

Product Data Sheet

Product Name: Taladegib hydrochloride

Cat. No.: GC81339

Chemical Properties

Cas. No. 1258861-21-0

Formula $C_{26}H_{25}ClF_4N_6O$

M.Wt 548.96

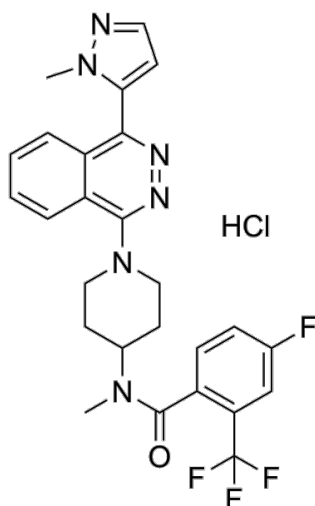
Solubility

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.

Structure



Background

Taladegib (LY2940680) hydrochloride is a Smoothed (SMO) antagonist. Taladegib hydrochloride inhibits the Hedgehog signaling pathway, with an IC_{50} of 5.5 nM for suppressing GLI1 mRNA expression in DAOY cells and an IC_{50} of 7.6 nM in CGNP cell proliferation assays. Taladegib hydrochloride binds to the extracellular loop region (site 1) of the transmembrane domain of the SMO receptor, competes with cyclopamine for SMO binding, and thereby inhibits Gli-dependent transcription. Taladegib hydrochloride can be used in studies of Hedgehog pathway-related cancers [1] [2] [3] [4].

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

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In Vivo, Taladegib (LY2940680) hydrochloride (100 μ M; p.o.; daily; 5-7 days) reverses A β -induced immediate (3 min) and intermediate (1 h) memory impairment in a *Drosophila* Alzheimer's disease model^[1]. Hydrochloride of Taladegib (1% (w/v); topical administration; single dose) potently inhibits Hedgehog pathway activity in the skin of depilated mice, reduces Gli1 mRNA by approximately 70%-80%, and results in low systemic plasma exposure^[4].

In Vitro, Hydrochloride of Taladegib (LY2940680) (1-100 μ M; 72 h) slightly inhibits the proliferation of primary cell cultures of mucinous-type IHCCA and mixed-type IHCCA, with IC₅₀ values of 49.8 μ M and 61.2 μ M, respectively^[2]. Taladegib hydrochloride potently inhibits SHH-induced GLI1 mRNA expression in human DAOY medulloblastoma cells, with a pIC₅₀ of 8.26 and full efficacy^[4]. Hydrochloride of Taladegib (20 μ M; 72 h) does not induce apoptosis in primary cell cultures of mucinous IHCCA or mixed-type IHCCA^[2]. Taladegib hydrochloride potently binds to wild-type human Smoothed, with a K_i value of 0.5 nM^[3]. Taladegib hydrochloride exhibits significantly reduced binding affinity for the D473H mutant human Smoothed, with a K_i value of 55 nM^[3]. Taladegib hydrochloride potently inhibits the constitutive activity of wild-type human SMO in CHO-K1 cell membranes, with a pIC₅₀ of 6.53, and exhibits full inverse agonist efficacy^[4]. Taladegib (LY2940680) hydrochloride potently inhibits the constitutive activity of the human SMOD473H mutant receptor on CHO-K1 cell membranes, with a pIC₅₀ of 6.22, and exhibits full inverse agonist efficacy^[4]. Taladegib hydrochloride inhibits the constitutive activity of the human SMOM2 (W535L) mutant receptor on CHO-K1 cell membranes, with a pIC₅₀ of 5.75, and exhibits full inverse agonist potency^[4]. Taladegib hydrochloride potently inhibits SHH-induced proliferation of rat CGNP cells, with a pIC₅₀ of 8.12 and full efficacy^[4].

References:

- [1]. Ma W, et al. Reduced Smoothed level rescues A β -induced memory deficits and neuronal inflammation in animal models of Alzheimer's disease. *Journal of genetics and genomics = Yi chuan xue bao*. 2018 May 20;45(5):237-246.
- [2]. Fraveto A, et al. Sensitivity of Human Intrahepatic Cholangiocarcinoma Subtypes to Chemotherapeutics and Molecular Targeted Agents: A Study on Primary Cell Cultures. *PloS one*. 2015;10(11):e0142124.
- [3]. Hoch L, et al. MRT-92 inhibits Hedgehog signaling by blocking overlapping binding sites in the

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transmembrane domain of the Smoothed receptor. FASEB journal: official publication of the Federation of American Societies for Experimental Biology. 2015 May;29(5):1817-29.

[4]. Laressergues E, et al. Pharmacological evaluation of a series of smoothed antagonists in signaling pathways and after topical application in a depilated mouse model. Pharmacology research & perspectives. 2016 Apr;4(2):e00214.

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