PF15

Cat. No.: HY-143286

CAS No.: 2892631-70-6

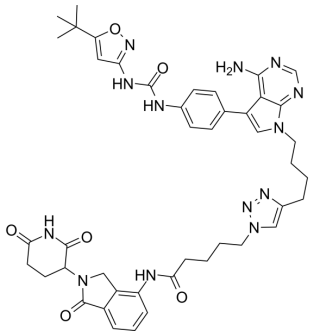
Molecular Formula: $C_{44}H_{49}N_{13}O_6$

Molecular Weight: 855.94

Target: PROTACs; FLT3

Pathway: PROTAC; Protein Tyrosine Kinase/RTK

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (116.83 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.1683 mL	5.8415 mL	11.6831 mL
	5 mM	0.2337 mL	1.1683 mL	2.3366 mL
	10 mM	0.1168 mL	0.5842 mL	1.1683 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 (2.92 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (2.92 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF15 is a PROTAC connected by ligands for FLT3 kinase and CRBN. PF15 is a high selective FLT3-ITD degrader, with a DC_{50} of 76.7 nM. PF15 significantly inhibits the proliferation of FLT3-ITD-positive cells, can down-regulate the phosphorylation of FLT3 and STAT5. PF15 also inhibits tumor growth in mouse models and can be used in study of leukemia[1].

In Vitro

PF15 (0-1000 nM; 72 h) shows good anti-proliferation activity in MV4-11, Molm-13 and BaF3 cells (transformed ITD, ITD-D835V, and ITD-F691L mutations)[1].

PF15 (1, 3, 10, 30, 100, 300, 1000 nM; 6 h) obviously induces FLT3 degradation in a dose-dependent manner and (10, 30, 100, 300, 1000 nM; 6 h) dramatically inhibits the phosphorylation of FLT3 and STAT5 in BaF3-FLT3-ITD cells[1].

PF15 (10, 30, 100, 300, 1000 nM; 6 h) sharply downregulates the phosphorylation of FLT3 and STAT5 at 100 nM in both BaF3-FLT3-ITD-D835V and BaF3-FLT3-ITD-F691L cells[1].

PF15 (100 nM; 1, 3, 6, 12, 24 h) induces FLT3 degradation in a time-dependent manner from 1 h to 24 h[1].

PF15 (15.6, 31.2, 62.5, 125, 250, 500, 1000, 2000 nM; 24 h) induces FLT3 degradation with a DC_{50} of 76.7 nM[1].

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

Cell Proliferation Assay[1]

Cell Line:	MV4-11, Molm-13, BaF3 cells (transformed ITD, ITD-D835V, and ITD-F691L mutations)
Concentration:	0-1000 nM
Incubation Time:	72 h
Result:	Exhibited anti-proliferation activity with IC_{50}s of 4.83 nM (MV4-11), 4.01 nM (Molm-13) and 7.85, 120.1, 116.6 nM (for transformed BaF3 cells harboring ITD, ITD-D835V, and ITD-F691L mutations respectively).

Western Blot Analysis[1]

Cell Line:	BaF3-FLT3-ITD, BaF3-FLT3-ITD-D835V, BaF3-FLT3-ITD-F691L cells
Concentration:	1, 3, 10, 30, 100, 300, 1000 nM
Incubation Time:	6 h
Result:	Induced FLT3 degradation when at 3 nM and in a dose-dependent manner in BaF3-FLT3-ITD cells. Dramatically inhibited the phosphorylation of FLT3 and STAT5 when concentration up to 30 nM in BaF3-FLT3-ITD cells, and at 100 nM in both BaF3-FLT3-ITD-D835V and BaF3-FLT3-ITD-F691L cells.

Western Blot Analysis[1]

Cell Line:	BaF3-FLT3-ITD cells
Concentration:	100 nM
Incubation Time:	1, 3, 6, 12, 24 h
Result:	Significantly induced FLT3 degradation in a time-dependent manner, and FLT3 completely degraded when at 24 h.

Western Blot Analysis[1]

Cell Line:	BaF3-FLT3-ITD cell
Concentration:	15.6, 31.2, 62.5, 125, 250, 500, 1000, 2000 nM
Incubation Time:	24 h
Result:	Notably induced FLT3 degradation when at 125 nM, and DC_{50} was 76.7 nM.

In Vivo

PF15 (10 or 20 mg/kg; i.p.; once daily for 10 days) shows good tumor growth inhibition with an inhibitory rate of 58.4% at dosage of 10 mg/kg, and when up to 20 mg/kg displays higher inhibitory rate[1].

PF15 (twice daily (20 mg/kg), once daily (40 mg/kg); 12 days; i.p.) prolongs the median survival up to 15 days (negative control group is 11 days) in BaF3-FLT3-ITD in situ model[1].

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

Animal Model:	Female NOD/SCID mice (BaF3-FLT3-ITD xenograft model)[1].

Dosage:	10 or 20 mg/kg
Administration:	Intraperitoneal injection; once daily for 10 days.
Result:	Achieved good tumor growth inhibition with an inhibitory rate of 58.4% (10 mg/kg), meanwhile, when at 20 mg/kg displayed higher inhibitory rate. Hardly caused side effects on heart, liver, and kidney (both of the treatment groups).

Animal Model:	Female BALB/c nude mice (BaF3-FLT3-ITD in situ model)[1].
Dosage:	20, 40 mg/kg
Administration:	Intraperitoneal injection; twice daily (20 mg/kg), once daily (40 mg/kg); 12 days.
Result:	Prolonged the median survival from 11days to 15 days (both of the treatment groups).

REFERENCES

[1]. Chen Y, et al. Degrading FLT3-ITD protein by proteolysis targeting chimera (PROTAC). Bioorg Chem. 2022 Feb;119:105508.

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