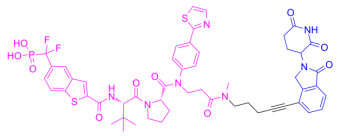
AK-2292

Cat. No.:	HY-148813
CAS No.:	2984506-77-4
Molecular Formula:	$C_{52}H_{54}F_2N_7O_{10}PS_2$
Molecular Weight:	1070.13
Target:	STAT; PROTACs
Pathway:	JAK/STAT Signaling; Stem Cell/Wnt; PROTAC
Storage:	4°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (116.81 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	0.9345 mL	4.6723 mL	9.3447 mL
5 mM	0.1869 mL	0.9345 mL	1.8689 mL
10 mM	0.0934 mL	0.4672 mL	0.9345 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: ≥ 10 mg/mL (9.34 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AK-2292 is a potent and selective STAT5 PROTAC degrader, with a DC_{50} of 0.10 μM. AK-2292 induces degradation of STAT5A/B proteins in vitro and in vivo. AK-2292 can induce tumor regression in acute myeloid leukemia and chronic myeloid leukemia xenograft mouse models[1][2]. AK-2292 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

STAT5
0.10 μM (DC50)

In Vitro

AK-2292 (0.0015-15 μM; 4 days) inhibits the cell growth of SKNO1, MV4;11, and Kasumi-3 cells, with IC_{50}s of 0.36, 0.35, and 0.18 μM, respectively[1].
AK-2292 (0.008-5 μM; 18 h) reduces the levels of STAT5A, STAT5B and $pSTAT5^{Y694}$ proteins in the SKNO1 cell line[1].
AK-2292 (0.008-5 μM; 6 h) effectively reduces the levels of STAT5 and $pSTAT5^{Y694}$ in the MV4;11 acute leukemia cell line[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	SKNO1 cells
Concentration:	0.008, 0.04, 0.2, 1, 5 μM
Incubation Time:	18 hours
Result:	Reduced the levels of STAT5A, STAT5B, and pSTAT5^{Y694} by >75% at 0.2 μM and by >95% at 1 μM. Has no obvious effect on the levels of STAT1, STAT2, STAT3, STAT4, and STAT6 proteins at concentrations up to 5 μM.

Cell Viability Assay[1]

Cell Line:	SKNO1, MV4;11, and Kasumi-3 cells
Concentration:	0.0015, 0.015, 0.15, 1.5, 15 μM
Incubation Time:	4 days
Result:	Effectively inhibited cell growth with IC_{50}s of 0.36, 0.18, and 0.35 μM, respectively.

In Vivo

AK-2292 (50-200 mg/kg; i.p. once a day, 5 days a week for 3 weeks) inhibits tumor growth in the MV4;11 xenograft model in mice[1].

AK-2292 (150 mg/kg; a single i.p.) induces rapid and >95% depletion of STAT5 and pSTAT5^{Y694} proteins in the MV4;11 xenograft tissues in mice[1].

AK-2292 (i.p.) exhibits good plasma exposure and has a plasma half-life of 1.9 h, moderate clearance (CL=0.77 L/h/kg), and good volume distribution (V_z=2.1 L/kg)[1].

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

Animal Model:	SCID mice bearing MV4;11 tumors[1]
Dosage:	50, 100, 200 mg/kg
Administration:	I.p. injection, once a day, 5 days per week for 3 weeks
Result:	Inhibited tumor growth in a dose-dependent manner and achieved 50, 60, and 80% of tumor growth inhibition at doses of 50, 100, and 200 mg/kg, respectively. Did not induce animal weight loss or any other signs of toxicity.

REFERENCES

[1]. Kaneshige A, et, al. Discovery of a Potent and Selective STAT5 PROTAC Degrader with Strong Antitumor Activity In Vivo in Acute Myeloid Leukemia. J Med Chem. 2023 Feb 3.

[2]. Kaneshige A, et, al. A selective small-molecule STAT5 PROTAC degrader capable of achieving tumor regression in vivo. Nat Chem Biol. 2023 Feb 2.

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

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