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：KX2-391 (dihydrochloride)
产品别名：Tirbanibulin dihydrochloride

生物活性：

Description	Tirbanibulin (dihydrochloride) (KX2-391 (dihydrochloride)) is an inhibitor of Src that targets the peptide substrate site of Src, with GI50 of 9-60 nM in cancer cell lines.
IC_{50} & Target	GI50: 9 nM (Src HuH7), 13 nM (Src PLC/PRF/5), 26 nM (Src Hep3B), 60 nM (Src HepG2)
In Vitro	Tirbanibulin (KX2-391) is a Src inhibitor that is directed to the Src substrate pocket. KX2-391 shows steep dose-response curves against Huh7 (GI50=9 nM), PLC/PRF/5 (GI50=13 nM), Hep3B (GI50=26 nM), and HepG2 (GI50=60 nM), four hepatic cell cancer (HCC) cell lines[1]. Tirbanibulin (KX2-391) is found to inhibit certain leukemia cells that are resistant to current commercially available drugs, such as those derived from chronic leukemia cells with the T3151 mutation. Tirbanibulin (KX2-391) is evaluated in engineered Src driven cell growth assays inNIH3T3/c-Src527F and SYF/c-Src527F cells and exhibits GI50 with 23 nM and 39 nM, respectively[2].
In Vivo	Orally administered Tirbanibulin (KX2-391) is shown to inhibit primary tumor growth and to suppress metastasis, in pre-clinical animal models of cancer[2].
Solvent&Solubility	***In Vitro:*** **DMSO : 33.33 mg/mL (66.07 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9824 mL	9.9118 mL	19.8236 mL
	5 mM	0.3965 mL	1.9824 mL	3.9647 mL
	10 mM	0.1982 mL	0.9912 mL	1.9824 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 (4.96 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.96 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% (20% SBE-β-CD in saline)

Solubility: ≥ 2.5 mg/mL (4.96 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (4.96 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 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (4.96 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.96 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]. Lau GM, et al. Expression of Src and FAK in hepatocellular carcinoma and the effect of Src inhibitors on hepatocellular carcinoma in vitro. Dig Dis Sci, 2009, 54(7), 1465-1474. [2]. Fallah-Tafti A, et al. Thiazolyl N-benzyl-substituted acetamide derivatives: synthesis, Src kinase inhibitory and anticancer activities. Eur J Med Chem, 2011, 46(10), 4853-4858.

实验参考：

Cell Assay	Liver cell lines including Huh7, PLC/PRF/5, Hep3B, and HepG2 are routinely cultured and maintained in basal medium containing 2% fetal bovine serum (FBS) at 37°C and 5% CO_2. Cells are seeded at 4.0×10^3/190 μL and 8.0×10^3/190 μL per well of 96-well plate in basal medium containing 1.5% FBS. These are cultured overnight at 37°C and 5% CO_2 prior to the addition of Tirbanibulin (KX2-391), at concentrations ranging from 6,564 to 0.012 nM in triplicates. Treated cells are incubated for 3 days. Ten μLs of 3-(4,5-dimethylthiazol- 2-yl)-2,5-diphenyltetrazolium bromide (MTT) solution (5 mg/mL) is then added to each well on day 3 and cells incubated for 4 hours. The formazan product is dissolved with 10% SDS in dilute HCl. Optical density at 570 nm is measured. For comparison of activity and potency, parallel experiments are performed using Tirbanibulin (KX2-391). Growth inhibition curves, 50% inhibition concentration (GI_{50}), and 80% inhibition concentration (GI_{80}) are determined using GraphPad Prism 5 statistical software. Data are normalized to represent percentage of maximum response as well as reported in optical density at wavelength of 570 nm (OD570) signal format. [1]
References	[1]. Lau GM, et al. Expression of Src and FAK in hepatocellular carcinoma and the effect of Src inhibitors on hepatocellular carcinoma in vitro. Dig Dis Sci, 2009, 54(7), 1465-1474. [2]. Fallah-Tafti A, et al. Thiazolyl N-benzyl-substituted acetamide derivatives: synthesis, Src kinase inhibitory and anticancer activities. Eur J Med Chem, 2011, 46(10), 4853-4858.