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PFI-3

Epigenetic modifier; Inhibits SMARCA2 and SMARCA4

Catalog #100-1641 5 mg

Product Description

PFI-3 is a bromodomain inhibitor of SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A member 2 (SMARCA2; IC_{50} = 89 nM) and SMARCA4, disrupting their function in gene regulation. SMARCA2 and SMARCA4 are catalytic ATPases in the SWI/SNF chromatin-remodeling complex and have been associated with regulating genes for stem cell maintenance and lineage specification (Fedorov et al.). Bromodomains bind to acetylated lysine residues in histone tails to recruit transcriptional complexes, which are involved in DNA damage repair (Filippakopoulos & Knapp). PFI-3 can enhance the effectiveness of DNA-damaging chemotherapeutics on cancer cells by inhibiting SWI/SNF chromatin binding (Pérez-Salvia & Esteller).

Alternative Names: PF-06687252

CAS Number: 1819363-80-8

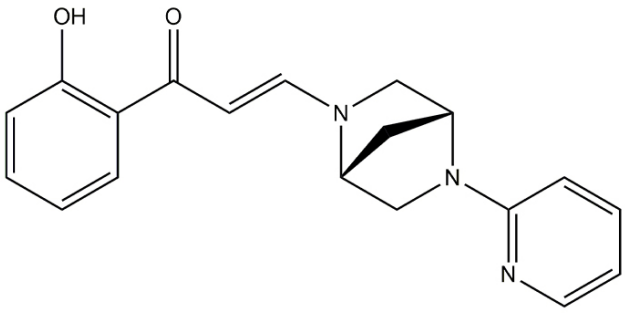
Chemical Formula: $C_{19}H_{19}N_3O_2$

Molecular Weight: 321.4 g/mol

Purity: ≥ 98%

Chemical Name: (2E)-1-(2-Hydroxyphenyl)-3-[(1R,4R)-5-(pyridine-2-yl)-2,5-diazabicyclo{2.2.1]heptan-2-yl]prop-2-en-1-one

Structure:



Properties

Product Format: A yellow powder

Stability and Storage: Product stable at -20°C as supplied. As a precaution, STEMCELL recommends storing all small molecules away from direct light. For long-term storage, store with a desiccant. Stable as supplied for 12 months from date of receipt.

Preparation:

- DMSO ≤ 75 mM

For example, to prepare a 10 mM stock solution in DMSO, resuspend 1 mg in 311 µL of DMSO.

Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported; however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application.

Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO concentration above 0.1% due to potential cell toxicity.

Published Applications

DIFFERENTIATION

- Reduces stemness and deregulates lineage specification in mouse embryonic stem cells and enhances differentiation of trophoblast stem cells (Fedorov et al.).
- Decreases the fusion index of mouse myoblasts and reduces skeletal muscle regeneration after injury in a mouse model (Sharma et al.).

CANCER RESEARCH

- Sensitizes human lung, colorectal, and osteosarcoma cancer cells to DNA damage caused by chemotherapeutics by blocking chromatin binding of bromodomains (Lee et al.).
- Enhances anti-cancer effects of temozolomide on human glioblastoma cells and glioblastoma mouse models (Yang et al.).

References

Fedorov O et al. (2015) Selective targeting of the BRG/PB1 bromodomains impairs embryonic and trophoblast stem cell maintenance. Sci Adv 1 (10): e1500723.
Filippakopoulos P & Knapp S. (2014) Targeting bromodomains: epigenetic readers of lysine acetylation. Nat Rev Drug Discov 13(5): 337–56.
Lee D et al. (2021) The bromodomain inhibitor PFI-3 sensitizes cancer cells to DNA damage by targeting SWI/SNF. Mol Cancer Res 19(5): 900–12.
Pérez-Salvia M & Esteller M. (2017) Bromodomain inhibitors and cancer therapy: From structures to applications. Epigenetics 12(5): 323–39.
Sharma T et al. (2021) The Bromodomains of the mammalian SWI/SNF (mSWI/SNF) ATPases Brahma (BRM) and Brahma Related Gene 1 (BRG1) promote chromatin interaction and are critical for skeletal muscle differentiation. Nucleic Acids Res 49(14): 8060–77.
Yang C et al. (2021) Targeting the bromodomain of brg-1/brm subunit of the swi/snf complex increases the anticancer activity of temozolomide in glioblastoma. Pharmaceuticals (Basel) 14(9): 904.

Related Products

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