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Lieferung & Zahlungsart

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Zuschläge

- Mindermengenzuschlag
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- Expressversand

SZABO-SCANDIC HandelsgmbH

Quellenstraße 110, A-1100 Wien

T. +43(0)1 489 3961-0

F. +43(0)1 489 3961-7

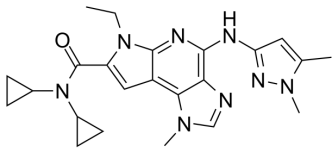
mail@szabo-scandic.com

www.szabo-scandic.com

linkedin.com/company/szaboscandic

BMS-911543

Cat. No.:	HY-15270
CAS No.:	1271022-90-2
Molecular Formula:	$C_{23}H_{28}N_8O$
Molecular Weight:	432.52
Target:	JAK
Pathway:	Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt
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 : 25 mg/mL (57.80 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3120 mL	11.5602 mL	23.1203 mL
	5 mM	0.4624 mL	2.3120 mL	4.6241 mL
	10 mM	0.2312 mL	1.1560 mL	2.3120 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: ≥ 2.5 mg/mL (5.78 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.78 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BMS-911543 is a selective JAK2 inhibitor, with IC_{50}s of 1.1 nM, less selective at JAK1, JAK3 and TYK2 (IC_{50}, 75, 360, 66 nM, respectively).

IC_{50} & Target			
JAK2	Tyk2	JAK1	JAK3
1.1 nM (IC_{50})	66 nM (IC_{50})	75 nM (IC_{50})	360 nM (IC_{50})

In Vitro

BMS-911543 is a selective JAK2 inhibitor, with IC_{50}s of 1.1 nM, less selective at JAK1, JAK3 and TYK2 (IC_{50}, 75, 360, 66 nM, respectively). BMS-911543 displays IC_{50} of >25 μM for all targets except PDE4 (IC_{50}, 5.6 μM). BMS-911543 exhibits potent antiproliferative effect on the SET-2 and BaF3-V617F engineered cell lines (both dependent upon JAK2 pathway), with IC_{50}s of 60 and 70 nM, respectively, and such an effect on SET-2 and BaF3-V617F cells is correlated with similar activity on

	constitutively active pSTAT5 (IC_{50}, 80 and 65 nM, respectively)[1]. BMS-911543 (>20 μM) is cytotoxic to murine or human pancreatic ductal adenocarcinoma (PDAC) cell lines. BMS-911543 (5 and 10 μM) also blocks T regulatory cell differentiation in vitro[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	BMS-911543 is well tolerated up to 100 mg/kg in rats (mean $AUC_{0\text{-}72\ h}$, 11300 μM·h) and dogs ($AUC_{0\text{-}24\ h}$, 610 μM·h). A 15 mg/kg/day dose (Day 14 $AUC_{0\text{-}24\ h}$, 3200 μM·h) is well tolerated[1] in two-week repeat dose studies in rats. BMS-911543 (30 mg/kg, p.o.) suppresses the growth of tumor and prolongs the median survival in KPC-Brca1 mice. BMS-911543 also selectively reduces pSTAT5 expression in pancreatic tumors and decreases levels of intratumoral $FoxP3^+$ T regulatory cells in mice administered BMS-911543[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Human and murine pancreatic ductal adenocarcinoma (PDAC) tumor cells or PSC are cultured in 96 well plates and the following day treated with BMS-911543 or DMSO vehicle control for 48 hours. After 48 hours, MTT reagent (ATCC) is added for 2 hours at 37°C. Samples are analyzed on a plate reader testing for absorbance at 450 nM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] Pancreatic tumors are confirmed in KPC-Brca1 mice by bioluminescent imaging (BLI) at 5-6 weeks of age. Briefly, mice are maintained on isofluorane anesthesia and imaged 10-15 minutes following intraperitoneal injection of Luciferin on a heated platform. Animals with a pancreatic mass of approximately 50-100 mm^3 are randomized, and treatment is initiated the day following imaging. Mice are then treated for 2 weeks by daily oral gavage at a dose of 30 mg/kg BMS-911543. Following 2 weeks of treatment, animals are euthanized via CO_2 asphyxiation followed by cardiac puncture. Plasma, splenocytes and tumor tissue are collected for further analysis. Pathology is assessed by H&E to determine differentiation state of the tissue as PanIN, papillary carcincoma or PDAC. For long term in vivo experiments, 8 week old KPC-Brca1 mice with advanced disease are continuously treated by oral gavage at 30 mg/kg of BMS-911543 until mice meet specified early removal criteria [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- IUBMB Life. 2018 Jan;70(1):81-91.

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REFERENCES

[1]. Wan H, et al. Discovery of a Highly Selective JAK2 Inhibitor, BMS-911543, for the Treatment of Myeloproliferative Neoplasms. ACS Med Chem Lett. 2015 Jul 12;6(8):850-5.

[2]. Mace TA, et al. Single agent BMS-911543 Jak2 inhibitor has distinct inhibitory effects on STAT5 signaling in genetically engineered mice with pancreatic cancer. Oncotarget. 2015 Dec 29;6(42):44509-22.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA