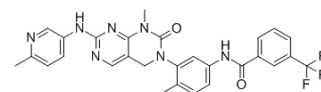


## GNF-7

Cat. No.:	HY-10943		
CAS No.:	839706-07-9		
Molecular Formula:	C <sub>28</sub> H <sub>24</sub> F <sub>3</sub> N <sub>7</sub> O <sub>2</sub>		
Molecular Weight:	547.53		
Target:	Bcr-Abl; Ack1		
Pathway:	Protein Tyrosine Kinase/RTK		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



## SOLVENT & SOLUBILITY

### In Vitro

DMSO : ≥ 33 mg/mL (60.27 mM)  
 \* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		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

Please refer to the solubility information to select the appropriate solvent.

### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
 Solubility: ≥ 2 mg/mL (3.65 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
 Solubility: ≥ 2 mg/mL (3.65 mM); Clear solution

## BIOLOGICAL ACTIVITY

### Description

GNF-7 is a multikinase inhibitor. GNF-7 is a Bcr-Abl inhibitor, with IC<sub>50</sub>s of 133 nM and 61 nM for Bcr-Abl<sup>WT</sup> and Bcr-Abl<sup>T315I</sup>, respectively. GNF-7 also possesses inhibitory activity against both ACK1 (activated CDC42 kinase 1) and GCK (germinal center kinase) with IC<sub>50</sub>s of 25 nM and 8 nM, respectively. GNF-7 can be used for the research of hematologic malignancies<sup>[1]</sup> [2][3].

### IC<sub>50</sub> & Target

IC<sub>50</sub>: 133 nM (Bcr-Abl<sup>WT</sup>)<sup>[1]</sup>, 61 nM (Bcr-Abl<sup>T315I</sup>)<sup>[1]</sup>, 25 nM (ACK1)<sup>[3]</sup>, 8 nM (GCK)<sup>[3]</sup>

### In Vitro

GNF-7 potently inhibits wild-type Bcr-Abl (IC<sub>50</sub><5 nM) and Bcr-Abl mutants such as T315I (IC<sub>50</sub>=11 nM), G250E (IC<sub>50</sub><5 nM), E255V (IC<sub>50</sub>=10 nM), F317L (IC<sub>50</sub><5 nM) and M351T (IC<sub>50</sub><5 nM) in cellular assays<sup>[2]</sup>.

GNF-7 (1  $\mu$ M; 2 hours) suppresses AKT/mTOR signaling and GCK downstream<sup>[3]</sup>.  
 GNF-7 (1  $\mu$ M; 24 hours) induces of apoptosis and cell cycle arrest in NRAS mutant cell lines<sup>[3]</sup>.  
 MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### Western Blot Analysis<sup>[3]</sup>

Cell Line:	Ba/F3-NRAS-G12D cells, OCI-AML3 cells
Concentration:	1 $\mu$ M
Incubation Time:	2 hours
Result:	Caused a decreased level of phosphorylation of p70S6K1, AKT (S473), JNK, and p38.

#### Apoptosis Analysis<sup>[3]</sup>

Cell Line:	OCI-AML3 cells
Concentration:	1 $\mu$ M
Incubation Time:	24 hours
Result:	Increased the levels of both cleaved PARP and cleaved caspase 3 and diminished bcl-2 and MCL1.

#### Cell Cycle Analysis<sup>[3]</sup>

Cell Line:	OCI-AML3 cells
Concentration:	1 $\mu$ M
Incubation Time:	24 hours
Result:	Induced of G0-G1 arrest.

#### In Vivo

GNF-7 (10-20 mg/kg; o.p.; daily; for 7 days) displays significant in vivo efficacy against T315I Bcr-Abl in the bioluminescent xenograft mouse model<sup>[2]</sup>.  
 GNF-7 exhibits moderate oral bioavailability (mice 36%) and  $C_{max}$  (mice 3616 nM) following oral administration (mice 20 mg/kg)<sup>[2]</sup>.  
 GNF-7 exhibits terminal elimination half-lives (mice 3.8 h) due to high plasma clearance (8.6 mL/min/kg) following intravenous injection (mice 5 mg/kg)<sup>[2]</sup>.  
 MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	6-8 weeks old SCID beige female mice, with Ba/F3-T315I-Bcr-Abl cells xenograft <sup>[2]</sup>
Dosage:	10 mg/kg, 20 mg/kg
Administration:	Oral administration, daily, for 7 days
Result:	Effectively inhibited tumor growth of T315I-Bcr-Abl-Ba/F3 cells in mice at low doses (10 mg/kg).

Animal Model:	5-6 weeks old male Balb/c mice (20-25 g) <sup>[2]</sup>
Dosage:	5 mg/kg for i.v.; 20 mg/kg for i.g. (Pharmacokinetic Analysis)
Administration:	Intravenous injection and oral gavage

---

Result:

Oral bioavailability (36%), C<sub>max</sub> (3616 nM), T<sub>1/2</sub> (3.2 h).

---

## CUSTOMER VALIDATION

- Biochem Pharmacol. 2020 Jul;177:113947.

See more customer validations on [www.MedChemExpress.com](http://www.MedChemExpress.com)

## 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]. Cho, H., et al. First SAR study for overriding NRAS mutant driven acute myeloid leukemia. Journal of Medicinal Chemistry.
- 

**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](mailto:tech@MedChemExpress.com)

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