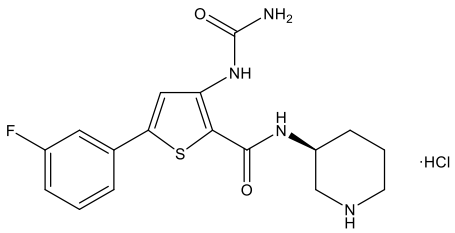
Catalog # 10-4771
AZD7762

CAS# 860352-01-8 (free base)

3-(Carbamoylamino)-5-(3-fluorophenyl)-N-[(3S)-piperidin-3-yl]thiophene-2-carboxamide

Lot # FBS2028



AZD7762 is a potent and selective inhibitor of checkpoint kinases 1 and 2 (IC_{50} = 5 nM for both).[1] It abrogates DNA damage-induced S and G2 checkpoints and enhances the efficacy of DNA damaging agents such as gemcitabine and irinotecan. AZD7762 also enhanced the radiation sensitivity of p53-mutant tumor cell lines.[2,3] AZD7762 was able to overcome imatinib resistance in CML cells.[4] AZD7762 has also been reported to be a potent inhibitor of MEKK2 (MAP3K2) – IC_{50} = 20 nM.[5] It has also recently been shown to inhibit antigen-stimulated degranulation from RBL-2H3 (IC_{50} = 28 nM) and BMMCs (IC_{50} = 99 nM) as well as suppressing degranulation of LAD2 human mast cells (IC_{50} = 50 nM) via Syk suppression through inactivation of Lyn and Fyn kinases.[6] Enhances CRISPR-Cpf1-mediated precise genome editing.[7]

1) Zabludoff *et al.* (2008) *AZD7762, a novel checkpoint kinase inhibitor, drives checkpoint abrogation and potentiates DNA-targeted therapies;* Mol. Cancer Ther. **7** 2955
2) Mitchell *et al.* (2010) *In vitro and in vivo radiation sensitization of human tumor cells by a novel checkpoint kinase inhibitor, AZD7762; Clin.* Cancer Res. **16** 2076
3) Morgan *et al.* (2010) *Mechanism of radiosensitization by the Chk1/2 inhibitor AZD7762 involves abrogation of the G2 checkpoint and inhibition of homologous recombinational DNA repair;* Cancer Res. **70** 4972
4) Lei *et al.* (2018) *Chk1 inhibitors overcome imatinib resistance in chronic myeloid leukemia cells;* Leuk. Res. **64** 17
5) Ahmad *et al.* (2015) *Identification of Ponatinib and Other Known Kinase Inhibitors with Potent MEKK2 Inhibitory Activity;* Biochem. Biophys. Res. Commun. **463** 888
6) Park *et al.* (2018) *Repositioning of anti-cancer drug candidate, AZD7762, to an anti-allergic drug suppressing IgE-mediated mast cells and allergic responses via the inhibition of Lyn and Fyn;* Biochem. Pharmacol. **154** 270
7) Ma *et al.* (2018) *Small molecules promote CRISPR-Cpf1-mediated genome editing in human pluripotent stem cells*; Nat. Commun. **9** 1303

PHYSICAL DATA

Molecular Weight:	398.88
Molecular Formula:	$C_{17}H_{19}FN_4O_2S{\cdot}HCl$
Purity:	>98% by HPLC
	NMR: (Conforms)
Solubility:	DMSO (>25 mg/ml)
Physical Description:	Yellow/brown solid
Storage and Stability:	Store as supplied at -20ºC for up to 1 year from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 1 month.

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