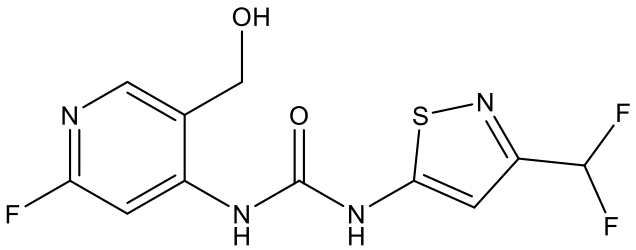
Catalog #10-5244

BRM014

CAS 2270879-17-7

1-[3-(Difluoromethyl)isothiazol-5-yl]-3-[2-fluoro-5-(hydroxymethyl)pyridine-4-yl]urea

Lot # E103775



SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin subfamily A member 2 (SMARCA2), also known as Brahma homologue (BRM), together with its close homologue Brahma-related gene 1 (BRG1), or SMARCA4, are ATPases of the large ATP-dependent SWI/SNF chromatin-remodeling complexes involved in transcriptional regulation of gene expression. BRM014 is an allosteric dual inhibitor of BRM and BRG1 (IC_{50}<5 nM for both).[1] It downregulated BRM-dependent gene expression and displayed antiproliferative activity in a BRG1-mutant-lung-tumor xenograft model after oral administration. Inhibition of BRG1/BRM ATPase by BRM014 inhibits chromatin openness.[2] For example, it reduced DNA accessibility to core regulatory factors (RUNX1, LM01 and MEIS1) at transcription factor PU.1 sites in AML cells.[3] P583 cells formed markedly large spheroids when treated with BRM014.[4] Cell permeable and active *in vivo*.

1) Papillon *et al.* (2018) *Discovery of orally active inhibitors of brahma homolog (BRM)/SMARCA2 ATPase activity for the treatment of brahma related gene 1 (BRG1)/SMARCA4-mutant cancers;* J. Med. Chem. **61** 10155
2) Hargreaves *et al.* (2021) *Chromatin openness requires continuous SW1/SNF activity;* Nat. Genet. **53** 263
3) Chambers *et al.* (2023) *SW1/SNF Blockade Disrupts PU.1-Directed Enhancer Programs in Normal Hematopoietic Cells and Acute Myeloid Leukemia;* Cancer Res. **83** 983
4) Krieg *et al.* (2023) *Chemical inhibition of SWI/SNF induces transformed growth in non-mutant cells, mimicking the effects of a SMARC4 mutation associated with small cell carcinoma of the ovary, hypercalcemic type;* Gynecol. Oncol. Rep. **48 Suppl 1** S32

PHYSICAL DATA

Molecular Weight:	318.27
Molecular Formula:	$C_{11}H_9F_3N_4O_2S$
Purity:	>98% HPLC
	NMR: (Conforms)
Solubility:	DMSO (70 mg/ml)
Physical Description:	White solid
Storage and Stability:	Store as supplied at -20°C for up to 2 years from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 3 months.

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