



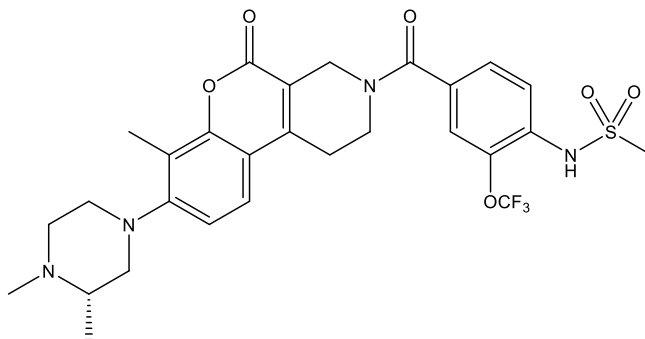
**Catalog # 10-4188**

**DS18561882**

CAS# 2227149-22-4

N-[4-[8-[(3S)-3,4-Dimethylpiperazin-1-yl]-7-methyl-5-oxo-2,4-dihydro-1H-chromeno[3,4-c]pyridine-3-carbonyl]-2-(trifluoromethoxy)phenyl]methanesulfonamide; DS18

Lot # FBA8137



DS18562881 is a potent ( $IC_{50} = 6.3$  nM) and selective (>90-fold over MTHFD1) inhibitor of the mitochondrial enzyme methylenetetrahydrofolate dehydrogenase 2 (MTHFD2), a key enzyme in one carbon metabolism in purine or thymidine biosynthesis.<sup>1</sup> It almost completely inhibited tumor growth in an MDA-MB-231 mouse xenograft model. DS18561882 treatment of triple-negative breast cancer cells lead to significant reduction of cancer cell proliferation but not apoptosis; however, in combination with Chk1 inhibitors it led to apoptotic cell death.<sup>2</sup> In combination with enzalutamide, it significantly inhibited castration resistant prostate cancer cells *in vitro* and *in vivo*.<sup>3</sup>

- 1) Kawai *et al.* (2019), *Discovery of a Potent, Selective, and Orally Available MTHFD2 Inhibitor (DS18561882) with In Vivo Antitumor Activity*; J. Med. Chem. **62** 10204
- 2) Lee *et al.* (2021), *A novel oral inhibitor for one-carbon metabolism and checkpoint kinase 1 inhibitor as a rational combination treatment for breast cancer*; Biochem. Biophys. Res. Commun. **584** 7
- 3) Zhao *et al.* (2022), *PPFIA4 promotes castration-resistant prostate cancer by enhancing mitochondrial metabolism through MTHFD2*; J. Exp. Clin. Cancer Res. **41** 125

#### **PHYSICAL DATA**

Molecular Weight:	608.63
Molecular Formula:	C <sub>28</sub> H <sub>31</sub> F <sub>3</sub> N <sub>4</sub> O <sub>6</sub> S
Purity:	>98% by HPLC
	NMR: (Conforms)
Solubility:	DMSO (at least 40 mg/mL)
Physical Description:	Pale yellow 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.

**Materials provided by Focus Biomolecules are for laboratory research use only and are not intended for human or veterinary applications.**

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