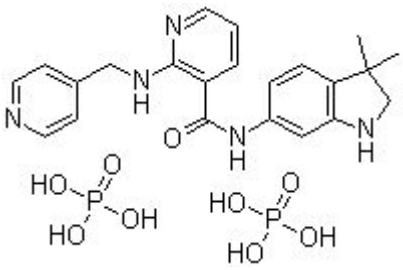
Product Introduction

Motesanib Diphosphate (AMG-706)

Motesanib Diphosphate (AMG-706) is a potent ATP-competitive inhibitor of **VEGFR1/2/3** with **IC50** of 2 nM/3 nM/6 nM, respectively; similar activity against Kit, ~10-fold more selective for VEGFR than PDGFR and Ret. Phase 1/2.

Technical Data:

Molecular Weight (MW):	569.44	
Formula:	C22H23N5O.2H3PO4	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 100 mg/mL	
	Water 100 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	857876-30-3	

Biological Activity

Motesanib Diphosphate has broad activity against the human VEGFR family, and displays >1000 selectivity against EGFR, Src, and p38 kinase. Motesanib Diphosphate significantly inhibits VEGF-induced cellular proliferation of HUVECs with an IC50 of 10 nM, while displaying little effect at bFGF-induced proliferation with an IC50 of >3,000 nM. Motesanib Diphosphate also potently inhibits PDGF-induced

proliferation and SCF-induced c-kit phosphorylation with IC50 of 207 nM and 37 nM, respectively, but not effective against the EGF-induced EGFR phosphorylation and cell viability of A431 cells. [1] Althouth displaying little antiproliferative activity on cell growth of HUVECs alone, Motesanib Diphosphate treatment significantly sensitizes the cells to fractionated radiation. [2]

Administration of Motesanib Diphosphate at 100 mg/kg significantly inhibits VEGF-induced vascular permeability in a time-dependent manner. Oral administration of Motesanib Diphosphate twice daily or once daily potently inhibits, in a dose-dependent manner, VEGF-induced angiogenesis using the rat corneal model with ED50 of 2.1 mg/kg and 4.9 mg/kg, respectively. Motesanib Diphosphate induces a dose-dependent tumor regression of established A431 xenografts by selectively targeting neovascularization in tumor cells. [1] Administration of Motesanib Diphosphate in combination with radiation displays significant anti-tumor activity in head and neck squamous cell carcinoma (HNSCC) xenograft models. [2] Motesanib Diphosphate treatment also induces significant dose-dependent reductions in tumor growth and blood vessel density of MCF-7, MDA-MB-231, or Cal-51 xenografts, which can be markedly enhanced when combined with docetaxel or tamoxifen. [3]

References

[1] Polverino A, et al. Cancer Res, 2006, 66(17), 8715-8721.
[2] Kruser TJ, et al. Clin Cancer Res, 2010, 16(14), 3639-3647.
[3] Coxon A, et al. Clin Cancer Res, 2009, 15(1), 110-118.

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