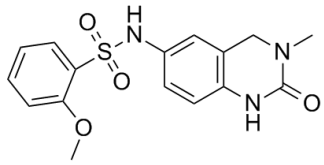
Data Sheet

Product Name:	PFI-1
Cat. No.:	HY-16586
CAS No.:	1403764-72-6
Molecular Formula:	$C_{16}H_{17}N_3O_4S$
Molecular Weight:	347.39
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
Solubility:	10 mM in DMSO



BIOLOGICAL ACTIVITY:

PFI-1 is a selective **BET** (bromodomain-containing protein) inhibitor for BRD4 with **IC_{50}** of 0.22 μM in a cell-free assay.
IC50 & Target: IC50: 0.22 μM (BRD4)
In Vitro: PFI-1 has antiproliferative effects on leukemic cell lines and efficiently abrogates their clonogenic growth. Exposure of sensitive cell lines with PFI-1 results in G1 cell-cycle arrest, downregulation of MYC expression, as well as induction of apoptosis and induces differentiation of primary leukemic blasts. Cells exposed to PFI-1 show significant downregulation of Aurora B kinase, thus attenuating phosphorylation of the Aurora substrate H3S10, providing an alternative strategy for the specific inhibition of this well-established oncology target[1]. PFI-1 binds to with cyclic AMP response binding protein with K_d of 49 μM. PFI-1 has an EC_{50} of 1.89 μM for the inhibition of IL6 production from human blood mononuclear cells stimulated by LPS[2]. PFI-1 induces dose-dependent reduction of cell viability in T4302 $CD133^+$ cells[3]. PFI-1 inhibits the proliferating of three NET cell lines (Bon-1 derived from a pancreatic NET, and H727 and H720 derived from lung NETs)[4].
In Vivo: PFI-1 administrated (1 mg/kg, i.v.) in the rat results in the volume of distribution of 1 L/kg, the plasma clearance of 18 mL/min/kg and half-life of 1 hour. PFI-1 oral dosed (2 mg/kg) in the rat results in the oral bioavailability as low as 32%. PFI-1 administrated (2 mg/kg, s.c.) in the mouse results in a Cmax of 58 ng/mL with a Tmax of 1 h and a half-life of approximately 2 hours[2].

References:

[1]. Picaud S, et al. PFI-1, a Highly Selective Protein Interaction Inhibitor, Targeting BET Bromodomains. Cancer Res. 2013 May 21. [Epub ahead of print]
[2]. Fish PV, et al. Identification of a chemical probe for bromo and extra C-terminal bromodomain inhibition through optimization of a fragment-derived hit. J Med Chem. 2012 Nov 26;55(22):9831-7.
[3]. Cheng Z, et al. Inhibition of BET bromodomain targets genetically diverse glioblastoma. Clin Cancer Res. 2013 Apr 1;19(7):1748-59.
[4]. Kate E Lines, et al. Epigenetic modifiers reduce proliferation of human neuroendocrine tumour cell lines. Endocrine Abstracts (2013) 31 P149

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