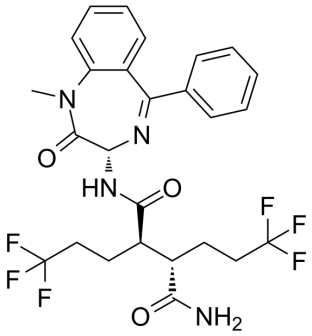
BMS-906024

Cat. No.:	HY-15670
CAS No.:	1401066-79-2
Molecular Formula:	$C_{26}H_{26}F_6N_4O_3$
Molecular Weight:	556.5
Target:	γ-secretase; Notch
Pathway:	Neuronal Signaling; Stem Cell/Wnt
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 9.5 mg/mL (17.07 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7969 mL	8.9847 mL	17.9695 mL
	5 mM	0.3594 mL	1.7969 mL	3.5939 mL
	10 mM	0.1797 mL	0.8985 mL	1.7969 mL

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

BIOLOGICAL ACTIVITY

Description

BMS-906024 is an orally active and selective γ-secretase (gamma secretase) inhibitor. BMS-906024 is a potent pan-Notch receptors inhibitor with IC_{50}s of 1.6 nM, 0.7 nM, 3.4 nM, and 2.9 nM for Notch1, -2, -3, and -4 receptors, respectively. BMS-906024 demonstrates broad-spectrum antineoplastic activity[1][2].

IC_{50} & Target

IC50: 1.6 nM (Notch1), 0.7 nM (Notch2), 3.4 nM (Notch3) and 2.9 nM (Notch4)[2]

In Vitro

BMS-906024 (5-100 nM; 72 hours) reduces Notch1 ICD levels in all six lung cancer cell lines. BMS-906024 at 100 nM, has no effect on total Notch1, and down-regulated Hes1 transcript[1].

In cancer cell proliferation assays, BMS-906024 inhibits both leukemia (TALL-1) and triple-negative breast cancer (MDA-MB-468) cells with IC_{50} of ~4 nM[2].

BMS-906024 (100 nM; for 72 hours) enhances the anti-tumor activity of Paclitaxel in vitro[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	NSCLC cell lines (A549, H358, H1975, H2444, H1792, HCC44)
Concentration:	5, 10, 25, 50, 100 nM
Incubation Time:	72 hours
Result:	Reduced Notch1 ICD levels in all six lung cancer cell lines tested at concentrations as low as 5 nM, with maximal depletion at 50-100 nM.

In Vivo

BMS-906024 (8.5 mg/kg; oral gavage; days 1 through 4 of each week for 3 weeks) significantly enhances the tumor growth inhibition of Paclitaxel (36 mg/kg). BMS-906024 enhances Paclitaxel-mediated cytotoxicity in vivo in NSCLC through a combination of inhibiting proliferation and promoting apoptosis, in a p21 and p57-independent manner[1].
BMS-906024 has a $T_{1/2}$ of 4.6/5.3 hours, a C_{max} of 1/0.3 μM and an AUC of 3.4/1.9 μM•hour for IV/PO[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Six to 12-week-old female NOD scid gamma (NSG) mice with KRAS- and BRAF-WT PDX-T42 xenografts[1]
Dosage:	8.5 mg/kg
Administration:	oral gavage; days 1 through 4 of each week for 3 weeks
Result:	Significantly enhanced the tumor growth inhibition of Paclitaxel (36 mg/kg), but had no significant effect on Cisplatin (2 mg/kg) treatment.

Animal Model:	Mouse[2]
Dosage:	1 mg/kg (Pharmacokinetic Analysis)
Administration:	IV or PO
Result:	Had a $T_{1/2}$ of 4.6/5.3 hours, a C_{max} of 1/0.3 μM and an AUC of 3.4/1.9 μM•hour for IV/PO.

CUSTOMER VALIDATION

- Research Square Preprint. 2020 Nov.

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REFERENCES

[1]. Morgan KM, et al. Gamma Secretase Inhibition by BMS-906024 Enhances Efficacy of Paclitaxel in Lung Adenocarcinoma. Mol Cancer Ther. 2017 Dec;16(12):2759-2769.

[2]. Gavai AV, et al. Discovery of Clinical Candidate BMS-906024: A Potent Pan-Notch Inhibitor for the Treatment of Leukemia and Solid Tumors. ACS Med Chem Lett. 2015 Mar 11;6(5):523-7.

Caution: Product has not been fully validated for medical applications. For research use only.

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