GNF-7

Cat. No.: HY-10943

CAS No.: 839706-07-9

Molecular Formula: $C_{28}H_{24}F_3N_7O_2$

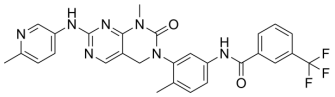
Molecular Weight: 547.53

Target: Bcr-Abl; Ack1

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20 mg/mL (36.53 mM; ultrasonic and warming and heat to 60°C)

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

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2 mg/mL (3.65 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2 mg/mL (3.65 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   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_{50}s of 133 nM and 61 nM for Bcr-Abl^{WT} and Bcr-Abl^{T315I}, respectively. GNF-7 also possesses inhibitory activity against both ACK1 (activated CDC42 kinase 1) and GCK (germinal center kinase) with IC_{50}s of 25 nM and 8 nM, respectively. GNF-7 can be used for the research of hematologic malignancies[1][2][3].

IC_{50} & Target

IC50: 133 nM (Bcr-Abl^{WT})[1], 61 nM (Bcr-Abl^{T315I})[1], 25 nM (ACK1)[3], 8 nM (GCK)[3]

In Vitro

GNF-7 potently inhibits wild-type Bcr-Abl (IC_{50}<5 nM) and Bcr-Abl mutants such as T315I (IC_{50}=11 nM), G250E (IC_{50}<5 nM), E255V (IC_{50}=10 nM), F317L (IC_{50}<5 nM) and M351T (IC_{50}<5 nM) in cellular assays[2].
GNF-7 (1 μM; 2 hours) suppresses AKT/mTOR signaling and GCK downstream[3].
GNF-7 (1 μM; 24 hours) induces of apoptosis and cell cycle arrest in NRAS mutant cell lines[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[3]

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

Apoptosis Analysis[3]

Cell Line:	OCI-AML3 cells
Concentration:	1 μM
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[3]

Cell Line:	OCI-AML3 cells
Concentration:	1 μM
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[2].
GNF-7 exhibits moderate oral bioavailability (mice 36%) and C_{max} (mice 3616 nM) following oral administration (mice 20 mg/kg)[2].
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)[2].
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[2]
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)[2]
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_{max} (3616 nM), $T_{1/2}$ (3.2 h).

CUSTOMER VALIDATION

- Biochem Pharmacol. 2020 Jul;177:113947.
- Arch Pharm (Weinheim). 2024 Sep;357(9):e2400066.

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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.

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