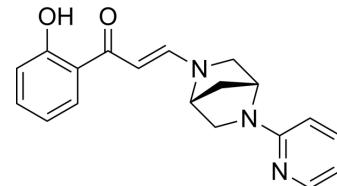


## PFI-3

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	Concentration	Solvent Mass		
		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:  $\geq 2.25 \text{ mg/mL}$  (7.00 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE- $\beta$ -CD in saline)  
Solubility:  $\geq 2.25 \text{ mg/mL}$  (7.00 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility:  $\geq 2.25 \text{ mg/mL}$  (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 <sub>50</sub> & Target	$K_d$ : 89 nM (SMARCA2/4) <sup>[1]</sup>
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<sup>[1]</sup>. 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<sup>[2]</sup>. 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<sup>[3]</sup>.

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

## PROTOCOL

### Kinase Assay<sup>[2]</sup>

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<sup>[2]</sup>.

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.

See more customer validations on [www.MedChemExpress.com](http://www.MedChemExpress.com)

## 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.

**Caution: Product has not been fully validated for medical applications. For research use only.**

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