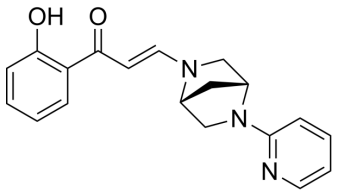
PFI-3

Cat. No.:	HY-12409
CAS No.:	1819363-80-8
Molecular Formula:	$C_{19}H_{19}N_3O_2$
Molecular Weight:	321.37
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
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 : 125 mg/mL (388.96 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1117 mL	15.5584 mL	31.1168 mL
	5 mM	0.6223 mL	3.1117 mL	6.2234 mL
	10 mM	0.3112 mL	1.5558 mL	3.1117 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: ≥ 2.25 mg/mL (7.00 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.25 mg/mL (7.00 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.25 mg/mL (7.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	PFI-3 is a selective, potent and cell-permeable SMARCA2/4 bromodomain inhibitor with a K_d of 89 nM.
IC_{50} & Target	Kd: 89 nM (SMARCA2/4)[1]
In Vitro	PFI-3 is a potent, cell-permeable probe capable of displacing ectopically expressed, GFP-tagged SMARCA2-bromodomain from chromatin. PFI-3 binds avidly to both SMARCA2 and SMARCA4 bromodomains (BROMOScan K_d's between 55 and 110 nM) consistent with the binding constant (K_d=89 nM) measured by isothermal titration calorimetry. PFI-3 does not

phenocopy the growth inhibitory effects of SMARCA2 knockdown in lung cancer[1]. Exposure of embryonic stem cells to PFI-3 leads to deprivation of stemness and deregulates lineage specification. Furthermore, differentiation of trophoblast stem cells in the presence of PFI-3 is markedly enhanced[2]. PFI-3 binds to certain family VIII bromodomains while displaying significant, broader bromodomain family selectivity. The high specificity of PFI-3 for family VIII is achieved through a novel bromodomain binding mode of a phenolic headgroup that leads to the unusual displacement of water molecules that are generally retained by most other bromodomain inhibitors reported to date[3].

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

PROTOCOL

Kinase Assay [2]

To establish whether PFI-3 intercalates DNA, the compound is assessed using a DNA unwinding assay. PFI-3 (1, 5, or 10 μM), cisplatin, or doxorubicin is incubated with supercoiled pBR322, in the presence of wheat germ topoisomerase I, for 30 min at 37°C. DNA incubated with DMSO in the presence or absence of the enzyme is run as control. After extraction by butanol and chloroform/isoamyl alcohol 24:1, the DNA is run in a 1% (w/v) agarose gel with a 1-kb DNA ladder for 4 hours at 80 V. The gel is then stained with SYBR Safe for 30 min before ultraviolet visualization[2].

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

CUSTOMER VALIDATION

- Nat Chem Biol. 2022 May 16.
- Mol Carcinog. 2023 May 5.
- Patent. US20180263995A1.

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REFERENCES

[1]. Vangamudi B, et al. The SMARCA2/4 ATPase Domain Surpasses the Bromodomain as a Drug Target in SWI/SNF-Mutant Cancers: Insights from cDNA Rescue and PFI-3 Inhibitor Studies. Cancer Res. 2015 Sep 15;75(18):3865-78.

[2]. Fedorov O, et al. Selective targeting of the BRG/PB1 bromodomains impairs embryonic and trophoblast stem cell maintenance. Sci Adv. 2015 Nov 13;1(10):e1500723.

[3]. Gerstenberger BS, et al. Identification of a Chemical Probe for Family VIII Bromodomains through Optimization of a Fragment Hit. J Med Chem. 2016 May 26;59(10):4800-11.

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