产品名称：GNF-7
产品别名：GNF-7

生物活性：

Description

GNF-7 inhibits Bcr-Abl WT and Bcr-Abl T315I with IC50 of 133 nM and 61 nM, respectively. IC50 value: 133 nM (Bcr-Abl WT), 61 nM (Bcr-Abl T315I) Target: Bcr-Abl in vitro: GNF-7 is amongst the first type II inhibitors capable of inhibiting T315I to be described and will serve as a valuable lead to design next generation Bcr-Abl kinase inhibitors. GNF-7 exhibits some selectivity (4 to 100-fold) for T315I Bcr-Abl (IC50 = 11 nM, in Ba/F3 cell line) relative to kinases such as TPR-Met, NPM-ALK, JAK-3, Flt-3. in vivo: GNF-7 displays significant efficacy against T315I-Bcr-Abl without appreciable toxicity in a bioluminescent xenograft mouse model using a transformed T315I-Bcr-Abl-Ba/F3 cell line that has a stable luciferase expression. GNF-7 exhibits excellent pharmacokinetic parameters in mice, with good systemic exposure (AUC = 26656 hrs*nM, Cmax = 3.6 uM) along with reasonable half life (t1/2=3.2 hrs) and favorable oral bioavailability (BAV=36%) being observed following oral administration of a single dose of 20 mg/kg.

Solvent&Solubility

In Vitro:

DMSO : ≥ 33 mg/mL (60.27 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8264 mL	9.1319 mL	18.2638 mL
	5 mM	0.3653 mL	1.8264 mL	3.6528 mL
	10 mM	0.1826 mL	0.9132 mL	1.8264 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 mg/mL (3.65 mM); Clear solution

此方案可获得 ≥ 2 mg/mL (3.65 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.0 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 mg/mL (3.65 mM); Clear solution

此方案可获得 ≥ 2 mg/mL (3.65 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.0 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。

References	[1]. Choi HG, et al. A type-II kinase inhibitor capable of inhibiting the T315I "gatekeeper" mutant of Bcr-Abl. J Med Chem. 2010 Aug 12;53(15):5439-48. [2]. Lu X, et al. Hybrid pyrimidine alkynyls inhibit the clinically resistance related Bcr-Abl(T315I) mutant. Bioorg Med Chem Lett. 2015 Sep 1;25(17):3458-63. [3]. Liang X, et al. Discovery of 2-((3-Amino-4-methylphenyl)amino)-N-(2-methyl-5-(3-(trifluoromethyl)benzamido)phenyl)-4-(methylamino) pyrimidine-5-carboxamide (CHMFL-ABL-053) as a Potent, Selective, and Orally Available BCR-ABL/SRC/p38 Kinase Inhibitor for Ch