Web: www.taiclone.com
Tel: +886-2-2735-9682
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XL019

Catalog No: tcsc1620

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg

Specifications

CAS No:
945755-56-6

Formula:
$C_{25}H_{28}N_6O_2$

Pathway:
Epigenetics;Stem Cell/Wnt;JAK/STAT Signaling

Target:
JAK;JAK;JAK

Purity / Grade:
>98%

Solubility:
10 mM in DMSO

Observed Molecular Weight:
444.53

Product Description

XL019 is a potent and selective JAK2 inhibitor with IC50 of 2.2 nM, 100 fold selectivity over JAK1; shows good biochemical and

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cellular potency against JAK2 with good selectivity against the Janus Kinase family as well as a broad kinase panel.

IC50 Value: 2.2 nM (JAK2); 214.2 nM (JAK3) [1]

XL019 was selected as a clinical candidate and advanced into human clinical trials where it was evaluated in patients with primary myelofibrosis, post-polycythemia vera, or post-essential thrombocythemia myelofibrosis.

in vitro: Analogue XL019 was also evaluated against a selectivity panel of 118 kinases. Targets for which XL019 exhibited IC50 50-fold selectivity against all kinases tested including JAK family members JAK1 and TYK2. Further in vitro evaluation of XL019 revealed that it demonstrated a desirable CYP (1A2, 2C9, 2D6, 3A4 20 μM), hERG (16 μM), and P-glycoprotein inhibition (>20 μM) profile [1].

in vivo: XL019 was administered orally to mice bearing HEL92.1.7 tumors and inhibition of STAT phosphorylation was measured after 4 h. A significant inhibition of downstream markers pSTAT1 and pSTAT3 is observed at 30, 100, and 300 mg/kg resulting in an ED50 of 42 mg/kg (pSTAT1) and 210 mg/kg (pSTAT3). XL019 had a superior pharmacodynamic profile and thus was evaluated in an efficacy experiment measuring growth inhibition of HEL.92.1.7 xenograft tumors in mice. Derivative XL019 demonstrated 60% and 70% inhibition when dosed orally at 200 mg/kg and 300 mg/kg respectively twice a day for 14 days. Harvested tumors were also subjected to immunohistochemical analysis of microvessel density (CD31), proliferation (Ki67) and apoptosis (TUNEL). Dosing at 300 mg/kg bid provided an 11.3-fold increase in apoptosis relative to vehicle control [1].