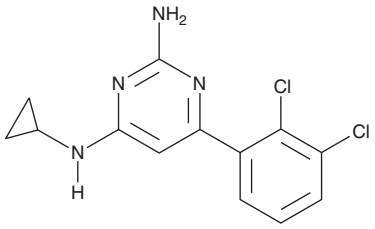
PRODUCT INFORMATION

TH588

Item No. 18133

CAS Registry No.:	1609960-31-7
Formal Name:	N^4-cyclopropyl-6-(2,3-dichlorophenyl)-2,4-pyrimidinediamine
MF:	$C_{13}H_{12}Cl_2N_4$
FW:	295.2
Purity:	≥98%
UV/Vis.:	λ_{max}: 297 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

TH588 is supplied as a crystalline solid. A stock solution may be made by dissolving the TH588 in the solvent of choice, which should be purged with an inert gas. TH588 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of TH588 in these solvents is approximately 2, 20, and 25 mg/ml, respectively.

TH588 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, TH588 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. TH588 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Human mutT homolog (MTH1) is a nucleotide pool sanitizing enzyme that cleaves oxidized nucleotides (dNTPs) to prevent incorporation of damaged bases during DNA replication. Cancer cells rely on MTH1 activity in order to avoid cell death. TH588 is an MTH1 inhibitor (IC_{50} = 5 nM) with improved metabolic stability over TH287 (Item No. 18132).[1] It selectively kills cancer cell lines (IC_{50s} = 2.48-6.37 µM) without significant cytotoxicity towards primary or immortalized cells (IC_{50}s = ≥20 µM) and demonstrates >1,000-fold selectivity for MTH1 over the related nudix hydrolase protein family members MTH2, NUDT5, NUDT12, NUDT14, and NUDT16, as well as other proteins with known nucleoside triphosphate pyrophosphatase activity (dCTPase, dUTPase, and ITPA).[1] At 30 mg/kg, TH588 induces incorporation of oxidized dNTPs in cancer cells, leading to DNA damage and cell death in B-Raf^{V600E} melanoma, SW480 colorectal, or MCF-7 breast tumor mouse xenografts.[1]

Reference

1. Gad, H., Koolmeister, T., Jemth, A.-S., *et al.* MTH1 inhibition eradicates cancer by preventing sanitation of the dNTP pool. *Nature* **508**, 215-242 (2014).

CAYMAN CHEMICAL
1180 EAST ELLSWORTH RD
ANN ARBOR, MI 48108 · USA
PHONE: [800] 364-9897
[734] 971-3335
FAX: [734] 971-3640
CUSTSERV@CAYMANCHEM.COM
WWW.**CAYMANCHEM**.COM