GNF-5

Cat. No.: HY-15738

CAS No.: 778277-15-9

Molecular Formula: $C_{20}H_{17}F_3N_4O_3$

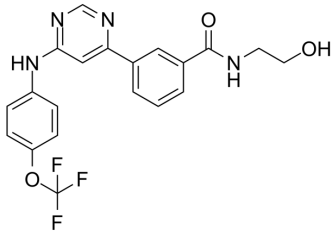
Molecular Weight: 418.37

Target: Bcr-Abl

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 : ≥ 49 mg/mL (117.12 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3902 mL	11.9511 mL	23.9023 mL
5 mM	0.4780 mL	2.3902 mL	4.7805 mL
10 mM	0.2390 mL	1.1951 mL	2.3902 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: ≥ 2.5 mg/mL (5.98 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.98 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.98 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GNF-5, the N-hydroxyethyl carboxamide analog of GNF-2, is an orally active Bcr-Abl inhibitor. GNF-5 has Bcr-Abl inhibition activity with an IC_{50} value of 0.22 μM. GNF-5 has good favorable pharmacokinetic properties. GNF-5 can be used for the research of kinds of cancer including chronic myelogenous leukemia (CML) and breast cancer[1][2].

IC_{50} & Target

IC50: 0.22 μM (Abl)[1]

In Vitro

GNF-5 has inhibition of wild-type Abl with an IC_{50} value of 0.22 μM but no inhibition for myristate site mutant E505K (IC_{50} ⊠ 10 μM)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	wild type and mutant Bcr-Abl expressing Ba/F3 cells
Concentration:	0.2, 0.8 and 1.6 μM
Incubation Time:	48 h
Result:	Inhibited wild-type Abl in a non-ATP competitive fashion.

In Vivo

GNF-5 (5 mg/kg iv. or 20 mg/kg oral) has suitable pharmacokinetic parameters[1].

GNF-5 (oral, 50 or 100 mg/kg, twice daily, for 7 days) shows efficacious in vivo but can observe relapses[1].

GNF-5 (75 mg/kg, b.i.d) inhibits T315I Bcr-Abl combination with nilotinib in vivo[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Balb/c mice[1]
Dosage:	5 mg/kg, 20 mg/kg
Administration:	5 mg/kg intravenously or 20 mg/kg orally
Result:	

AUC_inf (min*ug/mL)	292.37
AUC_inf (hrs*nM	11647
C_{max}(nM)	4386.08
T_{max}(hrs)	0.50
Clast (nM)	636.16
$T_{1/2}$(hrs)	2.30
V_{ss}(L/kg)	9.18
F (%)	44.82

Animal Model:	p210 xenograft model[1]
Dosage:	50 or 100 mg/kg
Administration:	oral, twice daily, for 7 days
Result:	Could normalize blood counts and spleen size.

Animal Model:	Bone marrow transduction/transplantation model[1]

Dosage:	75 mg/kg
Administration:	twice daily
Result:	Showed no significant response (alone). Showed no toxicity and had a strong and sustained inhibition of Bcr-Abl-mediated signaling combination with nilotinib.

CUSTOMER VALIDATION

- Nucleic Acids Res. 2021 Jan 8;49(D1):D1113-D1121.
- Oncotarget. 2018 Apr 24;9(31):22158-22183.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Zhang J, et al. Targeting Bcr-Abl by combining allosteric with ATP-binding-site inhibitors. Nature. 2010 Jan 28;463(7280):501-6.

[2]. Meirson T, et al. Targeting invadopodia-mediated breast cancer metastasis by using ABL kinase inhibitors. Oncotarget. 2018 Apr 24;9(31):22158-22183.

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