

Product Data Sheet

Product Name: GLPG1690

Cat. No.: GC19168

Chemical Properties

Cas. No. 1628260-79-6

SMILES N#CC1=C(C2=CC=C(F)C=C2)N=C(N(C3=C(CC)N=C4C(C)=CC(N5CCN(CC(N6CC(O)C6)=O)CC5)=CN43)C)S1

Formula $C_{30}H_{33}FN_8O_2S$ M.Wt 588.7

Solubility DMSO : 41.67 mg/mL (70.78 mM); Water : < 0.1 mg/mL (insoluble) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

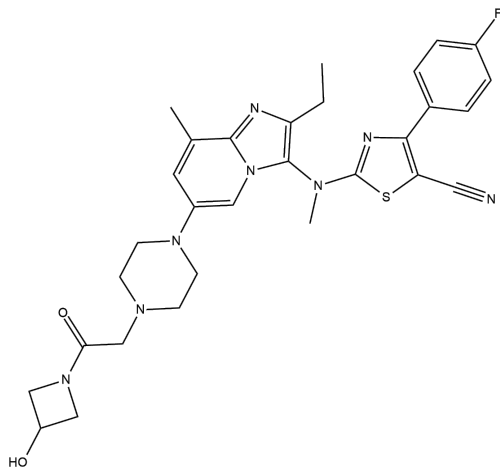
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment [1]:

Cell lines (Human renal angiomyolipoma-derived) TSC2-deficient cells

Preparation Method Cell were treated with specified concentration GLPG1690(Ziritaxestat).

Reaction Conditions 20 nM; 68-96h

Applications GLPG1690 inhibits the growth of TSC2-deficient cells where ATX is overexpressed.

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Animal experiment [2]:

Animal models BALB/c mice (4T1 tumor model)

Preparation Method GLPG1690 was finely ground in a mortar and suspended at a concentration of 10 mg/mL in 0.5% methyl cellulose. Mice were administered GLPG1690 by gavage at doses of 50 or 100 mg/kg, using 10 mL/kg of body weight. Control mice received the vehicle, which was 0.5% methyl cellulose.

Dosage form i.g; 50 or 100 mg/kg; every 12 hours for 19 days

Applications GLPG1690 decreases the activity of plasma ATX and the concentration of lysophosphatidic acid (LPA).

References:

[1]: Feng Y, Mischler WJ, et.al. Therapeutic Targeting of the Secreted Lysophospholipase D Autotaxin Suppresses Tuberous Sclerosis Complex-Associated Tumorigenesis. *Cancer Res.* 2020 Jul 1;80(13):2751-2763. doi: 10.1158/0008-5472.CAN-19-2884. Epub 2020 May 11. PMID: 32393662; PMCID: PMC7335343.

[2]: Tang X, Wuest M, et.al. Inhibition of Autotaxin with GLPG1690 Increases the Efficacy of Radiotherapy and Chemotherapy in a Mouse Model of Breast Cancer. *Mol Cancer Ther.* 2020 Jan;19(1):63-74. doi: 10.1158/1535-7163.MCT-19-0386. Epub 2019 Sep 23. PMID: 31548293.

Background

GLPG1690(Ziritaxestat) is a novel autotaxin (ATX) inhibitor with an IC₅₀ of 131 nM and a K_i of 15 nM. It effectively halts the progression of idiopathic pulmonary fibrosis [1-2].

GLPG1690 (20 nM; 68-96h) inhibits the proliferation of TSC2-deficient cells where ATX is upregulated. Additionally, GLPG1690 suppresses the migration and anchorage-independent growth of TSC2-deficient cells[3].

GLPG1690(i.g; 50 or 100 mg/kg; every 12 hours for 19 days) reduces plasma ATX activity and

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lysophosphatidic acid (LPA) concentration in mice. Furthermore, GLPG1690 enhances the inhibition of cancer cell proliferation in vivo when combined with irradiation^[4]. GLPG1690 reverses lysophosphatidylcholine (LPC)-induced endothelial dysfunction in mice^[5].

References:

- [1]. Desroy N, Housseman C, et.al. Discovery of 2-[[2-Ethyl-6-[4-[2-(3-hydroxyazetidin-1-yl)-2-oxoethyl]piperazin-1-yl]-8-methylimidazo[1,2-a]pyridin-3-yl]methylamino]-4-(4-fluorophenyl)thiazole-5-carbonitrile (GLPG1690), a First-in-Class Autotaxin Inhibitor Undergoing Clinical Evaluation for the Treatment of Idiopathic Pulmonary Fibrosis. J Med Chem. 2017 May 11;60(9):3580-3590. doi: 10.1021/acs.jmedchem.7b00032. Epub 2017 May 1. PMID: 28414242.
- [2]. Maher TM, van der Aar EM, et.al. Safety, tolerability, pharmacokinetics, and pharmacodynamics of GLPG1690, a novel autotaxin inhibitor, to treat idiopathic pulmonary fibrosis (FLORA): a phase 2a randomised placebo-controlled trial. Lancet Respir Med. 2018 Aug;6(8):627-635. doi: 10.1016/S2213-2600(18)30181-4. Epub 2018 May 20. PMID: 29792287.
- [3]. Feng Y, Mischler WJ, et.al. Therapeutic Targeting of the Secreted Lysophospholipase D Autotaxin Suppresses Tuberous Sclerosis Complex-Associated Tumorigenesis. Cancer Res. 2020 Jul 1;80(13):2751-2763. doi: 10.1158/0008-5472.CAN-19-2884. Epub 2020 May 11. PMID: 32393662; PMCID: PMC7335343.
- [4]. Tang X, Wuest M, et.al. Inhibition of Autotaxin with GLPG1690 Increases the Efficacy of Radiotherapy and Chemotherapy in a Mouse Model of Breast Cancer. Mol Cancer Ther. 2020 Jan;19(1):63-74. doi: 10.1158/1535-7163.MCT-19-0386. Epub 2019 Sep 23. PMID: 31548293.
- [5]. Janovicz A, Majer A, et.al. Autotaxin-lysophosphatidic acid receptor 5 axis evokes endothelial dysfunction via reactive oxygen species signaling. Exp Biol Med (Maywood). 2023 Oct;248(20):1887-1894. doi: 10.1177/15353702231199081. Epub 2023 Oct 14. PMID: 37837357; PMCID: PMC10792427.

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