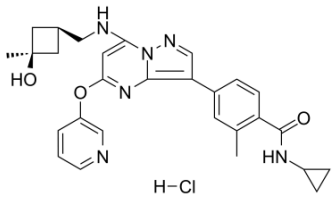
CFI-402257 hydrochloride

Cat. No.:	HY-101340A
CAS No.:	1610677-37-6
Molecular Formula:	$C_{28}H_{31}ClN_6O_3$
Molecular Weight:	535.04
Target:	Mps1
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton
Storage:	4°C, protect from light



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 125 mg/mL (233.63 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8690 mL	9.3451 mL	18.6902 mL
5 mM	0.3738 mL	1.8690 mL	3.7380 mL
10 mM	0.1869 mL	0.9345 mL	1.8690 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: **10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline**
   Solubility: ≥ 2.08 mg/mL (3.89 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: ≥ 2.08 mg/mL (3.89 mM); Clear solution
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 2.08 mg/mL (3.89 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CFI-402257 hydrochloride is a highly selective and orally bioavailable **TTK/Mps1** inhibitor with an **IC_{50}** of 1.7 nM for TTK in vitro. CFI-402257 hydrochloride has anti-cancer activity[1].

IC_{50} & Target

IC50: 1.7 nM (TTK in vitro)[1].

In Vitro

CFI-402257 is highly selective to TTK. CFI-402257 is tested against a panel of human kinases at 1 μM and inhibits none of the 262 kinases tested. CFI-402257 is a potent inhibitor of cell growth[1].

CFI-402257 (200 nM, 6 h) causes a massive increase in chromosome missegregations[2].
CFI-402257 (0, 50 or 100 nM) induces a dose-dependent dysregulation of the cell cycle, resulting in an increase in the frequency of cells exhibiting an aneuploid DNA content[2].
CFI-402257 exhibits effects consistent with Mps1 kinase inhibition, specifically SAC inactivation, leading to chromosome missegregation, aneuploidy, and ultimately cell death[2].

Cell Cycle Analysis[2]

Cell Line:	HCT116 cells.
Concentration:	0 nM, 50 nM, 100 nM, 300 nM, 1000 nM, 3000 nM.
Incubation Time:	48 hours
Result:	Resulted in an increase in the frequency of cells exhibiting an aneuploid DNA content.

Western Blot Analysis[2]

Cell Line:	HCT116 cells.
Concentration:	0 nM, 50 nM or 100 nM.
Incubation Time:	8, 16, 24 and 48 hours.
Result:	CFI-402257-induced aneuploidy was accompanied by a progressive accumulation of apoptotic cells that were detectable as early as 16 h following treatment.

In Vivo

CFI-402257 given orally QD shows dose-dependent activity in mice with established tumors from xenografted MDA-MB-231 human TNBC cells and MDA-MB-468 human TNBC cells in mice. CFI-402257 demonstrates antitumor activity in a platinum-resistant PDX model of high-grade serous ovarian cancer[2].

Animal Model:	Xenografted MDA-MB-231 human TNBC cells and MDA-MB-468 human TNBC cells in mice[2].
Dosage:	5, 6 mg/kg.
Administration:	Oral gavage, daily.
Result:	Xenografted MDA-MB-231 human TNBC cells: 5 mg/kg, tumor growth inhibition (TGI) = 74%; 6 mg/kg, TGI = 89%. Xenografted MDA-MB-468 human TNBC cells: 5 mg/kg, tumor growth inhibition (TGI) = 75%; 6 mg/kg, TGI = 94%.

Animal Model:	PDX model of high-grade serous ovarian cancer[2].
Dosage:	6.5, 7.5 mg/kg.
Administration:	Oral gavage, daily.
Result:	6.5 mg/kg, tumor growth inhibition (TGI) = 61%; 7.5 mg/kg, TGI = 97%.

CUSTOMER VALIDATION

- **Cancer Discov**. 2019 Feb;9(2):230-247.

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REFERENCES

[1]. Liu Y, et al. Discovery of Pyrazolo[1,5-a]pyrimidine TTK Inhibitors: CFI-402257 is a Potent, Selective, Bioavailable Anticancer Agent. ACS Med Chem Lett. 2016 May 6;7(7):671-5.

[2]. Mason JM, et al. Functional characterization of CFI-402257, a potent and selective Mps1/TTK kinase inhibitor, for the treatment of cancer. Proc Natl Acad Sci U S A. 2017 Mar 21;114(12):3127-3132.

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