ODM-203

Cat. No.: HY-119367

CAS No.: 1430723-35-5

Molecular Formula: $C_{26}H_{21}F_2N_5O_2S$

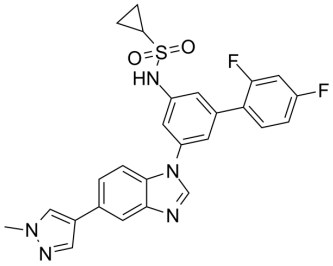
Molecular Weight: 505.54

Target: FGFR; VEGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 66.67 mg/mL (131.88 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9781 mL	9.8904 mL	19.7808 mL
	5 mM	0.3956 mL	1.9781 mL	3.9562 mL
	10 mM	0.1978 mL	0.9890 mL	1.9781 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.11 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.11 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.11 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ODM-203 is an orally active and selective FGFR/VEGFR inhibitor with IC_{50} values of 6, 11, 16, 5, 9, 26 and 35 nM for FGFR3/1/2 and VEGFR3/2/1/4, respectively. ODM-203 has strong anti-tumour activity and activates immune responses in the tumour microenvironment[1].

IC_{50} & Target

FGFR1 11 nM (IC_{50})	FGFR2 16 nM (IC_{50})	FGFR3 6 nM (IC_{50})	FGFR4 35 nM (IC_{50})
VEGFR1	VEGFR2	VEGFR3	DDR1

	26 nM (IC_{50})	9 nM (IC_{50})	5 nM (IC_{50})	6 nM (IC_{50})
	RET 8 nM (IC_{50})	SIK3 23 nM (IC_{50})	PDGFRa 35 nM (IC_{50})	MINK1 41 nM (IC_{50})
	MAP4K4 49 nM (IC_{50})			

In Vitro

ODM-203 (eight-dose concentration series up to 3 μM; 96 h) potently inhibits FGFR signaling and proliferation in several FGFR-dependent cell lines[1].
ODM-203 (eight-dose concentration series up to 3 μM; 10 days) inhibits endothelial tubule formation[1].
ODM-203 (1, 10, 100, 1000 nM; 1 h) inhibiting FGFR and VEGFR cellular signaling in HUVEC cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	H1581 (ATCC-CRL-5878), SNU16 (ATCC-CRL-5974) and RT4 (HTB2) cells
Concentration:	Eight-dose concentration series up to 3 μM
Incubation Time:	96 h
Result:	Suppressed cell proliferation in a dose-dependent manner in H1581 (IC_{50}=104 nM), SNU16 (IC_{50}=132 nM) and RT4 cells (IC_{50}=192 nM).

Cell Viability Assay[1]

Cell Line:	HUVECs and human umbilical vein endothelial cells (co-culture)
Concentration:	Eight-dose concentration series up to 3 μM
Incubation Time:	10 days (media and test agents were replaced every 2-3 days)
Result:	Inhibited endothelial tubule formation in a dose-dependent manner at non-toxic concentrations with an IC_{50} value of 33 nM.

Western Blot Analysis[1]

Cell Line:	HUVEC cells
Concentration:	1, 10, 100, 1000 nM
Incubation Time:	1 h
Result:	Suppressed both FGFR and VEGFR signaling.

In Vivo

ODM-203 (20, 40 mg/kg; p.o.; single daily for 21 days) inhibits FGFR phosphorylation and tumor growth in several FGFR-dependent xenografts by suppressing FGFR signaling in tumors[1].
ODM-203 (7, 20, 40 mg/kg; p.o.; single daily for 21 days) shows strong anti-tumor activity in a VEGFR-dependent angiogenic orthotopic syngenic model (Renca) and suppresses angiogenesis[1].
ODM-203 (20, 40 mg/kg; p.o.; single daily for 5 days) activates immune response in the tumor microenvironment[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Athymic Nude-Foxn1nu female mice (9-week-old; subcutaneous xenograft models)[1].
Dosage:	20, 40 mg/kg

Administration:	Oral administration; single daily for 21 days.
Result:	Significantly inhibited tumour growth for 21 consecutive days. Showed tumor growth inhibition (TGI) in RT4 xenografts was 37% and 92% with dosage of 20 and 40 mg/kg, respectively.

Animal Model:	Male balb/c mice (8-week-old; orthotopic renca syngenic model)[1].
Dosage:	7, 20, 40 mg/kg
Administration:	Oral administration; single daily for 21 days.
Result:	Showed tumor growth inhibition were 39%, 58% and 75% for dosage of 7, 20 and 40 mg/kg, respectively. Inhibited formation of lung metastasis, and suppressed angiogenesis.

Animal Model:	Male balb/c male mice (5 to 7-week-old; renca subcutaneous tumor model)[1].
Dosage:	20, 40 mg/kg
Administration:	Oral administration; single daily for 5 days.
Result:	Resulted in an increase in the percentage of total and CD4 T cells. Decreased the expression of immune check points PD-1 and PD-L1 and increased IFN-γ expression on both CD8 T cells and NK cells.

REFERENCES

[1]. Holmström TH, et al. ODM-203, a Selective Inhibitor of FGFR and VEGFR, Shows Strong Antitumor Activity, and Induces Antitumor Immunity. Mol Cancer Ther. 2019 Jan;18(1):28-38.

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