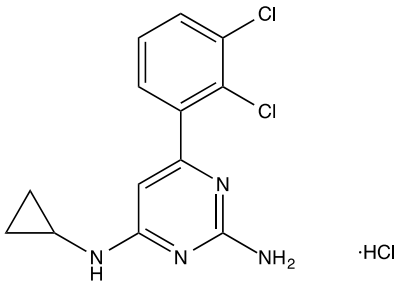
Catalog #10-4602

TH588

1609960-31-7 (free base)

N4-Cyclopropyl-6-(2,3-dichlorophenyl)pyrimidine-2,4-diamine hydrochloride

Lot # FBA3106



TH588 is a first-in-class nudix hydrolase family inhibitor.[1] MTH1/NUDT1 is a family member that "sanitizes" oxidized deoxynucleotide triphosphates (dNTP) preventing their incorporation into DNA and thus avoiding DNA damage and cell death. TH588 inhibits MTH1/NUDT1 (IC_{50} = 5 nM) leading to cell death in several cancer cell lines while not affecting normal cells. Active *in vitro* and *in vivo*. Recent evidence has raised doubts about the cancer-killing ability of MTH1 inhibition.[2,3] Conversely, TH588 has been also been shown to decrease osteosarcoma cell viability, impair cell cycle, and increase apoptosis via an MTH1-dependent pathway.[4]

1) Gad *et al.* (2014), *MTH1 inhibition eradicates cancer by preventing sanitation of the dNTP pool;* Nature **508** 215
2) Petrocchi *et al.* (2016) *Identification of potent and selective MTH1 inhibitors*; Bioorg.Med.Chem.Lett. **26** 1503
3) Kettle *et al.* (2016), *Potent and Selective Inhibitors of MTH1 Probe Its Role in Cancer Cell Survival;* J.Med.Chem. **59** 2346
4) Moukengue *et al.* (2020), *TH1579, MTH1 inhibitor, delays tumour growth and inhibits metastases development in osteosarcoma model;* EBioMedicine. **53** 102704

PHYSICAL DATA

Molecular Weight:	331.63
Molecular Formula:	$C_{13}H_{12}Cl_2N_4 \cdot HCl$
Purity:	>98% (TLC)
	NMR: (Conforms)
Solubility:	DMSO (5 mg/ml)
Physical Description:	White solid
Storage and Stability:	Store as supplied at -20°C for up to 1 year from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 3 months.

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