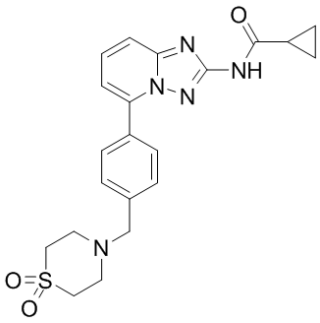
Data Sheet

Product Name:	GLPG0634
Cat. No.:	HY-18300
CAS No.:	1206161-97-8
Molecular Formula:	$C_{21}H_{23}N_5O_3S$
Molecular Weight:	425.50
Target:	JAK; JAK; JAK
Pathway:	Epigenetics; Stem Cell/Wnt; JAK/STAT Signaling
Solubility:	DMSO: 6.8 mg/mL



BIOLOGICAL ACTIVITY:

GLPG0634 is a selective **JAK1** inhibitor with **IC_{50}** of 10 nM, 28 nM, 810 nM, and 116 nM for JAK1, JAK2, JAK3, and TYK2, respectively.
IC50 & Target: IC50: 10 nM (JAK1), 28 nM (JAK2), 810 nM (JAK3), 116 nM (Tyk2)
In Vitro: GLPG0634 dose–dependently inhibits the differentiation of Th2 cells mediated by IL–4, a cytokine that signals through JAK1 and JAK3. GLPG0634 also inhibits Th1 differentiation with similar potencies of 1 μM or lower[1]. GLPG0634 does not inhibit JAK2 homodimer–mediated signaling induced by EPO or PRL (IC_{50} > 10 μM)[2].
In Vivo: GLPG0634 (3, 10, 30 mg/kg, p.o.) dose–dependently prevents disease progression in the therapeutic rat CIA model. GLPG0634 (50 mg/kg, o.p.) protects bone and cartilage from degradation, effectively reduces infiltration of T cells ($CD3^+$ cells) and macrophages ($F4/80^+$ cells) in the paw, and decreases the serum levels of all cytokines and chemokines measured, including IL–6, IP–10, XCL1, and MCP–1[1]. GLPG0634 (0.1 and 0.3 mg/kg) shows efficacy in the rat CIA model[2].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Recombinant JAK1, TYK2, JAK2, and JAK3 are used to develop activity assays in 50 mM HEPES (pH 7.5), 1 mM EGTA, 10 mM $MgCl_2$, 2 mM DTT, and 0.01% Tween 20. The amount of JAK protein is determined per aliquot, maintaining initial velocity and linearity over time. The ATP concentration is equivalent to 4× the experimental K_m value and the substrate concentration (ULight–conjugated JAK–1(Tyr1023) peptide) corresponds to the experimentally determined K_m value. After 90 min incubation at room temperature (RT), the amount of phosphorylated substrate is measured by addition of 2 nM europium–anti–phosphotyrosine Ab and 10 mM EDTA in Lance detection buffer. Compound IC_{50} values are determined by preincubating the enzyme with compound at RT for 60 min, prior to the addition of ATP.
Animal Administration: GLPG0634 is formulated in polyethyleneglycol 200/0.9% NaCl (60/40; v/v) for i.v. administration and in 0.5% (v/v) methylcellulose for oral administration.[1]GLPG0634 is orally dosed as a single esophageal gavage at 5 mg/kg (dosing volume of 5 mL/kg) and i.v. dosed as a bolus via the caudal vein at 1 mg/kg (dosing volume of 5 mL/kg). In the rat study, each group consists of three rats and blood samples are collected via the jugular vein. In the mouse study, each group consists of 21 mice (n=3/time point) and blood samples are collected by intracardiac puncture under isoflurane anesthesia. Lithium heparin is used as anticoagulant and blood is taken at 0.05, 0.25, 0.5, 1, 3, 5, and 8 h (i.v. route) and 0.25, 0.5, 1, 3, 5, 8, and 24 h (by mouth).

References:

[1]. Van Rompaey L, et al. Preclinical characterization of GLPG0634, a selective inhibitor of JAK1, for the treatment of inflammatory diseases. J Immunol. 2013, 191(7), 3568–3577.
[2]. Menet CJ, et al. Triazolopyridines as Selective JAK1 Inhibitors: From Hit Identification to GLPG0634. J Med Chem. 2014 Nov 17.

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

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