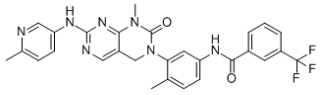
Data Sheet

Product Name:	GNF–7
Cat. No.:	HY-10943
CAS No.:	839706-07-9
Molecular Formula:	$C_{28}H_{24}F_3N_7O_2$
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, 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.

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