

Product Data Sheet

Product Name: Cathepsin S inhibitor

Cat. No.: GC14903

Chemical Properties

Cas. No. 1373215-15-6

Chemical Name [(3R,4S)-4-[(4-fluorobenzoyl)amino]-6-[4-(oxetan-3-yl)piperazin-1-yl]-3,4-dihydro-2H-chromen-3-yl] N-methylcarbamate

SMILES CNC(=O)OC1COC2=C(C1NC(=O)C3=CC=C(C=C3)F)C=C(C=C2)N4CCN(CC4)C5COC5

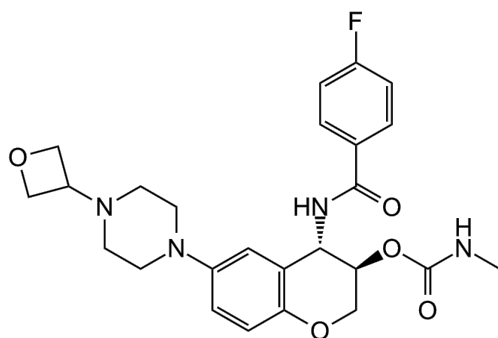
Formula $C_{25}H_{29}FN_4O_5$ M.Wt 484.52

Solubility ≥ 24.25 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

Kinase experiment [1]:

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

Kinase assays

Assays were performed for Cat S, mCat S, Cat B and Cat L by adding enzyme to a concentration of FRET substrate equal to the K_m in a 50 mM sodium phosphate buffer (pH 6.5) containing 2.5 mM DTT, 2.5 mM EDTA plus 0.01% Triton X-100. The Cat V and Cat K assays were performed as above, but in a 0.1 M sodium acetate (pH 5.5) buffer containing 2.5 mM DTT, 2.5 mM EDTA plus 0.01% Triton X-100. K_m values for the FRET substrate were 25 μ M, 25 μ M, 20 μ M, 37.5 μ M, 35 μ M, 35 μ M and 25 μ M for human Cat S, mouse Cat S, human Cat L, human Cat B, human Cat K, human Cat V and human Cat F respectively.

Animal experiment [1]:

Animal models

Mouse model of abdominal aortic aneurysm (AAA)

Dosage form

1, 3, 10, and 30 mg/kg, oral, BID dosing

Application

The efficacies of Cathepsin S inhibitor was studied in a mouse model of abdominal aortic aneurysm (AAA). Cathepsin S inhibitor exhibited a dose-responsive aortic diameter reduction at 1, 3, 10, and 30 mg/kg. At the lowest dose of 1 mg/kg of Cathepsin S inhibitor, the aortic diameter is reduced by 58%, then 83% at 3 mg/kg, and 87% at 10 mg/kg.

Other notes

Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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

References:

[1] Jadhav PK, et al. Discovery of Cathepsin S Inhibitor LY3000328 for the Treatment of Abdominal Aortic Aneurysm. ACS Med Chem Lett. 2014 Aug 27;5(10):1138-42.

Background

Ki: 0.185 nM

Cathepsin S is a lysosomal cysteine protease, playing an important role in antigen presentation. The inhibition of Cathepsin S is expected to result in immunosuppression, which makes this enzyme an attractive target to potentially treat autoimmune and inflammatory diseases. Cathepsin S inhibitor is a novel Cathepsin S inhibitor.

In vitro: Cathepsin S inhibitor was a slow, tight-binding reversible inhibitor of recombinant cathepsin S, exhibiting greater selectivity for cathepsin S compared to cathepsin B [1].

In vivo: No animal in vivo data available currently

Clinical trial: Oral Cathepsin S inhibitor that blocked MHCII antigen presentation could result in a T-cell-selective immunosuppressant agent with improved safety over the current standard of care for the treatment of rheumatoid arthritis, psoriasis, multiple sclerosis and other autoimmune-based inflammatory diseases [2].

References:

[1] Wiener JJ, Sun S, Thurmond RL. Recent advances in the design of cathepsin S inhibitors. Curr Top Med Chem. 2010;10(7):717-32.

[2] Lee-Dutra A, Wiener DK, Sun S. Cathepsin S inhibitors: 2004-2010. Expert Opin Ther Pat. 2011;21(3):311-37.

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