-15 min at 4°C, and plasma is harvested. The plasma samples are stored at -70 to -80°C until analysis. For neonate PK, 3-day old CD1 pups are injected with 25 mg/kg and 50 mg/kg GNE-495 intraperitoneally, blood samples are collected at the time points indicated, retinas are collected one hour post-dose and snap frozen in liquid nitrogen and stored at -80°C until analysis. Plasma and retinal lysate concentrations are determined by LC/MS/MS.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Oncogene. 2023 Mar 15.

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## REFERENCES

[1]. Ndubaku CO et al. Structure-Based Design of GNE-495, a Potent and Selective MAP4K4 Inhibitor with Efficacy in Retinal Angiogenesis. ACS Med Chem Lett. 2015 Jun 29;6(8):913-8.

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

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