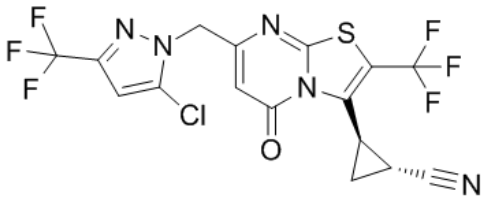
Product Data Sheet

Product Name: GNE 0723
Cat. No.: GC31270

Chemical Properties

Cas. No.	1883518-31-7		
SMILES	N#C[C@H]1[C@H](C2=C(C(F)(F)F)SC3=NC(CN4N=C(C(F)(F)F)C=C4Cl)=CC(N32)=O)C1		
Formula	$C_{16}H_8ClF_6N_5OS$	M.Wt	467.78
Solubility	DMSO : 190 mg/mL (406.17 mM; Need ultrasonic)	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



Protocol

Cell experiment [1]:

Cell lines CHO cell lines

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Preparation Method	Whole-cell patch-clamp recordings were made from CHO cell lines, 1μM GNE 0723 and 0.03-100μM Glu was applied for a 5ms pulse duration using a 2-barrel theta tube perfusion system with a P-601.30L PiezoMove linear actuator.
Reaction Conditions	1μM
Applications	GNE 0723 at 1μM enhanced NMDAR currents evoked by a wide range of Glu concentrations.

Animal experiment [1]:

Animal models	Sex-mixed 4–6-month-old J20
Preparation Method	Doses of GNE 0723 were administered via oral gavage as 0.5% methylcellulose and 0.2% Tween 80 (MCT) suspension. Vehicle was used as control. Drug doses for GNE 0723 are expressed as mg/kg of free base.
Dosage form	3mg/kg; oral; every other day for 5 weeks.
Applications	An early probe trial 24 h after 3 days of MWM training revealed a significant quadrant preference (reference memory) in GNE 0723-treated J20 mice.

References:

[1]. Hanson, Jesse E., et al. "GluN2A NMDA receptor enhancement improves brain oscillations, synchrony, and cognitive functions in Dravet syndrome and Alzheimer's disease models." Cell reports 30.2 (2020): 381-396.

Background

GNE 0723 is a GluN2A subunit-selective and brain-penetrant positive allosteric modulator (PAM) of NMDARs, with an EC_{50} of 0.021μM and a maximal potentiation of 152%[1,2].

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In vitro, Whole-cell recordings at room temperature (RT) from CHO cells expressing GluN2A-containing NMDARs showed that 1μM GNE 0723 enhanced the peak current and slowed the current deactivation in response to brief pulses of glutamate (Glu)[3].

In vivo, mouse clearance of GNE 0723 was 26mL·min^{-1}·kg^{-1} and oral bioavailability was 24%[1]. GNE 0723 (3mg/kg; oral; every other day for 5 weeks) treatment improved memory retention in J20 mice and improved long-term memory consolidation in J20 and WT mice by the Morris water maze (MWM) test[3]. GNE 0723 (3mg/kg; oral; every other day for 5 weeks) enhances fear learning in Scn1a-KI mice[3].

References:
[1]. Villemure, Elisia, et al. "GluN2A-selective pyridopyrimidinone series of NMDAR positive allosteric modulators with an improved in vivo profile." ACS Medicinal Chemistry Letters 8.1 (2017): 84-89.
[2]. Li, Zhongtang, et al. "Discovery of novel and potent N-methyl-d-aspartate receptor positive allosteric modulators with antidepressant-like activity in rodent models." Journal of Medicinal Chemistry 64.9 (2021): 5551-5576.
[3]. Hanson, Jesse E., et al. "GluN2A NMDA receptor enhancement improves brain oscillations, synchrony, and cognitive functions in Dravet syndrome and Alzheimer's disease models." Cell reports 30.2 (2020): 381-396.

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