

Product Data Sheet

Product Name: CFI-402257

Cat. No.: GC18491

Chemical Properties

Cas. No. 1610759-22-2

Chemical Name N-cyclopropyl-4-[7-[[[cis-3-hydroxy-3-methylcyclobutyl)methyl]amino]-5-(3-pyridinyloxy)pyrazolo[1,5-a]pyrimidin-3-yl]-2-methyl-benzamide

SMILES CC1=C(C(NC2CC2)=O)C=CC(C3=C4N=C(OC5=CN=CC=C5)C=C(NC[C@@H]6C[C@@](O)(C)C6)N4N=C3)=C1

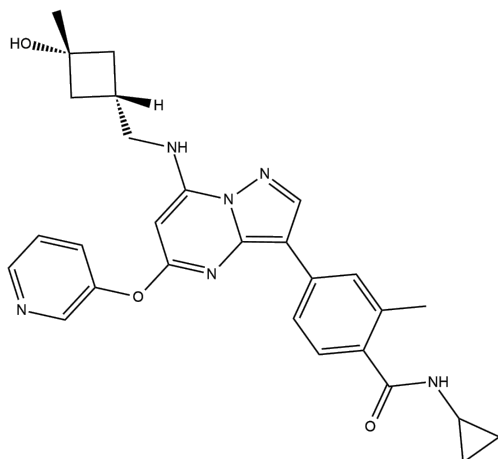
Formula $C_{28}H_{30}N_6O_3$ M.Wt 498.6

Solubility DMSO : ≥ 125 mg/mL (233.63 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.

Structure



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

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Protocol

Cell experiment [1]:	
Cell lines	Py8119 cells
Preparation Method	Py8119 cells were cultured in Ham's F12K medium, supplemented with 10% fetal bovine serum (FBS), and 5% penicillin/streptomycin at 37°C in an incubator with 5% CO ₂ . 3000 cells per well were plated in 96-well plates and treated with increasing concentrations of CFI-402257 (0, 0.001, 0.01, 0.1, 1, 10, and 100µM) 24 hours later. 72 hours post treatment, cell viability was measured.
Reaction Conditions	0, 0.001, 0.01, 0.1, 1, 10, and 100µM; 72h
Applications	CFI-402257 treatment decreased cell viability of Py8119 cells in a dose-dependent manner.
Animal experiment [2]:	
Animal models	Male BALB/cAnN-nu mice
Preparation Method	Male BALB/cAnN-nu mice (6 weeks old) were housed in a standard environment, with free access to food and water. Suspension of 1.5×10^6 luciferase-labelled MHCC97L cells in 100% Matrigel, was injected into the left lobe of the livers of mice. 6mg/kg/day CFI-402257 or vehicle (90% PEG in ultrapure H ₂ O) was administered to mice daily via oral gavage, starting from day 14 post-orthotopic implantation, lasting for 19 days. Size of tumors was measured using an electronic caliper and calculated by $\text{length(mm)} \times \text{width(mm)} \times \text{height(mm)} \times 0.52$.

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Dosage form	6mg/kg/day; 19 days; p.o.
Applications	CFI-402257 treatment inhibited tumor growth in the mice with implantation of MHCC97L cells.
References: [1] Jungles K M, Bishop C R, Wilson C M, et al. Targeting monopolar spindle kinase I (Mps1 or TTK) induces radiosensitization in syngeneic models of triple negative breast cancer (TNBC) and potentiates type I interferon (T1IFN) signaling[J]. Neoplasia, 2025, 66: 101190. [2] Chan C Y K, Chiu D K C, Yuen V W H, et al. CFI-402257, a TTK inhibitor, effectively suppresses hepatocellular carcinoma[J]. Proceedings of the National Academy of Sciences, 2022, 119(32): e2119514119.	

Background

CFI-402257 is a potent, highly selective, and orally active small-molecule inhibitor of Threonine tyrosine kinase, with an IC_{50} value of 1.7nM and a K_i value of 0.1nM^[1]. CFI-402257 inhibits autophosphorylation of monopolar spindle 1 (Mps1) at threonine 12/serine 15 with an EC_{50} value of 6.5 ± 0.5 nM, leading to spindle assembly checkpoint (SAC) inactivation, chromosome missegregation, aneuploidy, and ultimately cell death^[2]. CFI-402257 has been widely used in preclinical tumor model studies to restrain the progression of breast cancer, lung cancer and liver cancer^[3].

In vitro, CFI-402257 treatment for 72 hours markedly suppressed the proliferation of Py8119, BT-549 and CAL-51 cells, with IC_{50} values of 20.78nM, 38.20nM and 42.90nM, respectively^[4]. Treatment with 1 μ M CFI-402257 for 24 hours increased the aneuploid DNA content in A549 cells and induced cell apoptosis^[5]. Incubation of Hmeso cells with 100nM CFI-402257 for 24 hours resulted in unequal division, multilobulation and formation of micronucleus, and cytoplasmic translocation of cytochrome c^[6].

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In vivo, CFI-402257 treatment via oral administration at a dose of 6mg/kg/day for 19 days delayed hepatocellular carcinoma progression and reduced lung metastasis in BALB/cAnN-nu mice^[7]. Oral administration of CFI-402257 (4mg/kg/day) for 4 consecutive weeks reduced the area of atherosclerotic plaques in the aorta of ApoE^{-/-} mice fed a high-fat diet without affecting the blood lipid levels^[8].

References:

- [1] Liu Y, Laufer R, Patel N K, et al. Discovery of pyrazolo [1, 5-a] pyrimidine TTK inhibitors: CFI-402257 is a potent, selective, bioavailable anticancer agent[J]. ACS Medicinal Chemistry Letters, 2016, 7(7): 671.
- [2] Mason J M, Wei X, Fletcher G C, et al. Functional characterization of CFI-402257, a potent and selective Mps1/TTK kinase inhibitor, for the treatment of cancer[J]. Proceedings of the National Academy of Sciences, 2017, 114(12): 3127-3132.
- [3] Thu K L, Jafari S, Silvester J, et al. Genome-Wide CRISPR Screens Identify ABCG2-Mediated Drug Resistance to the Threonine Tyrosine Kinase (TTK) Inhibitor CFI-402257 in Breast Cancer[J]. International Journal of Molecular Sciences, 2026, 27(6): 2665.
- [4] Jungles K M, Bishop C R, Wilson C M, et al. Targeting monopolar spindle kinase I (Mps1 or TTK) induces radiosensitization in syngeneic models of triple negative breast cancer (TNBC) and potentiates type I interferon (T1IFN) signaling[J]. Neoplasia, 2025, 66: 101190.
- [5] Zheng L, Chen Z, Kawakami M, et al. Tyrosine threonine kinase inhibition eliminates lung cancers by augmenting apoptosis and polyploidy[J]. Molecular cancer therapeutics, 2019, 18(10): 1775-1786.
- [6] Szymiczek A, Carbone M, Pastorino S, et al. Inhibition of the spindle assembly checkpoint kinase Mps-1 as a novel therapeutic strategy in malignant mesothelioma[J]. Oncogene, 2017, 36(46): 6501-6507.
- [7] Chan C Y K, Chiu D K C, Yuen V W H, et al. CFI-402257, a TTK inhibitor, effectively suppresses hepatocellular carcinoma[J]. Proceedings of the National Academy of Sciences, 2022, 119(32): e2119514119.
- [8] Wu J H, Liu Y X, Zong J B, et al. TTK inhibition alleviates Postinjury Neointimal formation and

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