# Product Data Sheet

Product Name: BMS-911543
Cat. No.: GC12454

## Chemical Properties

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|---|---|---|---|
| Cas. No. | 1271022-90-2 | | |
| SMILES | CCN1C(=CC2=C3C(=C(N=C21)NC4=NN(C(=C4)C)C)N=CN3C)C(=O)N(C5CC5)C6CC6 | | |
| Formula | $C_{23}H_{28}N_8O$ | M.Wt | 432.52 |
| Solubility | ≥ 43.3 mg/mL in DMSO with gentle warming, ≥ 9.8 mg/mL in EtOH with ultrasonic and warming | Storage | Store at -20°C |
| General tips | For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months. | | |
| Shipping Condition | Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request. | | |
| Structure | BMS-911543 | | |

## Protocol

### Cell experiment [1, 2]:

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| Cell lines | SET2 and Ba/F3 cells engineered to express JAK2V617F; human platelets; primary hematopoetic progenitor cells isolated from MPN patients that expressed JAK2V617F, JAK2EXON12 or MPLW515L mutations |
| Preparation method | This compound is soluble in DMSO. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months. |


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| Reacting condition | 0-10 μM; 6, 16 or 24 h |
| Applications | In SET2 and Ba/F3 cells engineered to express JAK2V617F, BMS-911543 exhibited a dose-dependent anti-proliferative effect with IC50 values of 60 and 70 nM, respectively. In human platelets, BMS-911543 inhibited TPO-stimulated pSTAT5 in a dose-dependent manner. In primary hematopoetic progenitor cells isolated from MPN patients that expressed JAK2V617F, JAK2EXON12 or MPLW515L mutations, BMS-911543 inhibited EPO-mediated burst forming unit-erythroid (BFU-E) colony growth with IC50 ranging from <0.150 to ~0.9 μM. |

**Animal experiment [1]:**

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| Animal models | BALB/c mice; athymic mice xenografted with SET2 cells |
| Dosage form | 5, 10 and 30mg/kg, 18h; 1, 2, 5 and 10 mg/kg, orally administered |


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| Application | In BALB/c mice treated with BMS-911543, platelets were isolated and treated with TPO to induce the pSTAT5. At 30mg/kg, BMS-911543 fully suppressed pSTAT5 induction at all time points (1–18 h post dose). BMS-911543 induced ~75% reduction up to 18 h at 10mg/kg. 5mg/kg BMS-911543 revealed a roughly 50% reduction in TPO-stimulated pSTAT5 by ~8 h. In athymic mice xenografted with SET2 cells, 10mg/kg BMS-911543 showed 90–100% inhibition of pSTAT5 up to 7 h post dose. |
| Other notes | Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal. |


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References:

[1] Purandare AV, McDevitt TM, Wan H, You D, Penhallow B, Han X, Vuppugalla R, Zhang Y, Ruepp SU, Trainor GL, Lombardo L, Pedicord D, Gottardis MM, Ross-Macdonald P, de Silva H, Hosbach J, Emanuel SL, Blat Y, Fitzpatrick E, Taylor TL, McIntyre KW, Michaud E, Mulligan C, Lee FY, Woolfson A, Lasho TL, Pardanani A, Tefferi A, Lorenzi MV. Characterization of BMS-911543, a functionally selective small-molecule inhibitor of JAK2. Leukemia. 2012 Feb;26(2):280-8.

[2]. Wan H1, Schroeder GM1, Hart AC1, 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.

## Background

BMS-911543 is a selective small-molecule inhibitor of JAK2 with IC50 value of 1.1nM [1].

BMS-911543 is a reversible pyrrolopyridine ATP-competitive JAK2 inhibitor with a high selectivity. In the in vitro assay using human recombinant JAK enzyme, BMS-911543 displays an IC50 value of 1.1nM against JAK2 and the Ki value is 0.48nM. The inhibition activity and affinity against JAK2 are both much higher than those against JAK1 and JAK3. Besides that, BMS-911543 also has efficacy against other kinases, such as Lyn and the c-FMS receptor tyrosine kinase. In JAK-dependent cells such as SET2 or Ba/F3, the treatment of BMS-911543 causes an anti-proliferative effect with IC50 values of 60 and 70nM, respectively. The cell lines depending on other JAK family members do not show significant anti-proliferative response to BMS-911543. The colony growth assays prove that BMS-911543 can suppress the growth of MPN patient-derived cells and is more potent in the JAK2V617F pathway compared with the JAK2WT pathway. BMS-911543 is also found to be potent in vivo in both the JAK2WT pathway and the JAK2V617F pathway through suppressing pSTAT5 induction [1].

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References:
[1] Purandare AV, McDevitt TM, Wan H, You D, Penhallow B, Han X, Vuppugalla R, Zhang Y, Ruepp SU, Trainor GL, Lombardo L, Pedicord D, Gottardis MM, Ross-Macdonald P, de Silva H, Hosbach J, Emanuel SL, Blat Y, Fitzpatrick E, Taylor TL, McIntyre KW, Michaud E, Mulligan C, Lee FY, Woolfson A, Lasho TL, Pardanani A, Tefferi A, Lorenzi MV. Characterization of BMS-911543, a functionally selective small-molecule inhibitor of JAK2. Leukemia. 2012 Feb;26(2):280-8.


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