VVD-118313

Cat. No.: HY-151385

CAS No.: 2875046-27-6

Molecular Formula: $C_{19}H_{22}Cl_2N_2O_3S$

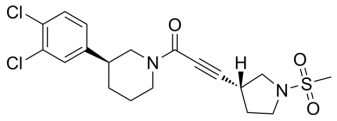
Molecular Weight: 429.36

Target: JAK; IFNAR; Interleukin Related; STAT

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

Storage:

Powder	-20°C	3 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (232.90 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3290 mL	11.6452 mL	23.2905 mL
	5 mM	0.4658 mL	2.3290 mL	4.6581 mL
	10 mM	0.2329 mL	1.1645 mL	2.3290 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.82 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.82 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.82 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

VVD-118313 (compound 5a) is a potent, selective JAK1 inhibitor. VVD-118313 targets an isoform-restricted allosteric cysteine to block JAK1-dependent trans-phosphorylation and cytokine signaling. VVD-118313 can be used for research of cancer[1]. VVD-118313 is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target

JAK1

In Vitro

VVD-118313 (compound 5a; 0.01-10 μM; 3 h; primary human PBMCs) inhibits JAK1 by engagement of C817 and JAK2 by engagement of C838. VVD-118313 inhibits cysteine reactivity in a dose-dependent manner[1].

VVD-118313 (2 μM, 2h) blocks IFNα-simulated STAT1 and IL-6-stimulated STAT3 phosphorylation in WT- or C810A-JAK1-expressing 22Rv1 cells. VVD-118313 also blocks the constitutive phosphorylation of WT- and C810A-JAK1[1].

VVD-118313 (0.01-10 μM) selectively inhibits JAK1 signaling in primary human immune cells. VVD-118313 inhibits JAK1-dependent IFNα-pSTAT1, IL-6-pSTAT3, and IL-2-pSTAT5 pathways in human PBMCs in a dose-dependent manner[1].

VVD-118313 (0.1-0.4 μM; 24 h) inhibits T-cell activation induction. VVD-118313 inhibits the activation of human T cells co-stimulated with αCD3/αCD28 by a reduction in the proportion of $CD25^+$ T cells. VVD-118313 blocks the secretion of the Th1-polarizing cytokine IFNγ and increases the production of IL-2[1].

VVD-118313 (0.1-0.5 μM; 2 h) inhibits on the production of pro-inflammatory cytokines and chemokines. VVD-118313 suppresses the induction of several pro-inflammatory chemokines, including CCL2/MCP-1, CXCL10/IP-10, and CCL4/MIP-1β[1].

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

Western Blot Analysis[1]

Cell Line:	22Rv1 cells
Concentration:	0.01, 0.1, and 1 μM
Incubation Time:	2 hours
Result:	Showed labeling of recombinant WT-JAK1 and C810A-JAK1, but not C817A-JAK1.

Western Blot Analysis[1]

Cell Line:	22Rv1 cells
Concentration:	2 μM
Incubation Time:	2 hours
Result:	Inhibited WT- and C810A-JAK1 phosphorylation with even greater potency than STAT1/STAT3 phosphorylation.

In Vivo

VVD-118313 (compound 5a; 25-50 mg/kg; i.h.; once) inhibits JAK1 signaling in TYK2 knockout mice[1].

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

Animal Model:	TYK2 knockout mice[1]
Dosage:	25 and 50 mg/kg
Administration:	Subcutaneous injection; once
Result:	Revealed 75% engagement of JAK1_C816 at 25 and 50 mg/kg, while other JAK1 cysteines were unaffected in reactivity.

REFERENCES

[1]. Kavanagh ME, et, al. Selective inhibitors of JAK1 targeting an isoform-restricted allosteric cysteine. Nat Chem Biol. 2022 Sep 12.

Caution: Product has not been fully validated for medical applications. For research use only.

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