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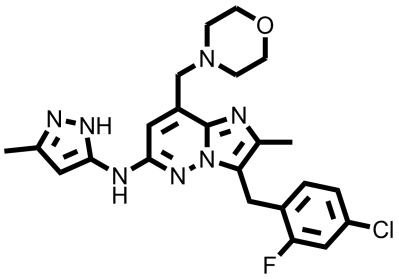
LY2784544 --- JAK2 inhibitor

Chemical Name: 3-(4-chloro-2-fluorobenzyl)-2-methyl-N-(3-methyl-1H-pyrazol-5-yl)-8-(morpholinomethyl)imidazo[1,2-b]pyridazin-6-amine



Molecular Weight:	469.94
Formula:	$C_{23}H_{25}ClFN_7O$
Purity:	≥ 98%
CAS#:	1229236-86-5
Solubility:	DMSO up to 100 mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

Biological Activity:

LY2784544 is highly potent and selective mutant JAK2 (V617F) inhibitor with an IC_{50} of ~55 nM. It also inhibits IL-3-activated wild type JAK2 with an IC_{50} of 2.26 μM. Similarly in the proliferation assay, LY2784544 shows anti-proliferative activity in JAK2 V617F-driven cells with an IC_{50} of 68 nM, compared to 1.36 μM in wild type JAK2-driven cells and 0.94 μM in JAK3-driven cells. LY2784544 significantly inhibits STAT5 phosphorylation in JAK2-V617F Ba/F3 xenografts. Currently LY2784544 is being investigated in a clinical trial for the treatment of essential thrombocythemia, polycythemia vera, and primary myelofibrosis.

How to Use:

In vitro: LY2784544 was used at 5-10 μM final concentration in vitro and in cellular assays.

In vivo: LY2784544 significantly inhibits STAT5 phosphorylation in JAK2-V617F Ba/F3 xenografts with a Threshold Effective Dose 50 (TED50) of 12.7 mg/kg. LY2784544 also reduces JAK2-V617F Ba/F3 tumor burden in the JAK2-V617F-induced MPN model with a TED50 of 13.7 mg/kg after oral treatment. LY2784544 has no effect on CD71/Ter119 positive erythroid progenitors in spleens of SCID mice after oral treatment.

Reference:

1. Srdan Verstovsek . Phase I Study of the JAK2 V617F Inhibitor, LY2784544, in Patients with Myelofibrosis (MF), Polycythemia Vera (PV), and Essential Thrombocythemia (ET). (2011) 53rd ASH Annual Meeting and Exposition.
2. Liandong Ma. Efficacy of LY2784544, a Small Molecule Inhibitor Selective for Mutant JAK2 Kinase, In JAK2 V617F-Induced Hematologic Malignancy Models. (2011) 53rd ASH Annual Meeting and Exposition.
3. David Mitchell, et al. Development and a Practical Synthesis of the JAK2 Inhibitor LY2784544. (2012) Org. Process Res. Dev., 16 (1), pp 70–81