

HG-7-85-01

Chemical Properties

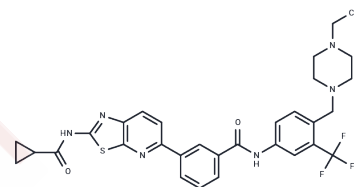
CAS No. : 1258391-13-7

Formula: C₃₁H₃₁F₃N₆O₂S

Molecular Weight: 608.68

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Actual storage temperature shall be subject to the COA.



Biological Description

Description	HG-7-85-01 is a novel ATP-competitive and type II tyrosine kinase inhibitor targeting both wild-type and watchman mutant BCR-ABL, PDGFR α , Kit, and Src kinases, with inhibitory effects on the proliferation of a variety of cancer cell lines, leading to G ₀ /G ₁ -phase blockade and apoptosis induction in BCR-ABL-expressing cells.
Targets(IC ₅₀)	Apoptosis,Bcr-Abl,c-Kit,JAK,PDGFR,Src
In vitro	HG-7-85-01 (0-1 μ M; 24 hours; BCR-ABL-, BCR-ABL-T315I-, Kit-T670I-, PDGFR α -T674M-, and PDGFR α -T674I-expressing cells) treatment leads to G ₀ G ₁ arrest of BCR-ABL-expressing cells [1]. HG-7-85-01 (0-1 μ M; 72 hours; BCR-ABL-, BCR-ABL-T315I-, Kit-T670I-, PDGFR α -T674M-, and PDGFR α -T674I-expressing cells) treatment also leads to induction of apoptosis of BCR-ABL-expressing cells [1]. HG-7-85-01 treatment potently and selectively inhibits the proliferation of 32D- and Ba/F3 cells expressing nonmutant BCR-ABL and the BCR-ABL-T315I gatekeeper mutant. HG-7-85-01 shows higher potency against nonmutant BCR-ABL and BCR-ABL-T315I (IC ₅₀ = 0.06-0.14 μ M) [1]. HG-7-85-01 inhibits BCR-ABL kinase activity in a concentration-dependent manner, suggesting selective targeting of the BCR-ABL kinase as the mechanism of action of HG-7-85-01 [1]. HG-7-85-01 potently inhibits the proliferation of Ba/F3 cells expressing the Kit-T670I gatekeeper mutation (Ba/F3- Kit-T670I) and Ba/F3 cells expressing TEL/PDGFR β and no effect on parental Ba/F3 cells. HG-7-85-01 inhibits Kit, PDGFR phosphorylation in a concentration-dependent manner [1]. The PDGFR α -T674M and PDGFR α -T674I gatekeeper mutant variants are highly responsive to HG-7-85-01 and significant IL-3 rescue [1]. HG-7-85-01 inhibits the proliferation of Ba/F3 cells transformed with human c-Src (EC ₅₀ = 190 nM), T338I Src (EC ₅₀ = 290 nM), and T338M Src (EC ₅₀ = 150 nM; chicken c-Src numbering). And potently inhibits the proliferation of exon 11 Kit mutant-expressing cells, exon 9 kit mutant-expressing cells are significantly less responsive [1]. Cell Cycle Analysis [1] Cell Line: BCR-ABL-, BCR-ABL-T315I-, Kit-T670I-, PDGFR α -T674M-, and PDGFR α -T674I-expressing cells Concentration: 0 μ M, 0.01 μ M, 0.1 μ M and 1 μ M Incubation Time: 24 hours Result: Led to G ₀ G ₁ arrest of BCR-ABL-expressing cells. Apoptosis Analysis [1] Cell Line: BCR-ABL-, BCR-ABL-T315I-, Kit-T670I-, PDGFR α -T674M-, and PDGFR α -T674I-expressing cells Concentration: 0 μ M, 0.01 μ M, 0.1 μ M and 1 μ M Incubation Time: 72 hours Result: Led to induction of apoptosis of BCR-ABL-expressing cells.
In vivo	HG-7-85-01 has limited oral bioavailability (BAV % F mouse = 5 %, rat = 19 %), a moderate half life (T _{1/2} mouse =1.1 h rat = 5.8 hours), a relative low maximal serum

In vivo	concentration (C max mouse = 106 ng/mL at 10 mg/kg , rat = 292 ng/mL and 2 mg/kg) and a relatively high clearance (Cl mouse = 23 ml/min/kg, rat = 13 ml/min/kg) [1] .
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Solubility Information

Solubility	DMSO: 100 mg/mL (164.29 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.6429 mL	8.2145 mL	16.429 mL
5 mM	0.3286 mL	1.6429 mL	3.2858 mL
10 mM	0.1643 mL	0.8214 mL	1.6429 mL
50 mM	0.0329 mL	0.1643 mL	0.3286 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Ellen Weisberg, et al. Discovery of a Small-Molecule Type II Inhibitor of Wild-Type and Gatekeeper Mutants of BCR-ABL, PDGFRalpha, Kit, and Src Kinases: Novel Type II Inhibitor of Gatekeeper Mutants. Blood. 2010 May 27;115(21):4206-16.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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