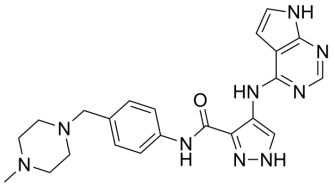
FN-1501

Cat. No.:	HY-111361
CAS No.:	1429515-59-2
Molecular Formula:	$C_{22}H_{25}N_9O$
Molecular Weight:	431.49
Target:	CDK; FLT3
Pathway:	Cell Cycle/DNA Damage; 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 : ≥ 50 mg/mL (115.88 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3176 mL	11.5878 mL	23.1755 mL
5 mM	0.4635 mL	2.3176 mL	4.6351 mL
10 mM	0.2318 mL	1.1588 mL	2.3176 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 (5.79 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.79 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

FN-1501 is a potent inhibitor of FLT3 and CDK, with IC_{50}s of 2.47, 0.85, 1.96, and 0.28 nM for CDK2/cyclin A, CDK4/cyclin D1, CDK6/cyclin D1 and FLT3, respectively. FN-1501 has anticancer activity.

IC_{50} & Target

Cdk4/cyclin D1 0.85 nM (IC_{50})	CDK6/cyclinD1 1.96 nM (IC_{50})	cdk2/cyclin A 2.47 nM (IC_{50})	FLT3 0.28 nM (IC_{50})

In Vitro

FN-1501 is a potent inhibitor of FLT3 and CDK, with IC_{50}s of 2.47 ± 0.21, 0.85 ± 0.28, 1.96 ± 0.08 and 0.28 ± 0.01 nM for CDK2/cyclin A, CDK4/cyclin D1, CDK6/cyclin D1 and FLT3, respectively. FN-1501 shows potent inhibitory activity against several tumor cells, such as MGC803, RS4 11, MCF-7, HCT-116, and NCI-H82, with GI_{50}s of 0.37 ± 0.04, 0.05 ± 0.01, 2.84 ± 0.25,

	0.09 ± 0.04, 0.11 ± 0.02 nM, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	FN-1501 exhibits potent antitumor activity, and shows little cytotoxicity on normal lymphocyte cells, with LD_{50} of 185.67 mg/kg in ICR mice. FN-1501 (15. 30, or 40 mg/kg/d, i.v.) dose-dependently and significantly suppresses the growth of tumor in MV4-11-cell-inoculated-xenograft mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The activity of the CDKs and FLT3 are assayed in reaction buffer (20 mM HEPES pH 7.5, 10 mM $MgCl_2$, 1 mM EGTA, 0.02% Brij35, 0.02 mg/mL BSA, 0.1 mM Na_3VO_4, 2 mM DTT, 1% DMSO) at room temperature at a final ATP concentration of 10 mM. Then FLT3, dissolved in 100% DMSO at the indicated doses, are delivered into the kinase reaction mixture by acoustic technology and incubated for 20 min at room temperature. After 10 μM [γ-^{33}P] ATP (specific activity 10 Ci/μL) is added to initiate the reaction, the reactions are carried out at 25°C for 120 min. The kinase activities are detected by the filterbinding method. IC_{50} values and curve fits are obtained by Prism[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	The human AML cell line MV4-11 is cultured in IMDM media with 10% FBS and supplemented with 2% l-glutamine and 1% penicillin/streptomycin. The MV4-11 cell line is maintained in culture media at 37°C with 5% CO_2. The effects of FN-1501 on MV4-11 proliferation are performed. Cells are cultured in 96-well culture plates (10 000 cells/well). FN-1501 at various concentrations is added to the plates. Cell proliferation is determined after treatment with FN-1501 for 72 h. Cell viability is measured using the CellTiter-Glo assay, and luminescence is measured in a multilabel reader. Data are normalized to control groups (DMSO) and represented as the means of three independent measurements with standard errors of <20%. IC_{50} values are calculated using Prism 5.0[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Six-week-old female nu/nu mice are housed in a specific pathogen-free facility. Prior to implantation, cells are harvested during exponential growth. Five million MV4-11 cells in PBS are formulated as a 1:1 mixture with a Matrigel and injected into the subcutaneous space on the right flank of each nu/nu mouse. Daily intravenous injections are initiated when MV4-11 tumors have reached sizes of 100-200 mm^3. The animals are then randomized into treatment groups of 8 mice each for the efficacy studies and dosed with FN-1501 (0, 15, 30, or 40 (mg/kg)/d) or cytarabine (50 (mg/kg)/d). The compounds (FN-1501, etc.) are dissolved in a solution of PEG400 (25%), ethanol (3.7%), glucose (5%), and acetic acid/sodium acetate buffer (pH 4.5, 7.5%). Tumor growth is measured every 3 days using Vernier calipers for the duration of the treatment. The volume is calculated as follows: tumor volume = a × b^2/2, where a is the long diameter, and b is the short diameter. The percentage of tumor-growth inhibition (GI) is calculated as follows: GI = 100% × {1 - [(tumor volumefinal - tumor volumeinitial for the compound-treated group)/(tumor volumefinal - tumor volumeinitial for the vehicle-treated group)]}. The percent tumor regression (PTR) is calculated as follows: PTR = 100% × (tumor volumeinitial - tumor volumefinal)/(tumor volumeinitial)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Comput Biol Med. 2023 Dec 21, 107889.

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REFERENCES

[1]. Wang Y, et al. Discovery of 4-((7H-Pyrrolo[2,3-d]pyrimidin-4-yl)amino)-N-(4-((4-methylpiperazin-1-yl)methyl)phenyl)-1H-pyrazole-3-carboxamide (FN-1501), an FLT3- and CDK-Kinase Inhibitor with Potentially High Efficiency against Acute Myelocytic Leukemia. J Med Chem. 2018 Feb 22;61(4):1499-1518.

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