

Product Data Sheet

Product Name: Complement factor D-IN-1

Cat. No.: GC31846

Chemical Properties

Cas. No. 1386455-76-0

SMILES O=C(N)C1=NN(CC(N2[C@H](C(NC3=CC=CC(Br)=N3)=O)C[C@@H]4[C@H]2C4)=O)C5=C1C=CC=C5

Formula $C_{21}H_{19}BrN_6O_3$ M.Wt 483.32

Solubility DMSO: 250 mg/mL (517.26 mM) 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.

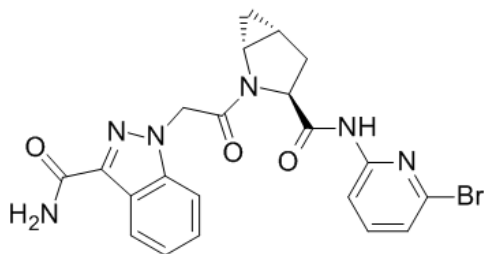
Caution: Product has not been fully validated for medical applications. For research use only.

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

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

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Structure



Protocol

Animal experiment:

Mice[1] Complement factor D-IN-1 is tested at 30 mg/kg in the human factor D knock-in mouse pharmacodynamic model. Groups of mice (n=4, female human FD knock-in) are treated either with Complement factor D-IN-1 or dosing vehicle by oral gavage at 24, 16, 12, 8, 6, and 4 h, respectively, prior to the termination of the study. All animals are given intraperitoneal LPS to activate complement 7.5 h prior to study termination. Baseline complement levels are obtained from mice that received oral dosing vehicle and intraperitoneal saline (indicated by PBS line on graph). The positive control group receives oral dosing vehicle and intraperitoneal LPS[1].

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References:

[1]. Lorthiois E, et al. Discovery of Highly Potent and Selective Small-Molecule Reversible Factor D Inhibitors Demonstrating Alternative Complement Pathway Inhibition in Vivo. J Med Chem. 2017 Jul 13;60(13):5717-5735.

Background

Complement factor D-IN-1 is a potent and selective small-molecule reversible factor d inhibitor, with IC₅₀s of 0.006 and 0.05 μ M in FD Thioesterolytic Fluorescent Assay and a MAC Deposition Assay, respectively.

The highly specific S1 serine protease factor D (FD) plays a central role in the amplification of the complement alternative pathway (AP) of the innate immune system. Complement factor D-IN-1 (compound 2) shows similar potency against human and monkey FD (IC₅₀s in FD thioesterolytic assays of 0.005 μ M and in 50% serum MAC deposition assays of 0.011 μ M for both human and monkey)[1].

Complement factor D-IN-1 displays an excellent oral PK profile in Sprague-Dawley rats and, following an oral dose (10 mg/kg) in Brown Norway rats, demonstrates a good distribution and sustained exposure in ocular tissues including the neural retina and the posterior eye cup (PEC), which comprises the sclera, retinal pigmented epithelium, and choroid. Mean exposure levels in plasma, the PEC, and the retina at 6 h after dosing are 0.36, 0.43, and 0.09 μ M, respectively[1].

[1]. Lorthiois E, et al. Discovery of Highly Potent and Selective Small-Molecule Reversible Factor D Inhibitors Demonstrating Alternative Complement Pathway Inhibition in Vivo. J Med Chem. 2017 Jul 13;60(13):5717-5735.

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