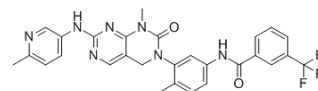


Data Sheet

Product Name:	GNF-7
Cat. No.:	HY-10943
CAS No.:	839706-07-9
Molecular Formula:	C ₂₈ H ₂₄ F ₃ N ₇ O ₂
Molecular Weight:	547.53
Target:	Bcr-Abl
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO: ≥ 33 mg/mL



BIOLOGICAL ACTIVITY:

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, C_{max} = 3.6 uM) along with reasonable half life (t_{1/2}=3.2 hrs) and favorable oral bioavailability (BAV=36%) being observed following oral administration of a single dose of 20 mg/kg.

PROTOCOL (Extracted from published papers and Only for reference)

Animal administration [1] GNF-7 was dissolved in a 100% PEG300 solution formulation (2.5 mg/mL) and dosed at 5 mg/kg intravenously via the lateral vein (n=3). Five to six week old male Balb/c mice (20–25 g) were obtained from Jackson Laboratory. The oral dose was prepared in a 1:1 formulation of PEG300 and distilled water and administered at 20 mg/kg via oral gavage (n=3). Five blood samples (50 µL) were serially drawn via retro orbital sinus within 24 hours after dosing. Plasma concentrations of GNF-7 were quantified utilizing a Liquid Chromatography/Mass Spectrometry (LC/MS/MS) assay. Pharmacokinetic parameters were calculated by non-compartmental regression analysis using Winnonlin 4.0 software.

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 Chronic Myeloid Leukemia. *J Med Chem.* 2016 Mar 10; 59(5):1984–2004.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA