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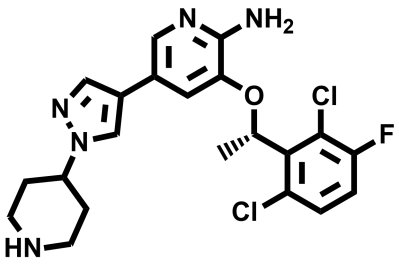
MTH1 Inhibitor (S)-crizotinib

Chemical Name: (S)-3-(1-(2,6-dichloro-3-fluorophenyl)ethoxy)-5-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)pyridin-2-amine



Molecular Weight:	450.34
Formula:	$C_{21}H_{22}Cl_2FN_5O$
Purity:	≥98%
CAS#:	1374356-45-2
Solubility:	DMSO up to 50 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

(S)-Crizotinib is a novel potent, selective and cell permeable MTH1 inhibitor with an IC_{50} of ~72 nM. MTH1 is a nucleotide pool sanitizing enzyme. (S)-Crizotinib disrupts nucleotide pool homeostasis via MTH1 inhibition and induces an increase in DNA single-strand breaks in cancer cells. In vivo it can effectively suppress tumor growth in colon carcinoma xenograft model by once per day oral dosing. (R)-Crizotinib, which is (R)-enantiomer of the drug, is inactive against MTH1 in vitro. Loss-of-function of MTH1 impaired growth of KRAS tumor cells. (S)-Crizotinib is a useful chemical probe to further validate MTH1 as a promising novel class of anticancer target.

How to Use:

In vitro: (S)-Crizotinib was used at 2-10 μM final concentration in various in vitro and cellular assays.

In vivo: (S)-Crizotinib was dosed to mice orally at 50 mg/kg once per day to impair tumor growth in an SW480 colon carcinoma xenograft model. Formulation is 1% DMSO, 10% ethanol, 10% Cremophor, 10% Tween 80, 69% PBS.

Reference:

1. Huber KV, et al. Stereospecific targeting of MTH1 by (S)-crizotinib as an anticancer strategy. (2014) Nature. 508(7495):222-7.