

Product Data Sheet

Product Name: LP533401 hcl

Cat. No.: GC13293

Chemical Properties

Cas. No. 1040526-12-2

Chemical Name (2S)-2-amino-3-(4-(2-imino-6-(2,2,2-trifluoro-1-(3'-fluoro-[1,1'-biphenyl]-4-yl)ethoxy)-2,3-dihydropyrimidin-4-yl)phenyl)propanoic acid hydrochloride

SMILES FC1=CC=CC(C2=CC=C(C(OC(C=C(N3)C4=CC=C(C[C@@](N)([H])C(O)=O)C=C4)=NC3=N)([H])C(F)(F)F)C=C2)=C1.Cl

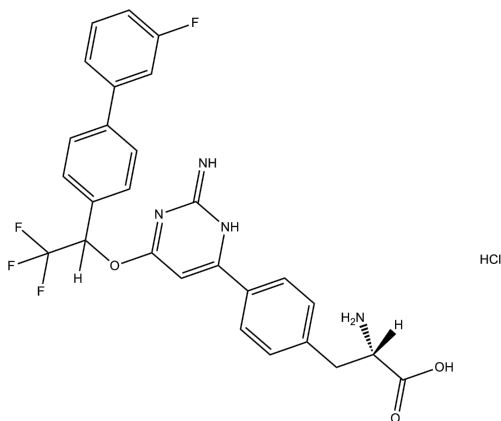
Formula $C_{27}H_{23}ClF_4N_4O_3$ M.Wt 562.94

Solubility $\geq 56.3\text{mg/mL}$ in DMSO 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



Protocol

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Animal experiment: Mice[1] Mice are treated from day 1 post-ovariectomy for 4 weeks with LP-533401 (1, 10, 100 or 250 mg per kg body weight per day) or vehicle. Next mice are treated for 4 weeks starting 2 weeks post-ovariectomy with LP-533401 (250 mg per kg body weight per day) or vehicle. lastly, mice are treated for 6 weeks starting 6 weeks post-ovariectomy with LP-533401 (25, 100 or 250 mg per kg body weight per day) or vehicle[1].

References:

- [1]. Yadav, V.K., et al. Inhibition of gut-derived serotonin synthesis: A potential bone anabolic treatment. Nat. Med. 16(3), 308-312 (2010).
- [2]. Abid S, et al. Inhibition of gut- and lung-derived serotonin attenuates pulmonary hypertension in mice. Am J Physiol Lung Cell Mol Physiol. 2012 Sep 15;303(6):L500-8.
- [3]. Krevvata M, et al. Inhibition of leukemia cell engraftment and disease progression in mice by osteoblasts. Blood. 2014 Oct 30;124(18):2834-46.

Background

LP533401 hcl is an inhibitor of Tph-1 [1].

Tryptophan hydroxylase-1 (Tph-1) is an isoenzyme of tryptophan hydroxylase and the initial enzyme in gut- and lung-derived serotonin biosynthesis. Tph-1 is mainly expressed in the gut and lung [2].

LP533401 hcl is a Tph-1 inhibitor. In rat RBL2H3 cells expressing Tph1, LP533401 (1 μ M) completely inhibited serotonin production. LP533401 reduced the activity of recombinant wild-type TPH-1 by 70% by interacting with residues Tyr235 and Phe241 [1].

In rodents, LP533401 orally administration was incapable of crossing the blood-brain barrier. In mice, LP533401 (250 mg/kg) dose-dependently reduced serum serotonin concentration by 30%. In ovariectomized female C57BL6/J mice, LP533401 (10, 100, 250 mg/kg for 28 days) increased bone mass and bone-formation parameters such as osteocalcin serum concentration, osteoblast numbers and bone formation rate. Also, LP533401 dose-dependently decreased serum serotonin concentration but didn't affect brain serotonin content. In ovariectomized female rats, LP533401 completely rescued the ovariectomy-induced osteopenia [1]. In transgenic SM22-5-HTT+ mice

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

overexpressing 5-HT transporter (5-HTT) in smooth muscle cells and spontaneously developing pulmonary hypertension (PH), LP533401 (250 mg/kg for 21 days) significantly reduced lung and blood 5-HT levels, vascular Ki67-positive cells, distal pulmonary artery muscularization, right ventricular (RV) hypertrophy and RV systolic pressure [2].

References:

- [1]. Yadav VK, Balaji S, Suresh PS, et al. Pharmacological inhibition of gut-derived serotonin synthesis is a potential bone anabolic treatment for osteoporosis. *Nat Med*, 2010, 16(3): 308-312.
- [2]. Abid S, Houssaini A, Chevarin C, et al. Inhibition of gut- and lung-derived serotonin attenuates pulmonary hypertension in mice. *Am J Physiol Lung Cell Mol Physiol*, 2012, 303(6): L500-508.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA