产品名称：TAE226 (NVP-TAE226)
产品别名：TAE226；NVP-TAE 226

生物活性：

Description	NVP-TAE 226 (TAE226) is a potent and ATP-competitive dual FAK and IGF-1R inhibitor with IC50s of 5.5 nM and 140 nM, respectively. NVP-TAE 226 (TAE226) also effectively inhibits Pyk2 and insulin receptor (InsR) with IC50s of 3.5 nM and 44 nM, respectively[1][2].
IC_{50} & Target	IC50: 5.5 nM (FAK), 3.5 nM (Pyk2), 140 nM (IGF-IR), 40 nM (InsR), 0.16 μM (c-Met), 0.36 μM (KDR), 0.48 μM (Flt3)[1]
In Vitro	NVP-TAE 226 (TAE226), a potent ATP-competitive inhibitor of several tyrosine protein kinases, in particular FAK and IGF-IR kinases. In a cell-based kinase assays, FAK, IGF-IR kinase, and IR kinase are inhibited with an IC50 range of 100 to 300 nM compared with the other kinases tested, which are >10-fold less sensitive. In culture, NVP-TAE 226 inhibits extracellular matrix-induced autophosphorylation of FAK (Tyr^{395}). NVP-TAE 226 also inhibits IGF-I-induced phosphorylation of IGF-IR and activity of its downstream target genes such as MAPK and Akt. NVP-TAE 226 retards tumor cell growth as assessed by a cell viability assay and attenuates G_2-M cell cycle progression associated with a decrease in cyclin B1 and phosphorylated cdc2 (Tyr^{15}) protein expression. NVP-TAE 226 treatment inhibits tumor cell invasion by at least 50% compared with the control in an in vitro Matrigel invasion assay. Interestingly, TAE226 treatment of tumor cells containing wild-type p53 mainly exhibits G_2-M arrest, whereas tumor cells bearing mutant p53 underwent apoptosis[1].
In Vivo	Treatment with NVP-TAE 226 (TAE226) at 50 or 75 mg/kg extends the median survival of U87 xenograft animals by 6 and 7 days, respectively (P=0.084 and P=0.042, respectively, compared with vehicle-treated animals). However, NVP-TAE 226 treatment of LN229-engrafted animals significantly prolongs their median survival by 19 days (P<0.004 for both dosages, compared with vehicle-treated animals)[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL** (**106.62 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1325 mL	10.6623 mL	21.3247 mL
	5 mM	0.4265 mL	2.1325 mL	4.2649 mL
	10 mM	0.2132 mL	1.0662 mL	2.1325 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, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

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：

——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

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (5.33 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (5.33 mM，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 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.33 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.33 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 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。
References	[1]. Liu TJ, et al. Inhibition of both focal adhesion kinase and insulin-like growth factor-I receptor kinase suppresses glioma proliferation in vitro and in vivo. Mol Cancer Ther, 2007, 6(4), 1357-1367. [2]. Delimont D, et al. Laminin α2-mediated focal adhesion kinase activation triggers Alport glomerular pathogenesis. PLoS One. 2014 Jun 10;9(6):e99083. [3]. Lietha D, et al. Crystal structures of the FAK kinase in complex with TAE226 and related bis-anilino pyrimidine inhibitors reveal a helical DFG conformation. PLoS One. 2008;3(11):e3800.

实验参考：

Cell Assay	Glioma cell cultures are harvested with 0.05% trypsin and seeded in triplicate at 2×10^4 in 24-well culture plates for 24 h before drug treatment. Culture medium is used for mock treatment. Cells are harvested at the indicated day after treatment, and viable cells are counted using the Vi-cell viability analyzer. The antiproliferative activity of NVP-TAE 226 (ranging from 0.25 to 1 μM) on cells growing in culture is determined using a tetrazolium-based colorimetric MTT assay[1].
Animal Administration	Mice[1] Male nude mice used for this study are 6 to 8 weeks old. In DMEM/F12 serum-free media (5 μL), 5×10^5 of U87 cells and 1×10^6 of LN229 cells per mouse are implanted intracranially through a guide-screw system. Four days after injection of the tumor cells, mice are randomized into three groups for each cell line (n=6). Mice in group 1 are treated with 50 mg/kg NVP-TAE 226 in 200 μL of 0.5% methylcellulose, via an oral gavage. The mice in group 2 receive 75 mg/kg NVP-TAE 226 in 200 μL of 0.5% methylcellulose. The mice in group 3 the same vehicle used for administration of NVP-TAE 226 (control). Treatment frequency is once a day for 5 days and off for 2 days, for a duration of 4 weeks. Mice are monitored daily. Mice are euthanized when they are moribund, and the whole brain is extracted for rapid freezing in liquid nitrogen and storage at -70°C.
References	[1]. Liu TJ, et al. Inhibition of both focal adhesion kinase and insulin-like growth factor-I receptor kinase suppresses glioma proliferation in vitro and in vivo. Mol Cancer Ther, 2007, 6(4), 1357-1367. [2]. Delimont D, et al. Laminin α2-mediated focal adhesion kinase activation triggers Alport glomerular pathogenesis. PLoS One. 2014 Jun 10;9(6):e99083. [3]. Lietha D, et al. Crystal structures of the FAK kinase in complex with TAE226 and related bis-anilino pyrimidine inhibitors reveal a helical DFG conformation. PLoS One. 2008;3(11):e3800.