# GNF-7

**Cat. No.:** HY-10943

**CAS No.:** 839706-07-9

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

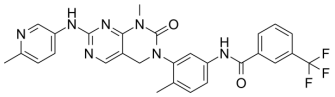
**Molecular Weight:** 547.53

**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 : ≥ 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 |

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

## 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.

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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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