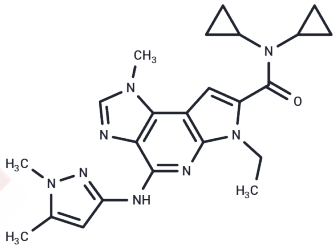
Data Sheet (Cat.No.T6790)

TargetMol

BMS-911543

Chemical Properties



CAS No. : 1271022-90-2

Formula: C23H28N8O

Molecular Weight: 432.52

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	BMS-911543 is a potent and selective inhibitor of JAK2 with IC50 of 1.1 nM, ~350-, 75- and 65-fold selective to JAK1, JAK3 and TYK2, respectively. Phase 1/2.
Targets(IC50)	Histone Methyltransferase,JAK,Tyrosine Kinases
In vitro	BMS-911543 shows potent antiproliferative activity in the SET-2 as well as BaF3-V617F engineered cell lines (both dependent upon JAK2 pathway), with IC50 values of 60 and 70 nM, respectively. The antiproliferative activity of BMS-911543 in SET-2 and BaF3-V617F cells correlates with similar activity on constitutively active pSTAT5 (IC50 80 and 65 nM, respectively). In contrast, non-JAK2-dependent cell lines (A549, MDA-MB-231, MiaPaCa-2) are significantly less sensitive to the inhibitor treatment. The excellent biochemical selectivity versus JAK1/3 translates to good cellular and functional selectivity in an IL-2 mediated T-cell proliferation assay (IC50 990 nM). Also, cell lines that rely on other JAK family members, including CTLL2 and parental BaF3 cells stimulated with IL-3, shows weak antiproliferative activity for BMS-911543 (IC50 2.9 and 3.5 μM, respectively)[1].
In vivo	BMS-911543 suppresses the pSTAT5 levels (mediated by wild type JAK2) relative to vehicle control when stimulated with thrombopoetin (TPO) in a mouse pharmacodynamic model. The responses are dose dependent and results in nearly complete normalization of pSTAT5 levels for 18 h at the highest oral dose of 30 mg/kg. At an intermediate 10 mg/kg oral dose, ~65% reduction is observed up to 18 h, whereas at the 5 mg/kg dose, approximately 50% reduction in pSTAT5 for 8 h is achieved. Observed pSTAT5 reductions correlates with exposures of BMS-911543, with AUC0-8h values of 23, 41, and 109 μM·h, respectively, for dose levels of 5, 10, and 30 mg/kg. In addition, BMS-911543 demonstrates a potent and sustained (2 mg/kg up to 7 h) PD effect in blocking pSTAT5 formation in mice grafted with human SET-2 cells harboring JAK2-V617F mutation. The absolute oral bioavailability in solution is >50% in mice, rats, dogs, and monkeys. In addition, the absorption of BMS-911543 is not significantly impacted by particle dissolution (suspension formulation), with a relative bioavailability (vs solution) of ~60% in rats and ~100% in dogs[1].

Solubility Information

Solubility	DMSO: 16.67 mg/mL (38.54 mM),Sonication is recommended. Ethanol: 21 mg/mL (48.55 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.62 mM),Sonication is recommended. 10% DMSO+90% Saline: 1.67 mg/mL (3.86 mM),Solution. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.312 mL	11.5602 mL	23.1203 mL
5 mM	0.4624 mL	2.312 mL	4.6241 mL
10 mM	0.2312 mL	1.156 mL	2.312 mL
50 mM	0.0462 mL	0.2312 mL	0.4624 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Wan H, et al. ACS Med Chem Lett. 2015, 6(8):850-5.