上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：JNJ40411813
CAS 号： 1127498-03-6
产品货号：S89226

生物活性：

Description	JNJ-40411813 (ADX-71149) 是一种新的 metabotropic Glutamate 2 receptor (mGlu2R) 的正变构调节剂，EC50 为 147 nM。JNJ-40411813 具有口服生物活性，可穿透血脑屏障。JNJ-40411813 具有抗抑郁的潜在特性。
IC50 & Target[1]	mGlu2 Receptor 147 nM (EC_{50})

Cellular Effect

Cell Line	Type	Value	Description
CHO	EC_{50}	147 nM	Positive allosteric modulation of human mGlu2 receptor expressed in CHO cells assessed as potentiation of glutamate-induced effect incubated for 30 mins prior to [35S]GTPgamma addition measured after 30 mins
CHO	EC_{50}	147 nM	Positive allosteric modulation of human mGlu2 receptor expressed in CHO cell membranes assessed as potentiation of glutamate-induced effect incubated for 30 mins prior to [35S]GTPgamma addition measured after 30 mins by scintillation counting method
CHO	IC_{50}	68 nM	Displacement of [3H]19 from human mGlu2 receptor expressed in CHO cells
CHO-K1	EC_{50}	1350 nM	Positive allosteric modulation at human mGlu2 receptor L639A mutant expressed in CHO-K1 cells assessed as potentiation of glutamate-induced effect incubated for 30 mins prior to [35S]GTPgamma addition measured after 30 mins by scintillation counting method
CHO-K1	EC_{50}	1630 nM	Positive allosteric modulation at human mGlu2 receptor N735D mutant expressed in CHO-K1 cells assessed as potentiation of glutamate-induced effect incubated for 30 mins prior to [35S]GTPgamma addition measured after 30 mins by scintillation counting method
CHO-K1	EC_{50}	2000 nM	Positive allosteric modulation at human mGlu2 receptor F643A mutant expressed in CHO-K1 cells assessed as potentiation of glutamate-induced effect incubated for 30 mins prior to [35S]GTPgamma addition measured after 30 mins by scintillation counting method
CHO-K1	EC_{50}	2570 nM	Positive allosteric modulation at human mGlu2 receptor W773A mutant expressed in CHO-K1 cells assessed as potentiation of glutamate-induced effect incubated for 30 mins prior to [35S]GTPgamma addition measured after 30 mins by scintillation counting method
CHO-K1	EC_{50}	265 nM	Positive allosteric modulation at human mGlu2 receptor F776A mutant expressed in CHO-K1 cells assessed as

上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

				potentiation of glutamate-induced effect incubated for 30 mins prior to [35S]GTPgamma addition measured after 30 mins by scintillation counting method
	CHO-K1	EC_{50}	65 nM	Positive allosteric modulation of wild-type human mGlu2 receptor expressed in CHO-K1 cells assessed as potentiation of glutamate-induced effect incubated for 30 mins prior to [35S]GTPgamma addition measured after 30 mins by scintillation counting method
	CHO-K1	EC_{50}	77 nM	Positive allosteric modulation at wild type human mGlu2 receptor L732A mutant expressed in CHO-K1 cells assessed as potentiation of glutamate-induced effect preincubated for 30 mins prior to glutamate challenge measured after 30 mins by [35S]GTP-gammaS binding assay

In Vivo

NJ-40411813 (ADX-71149) (5-20 mg/kg, 灌胃, 24 h 6 次) 在 Glutamate (HY-N0455B) 的协同作用下，明显增强了大脑区域对谷氨酸反应，特别是皮质区、纹状体和海马[2]。

药代动力学分析[2]

Route	Dose (mg/kg)	AUC_{INF_obs} (ng·h/mL)	$t_{1/2}$ (h)	T_{max} (h)	C_{max} (ng/mL)	Cl_{obs} (L·h/kg)	V_{ss_obs} (L/kg)
							2.31.4±0.
i.v.	2.5	1833±90	/	/	/	1.4±0.1	10.2
p.o.	10	2250±417	2.31±0.5	7	938	/	/

Animal Model:	Male Wistar Rats (150 mg)[2]
Dosage:	5 mg/kg, 20 mg/kg
Administration:	Oral Gavage (p.o.)
Result:	Showed increasing in basal binding with an EC50 of 48 μM and a Combined with 10 μM glutamate, [35S]GTPγS binding with an EC50 of 7.3 μM and a maximal effect of 380%.

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 ：25 mg/mL (72.49 mM; 超声助溶; 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO）

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8996 mL	14.4979 mL	28.9957 mL
	5 mM	0.5799 mL	2.8996 mL	5.7991 mL
	10 mM	0.2900 mL	1.4498 mL	2.8996 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 2 years; -20°C, 1 year。-80°C 储存时，请在 2 年内使用， -20°C 储存时，请在 1 年内使用。

动物实验：

请根据您的 实验动物和给药方式 选择适当的溶解方案。

以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

	——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 方案 一 请依序添加每种溶剂： 10% DMSO → 40% PEG300 → 5% Tween-80 → 45% Saline Solubility: 2.5 mg/mL (7.25 mM); 悬浊液; 超声加热助溶 此方案可获得 2.5 mg/mL 的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；再向上述体系中加入 50 μL Tween-80，混合均匀；然后再继续加入 450 μL 生理盐水 定容至 1 mL。 生理盐水的配制：将 0.9 g 氯化钠，溶解于 ddH₂O 并定容至 100 mL，可以得到澄清透明的生理盐水溶液。 方案 二 请依序添加每种溶剂： 10% DMSO → 90% (20% SBE-β-CD in Saline) Solubility: ≥ 2.5 mg/mL (7.25 mM); 澄清溶液 此方案可获得 ≥2.5 mg/mL（饱和度未知）的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液 中，混合均匀。 2 g SBE-β-CD（磺丁基醚 β-环糊精）粉末定容于 10 mL 的生理盐水中，完全溶解至澄清透明。 方案 三 请依序添加每种溶剂： 10% DMSO → 90% Corn Oil Solubility: 2.5 mg/mL (7.25 mM); 澄清溶液; 超声助溶 此方案可获得 2.5 mg/mL 的澄清溶液，此方案实验周期在半个月以上的动物实验酌情使用。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
参考文献	[1]. Cid JM, et al. Discovery of 1-Butyl-3-chloro-4-(4-phenyl-1-piperidinyl)-(1H)-pyridone (JNJ-40411813): A Novel Positive Allosteric Modulator of the Metabotropic Glutamate 2 Receptor. J Med Chem. 2014 Aug 14;57(15):6495-512. [2]. Hilde Lavreysen, et al. Pharmacological and pharmacokinetic properties of JNJ-40411813, a positive allosteric modulator of the mGlu2 receptor. Pharmacol Res Perspect 2015 Feb;3(1):e00096. [3]. Dunlop J, Schizophrenia, et al. Schizophrenia drug discovery and development in an evolving era: are new drug targets fulfilling expectations?. Journal of Psychopharmacology. 29 (2): 230–8.

完整储备液配制表：

请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80° C, 2 years; -20° C, 1 year。-80° C 储存时，请在 2 年内使用， -20° C 储存时，请在 1 年内使用。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	**1 mM**	2.8996 mL	14.4979 mL	28.9957 mL	72.4893 mL

上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

	5 mM	0.5799 mL	2.8996 mL	5.7991 mL	14.4979 mL
	10 mM	0.2900 mL	1.4498 mL	2.8996 mL	7.2489 mL
	15 mM	0.1933 mL	0.9665 mL	1.9330 mL	4.8326 mL
	20 mM	0.1450 mL	0.7249 mL	1.4498 mL	3.6245 mL
	25 mM	0.1160 mL	0.5799 mL	1.1598 mL	2.8996 mL
	30 mM	0.0967 mL	0.4833 mL	0.9665 mL	2.4163 mL
	40 mM	0.0725 mL	0.3624 mL	0.7249 mL	1.8122 mL
	50 mM	0.0580 mL	0.2900 mL	0.5799 mL	1.4498 mL
	60 mM	0.0483 mL	0.2416 mL	0.4833 mL	1.2082 mL