Brepocitinib

Cat. No.: HY-112708

CAS No.: 1883299-62-4

Molecular Formula: $C_{18}H_{21}F_2N_7O$

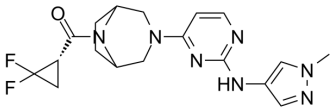
Molecular Weight: 389.4

Target: JAK

Pathway: Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt

Storage: 4°C, protect from light

* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (321.01 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5681 mL	12.8403 mL	25.6805 mL
	5 mM	0.5136 mL	2.5681 mL	5.1361 mL
	10 mM	0.2568 mL	1.2840 mL	2.5681 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Brepocitinib (PF-06700841) is a potent dual Janus kinase 1 (JAK1) and TYK2 inhibitor with IC_{50}s of 17 nM and 23 nM, respectively. Brepocitinib also inhibits JAK2 and JAK3 with IC_{50}s of 77 nM and 6.49 μM, respectively[1].

IC_{50} & Target

JAK1	JAK2	JAK3
17 nM (IC_{50})	77 nM (IC_{50})	6.9 μM (IC_{50})

In Vitro

Brepocitinib (PF-06700841; Compound 23) potently inhibits TYK2/JAK2 mediated IL-12/pSTAT4 and IL-23/pSTAT3 (human whole blood (HWB) IC_{50}s of 65 and 120 nM, respectively)[1].

Brepocitinib has good potency against IL6/pStat1 in the $CD3^+$ cellular subset (IC_{50} of 81 nM), but lower inhibition of IL6/pSTAT3, again in the $CD3^+$ cellular subset (IC_{50} of 641 nM)[1].

Brepocitinib also inhibits the JAK1/JAK3 driven γ-common chain cytokines, represented by IL-15/pStat5 and IL-21/pSTAT3 with reasonable potency (HWB IC_{50}s of 238 and 204 nM, respectively)[1].

Brepocitinib inhibits EPO/pSTAT5 (JAK2 homodimer) in HWB spiked with $CD34^+$ progenitor cells (IC_{50} of 577 nM).

IL10/pSTAT3 (TYK2/JAK1) and IL27/pSTAT3 (JAK1/JAK2/TYK2) are also inhibited by Brepocitinib with IC_{50}s of 305 nM and 86 nM, respectively[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Brepocitinib (PF-06700841; Compound 23; 3-30 mg/kg; oral administration; for 7 consecutive days; female Lewis rats) treatment significantly reduces paw volume increase in a dose-dependent manner. The plasma concentrations in animals dosed with Brepocitinib at peak (30 min) and trough (24 h) time intervals post final dose respectively are as follows: 3 mg/kg, 3.54 μM, 0.0221 μM; 10 mg/kg, 10.95 μM, 0.06 μM; and 30 mg/kg, 23.89 μM, 0.06 μM[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female Lewis rats with induced arthritis[1]
Dosage:	3 mg/kg, 10 mg/kg, or 30 mg/kg
Administration:	Oral administration; for 7 consecutive days
Result:	Increased in paw volume was significantly lower and dose-dependent.

CUSTOMER VALIDATION

- Inflamm Bowel Dis. 2020 Dec 9;izaa318.
- Heliyon. 2023 Jan 13.

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REFERENCES

[1]. Fensome A, et al. Dual Inhibition of TYK2 and JAK1 for the Treatment of Autoimmune Diseases: Discovery of ((S)-2,2-Difluorocyclopropyl)((1 R,5 S)-3-(2-((1-methyl-1 H-pyrazol-4-yl)amino)pyrimidin-4-yl)-3,8-diazabicyclo[3.2.1]octan-8-yl)methanone (PF-06700

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