

Product Data Sheet

Product Name: GNF 5
Cat. No.: GC15079

Chemical Properties

Cas. No. 778277-15-9

Chemical Name N-(2-hydroxyethyl)-3-[6-[4-(trifluoromethoxy)anilino]pyrimidin-4-yl]benzamide

SMILES C1=CC(=CC(=C1)C(=O)NCCO)C2=CC(=NC=N2)NC3=CC=C(C=C3)OC(F)(F)F

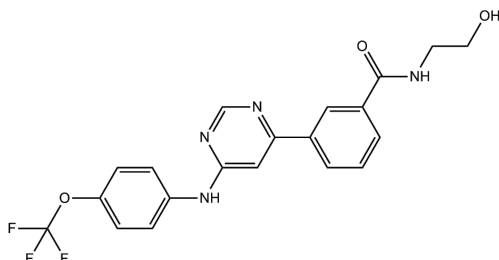
Formula $C_{20}H_{17}F_3N_4O_3$ M.Wt 418.37

Solubility $\geq 20.9\text{mg/mL}$ 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

Cell experiment:[1]

Cell lines Wild-type or Bcr-Abl transformed Ba/F3 cells

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

The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Preparation method

Reaction Conditions 0-3 µM

Applications

Inhibition of wild-type Abl was observed for both inhibitors with GNF-5 exhibiting an IC₅₀ value of 0.22 mM, dasatinib using an ATP concentration of 20 mM with an IC₅₀ value of 0.12 mM. The myristate site mutant E505K was inhibited by dasatinib with an IC₅₀ value of 0.02 mM, but not by GNF-5 (IC₅₀>10 mM).

Animal experiment:[2]

Animal models

Abl^{-lox} and SM22^{cre} mice on C57BL/6 background

Dosage form

Animals were intranasally instilled with 10 mg/kg GNF-5 or PBS 1 h before OVA instillation and 5 h after OVA instillation for last three weeks.

Applications

In conditional knockout of Abl mice, the levels of IL-13 and CCL2 in bronchoalveolar lavage fluid treated with ovalbumin has not been affected, but it works after treatment with imatinib and GNF-5 as well as airway resistance and smooth muscle growth in animals. Treatment with imatinib or GNF-5 inhibited the ACh-induced contraction in isolated mouse tracheal rings of OVA-sensitized and challenged mice. Treatment with imatinib or GNF-5 diminished the fluorescent intensity of PCNA in BALB/c mice treated with OVA.

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

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.

References:

[1]. Jacob RE, Zhang J, Gray NS et al. Allosteric interactions between the myristate- and ATP-site of the Abl kinase. PLoS One. 2011 Jan 10;6(1):e15929.

[2]. Cleary RA, Wang R, Wang T et al. Role of Abl in airway hyperresponsiveness and airway remodeling. Respir Res. 2013 Oct 11;14:105.

Background

GNF-5 is an analogue of GNF-2 and a selective non-ATP competitive inhibitor of Bcr-Abl with an IC₅₀ value of 0.1 to >10 μ M in various cancer cell lines.

Bcr-Abl is a fusion gene that results from the head-to-tail fusion of the Bcr and Abl genes[1]. Bcr-Abl upregulates production of tyrosine kinase and plays a central role in the pathogenesis of chronic myelogenous leukemia (CML) [1].

GNF-5 has the same chemical structure as its parent molecule (GNF-2) with the exception of N-hydroxyethyl carboxamide at its 4-position and such modification provided GNF-5 a longer half-life from (2.30 hrs)[2]. Similar with GNF-2, GNF-5 allosterically inhibits the proliferation of Bcr-Abl positive cell by binding to the myristate-binding site of Abl and induces cell apoptosis[3]. In steady-state kinetic analyses, GNF-5 was able to inhibit wild type Abl with an IC₅₀ value of 0.22 μ M[2]. In addition, GNF-5 also has a similar effectiveness against various imatinib® resistance cell lines: In E255V and T315I mutant Ba/F3 cells, a 12-day incubation of GNF-5 2 was able to inhibit the proliferation of cells with a IC₅₀ value of 0.38 and 5 μ M, respectively[2].

In mice injected with wild-type Bcr-Abl and luciferase expressing Ba/F3 cells, continuous injection of GNF-5 for 7 days (50 mg/kg, twice per day) normalized peripheral blood cell counts, as well as spleen size[2]. When treating mice that injected with imatinib® resistance T315I Bcr-Abl-transduced bone marrow, daily injection of GNF-5 (75 mg/ kg, twice per day) significantly extended the survival

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

day of mice from 24 days to 22 days[2].

References:

- [1]. Rumpold, H. & Webersinke, G. 2011. Molecular pathogenesis of Philadelphia-positive chronic myeloid leukemia - is it all BCR-ABL? Curr Cancer Drug Targets, 11, 3-19.
- [2]. Zhang, J., Adrian, F. J., Jahnke, W., et al. 2010. Targeting Bcr-Abl by combining allosteric with ATP-binding-site inhibitors. Nature, 463, 501-506.
- [3]. Karunakaran, U., Park, S. J., Jun, D. Y., et al. Non-receptor tyrosine kinase inhibitors enhances β -cell survival by suppressing the PKC δ signal transduction pathway in streptozotocin – induced β -cell apoptosis. Cellular Signalling.

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