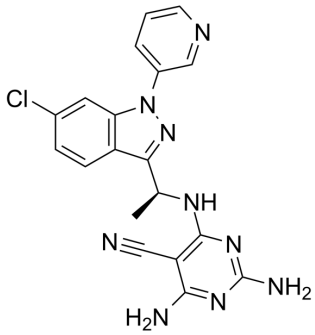
PI3Kδ-IN-10

Cat. No.:	HY-144254
CAS No.:	2409725-49-9
Molecular Formula:	$C_{19}H_{16}ClN_9$
Molecular Weight:	405.84
Target:	PI3K; Akt; Apoptosis
Pathway:	PI3K/Akt/mTOR; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	PI3Kδ-IN-10 is a highly potent and orally active PI3Kδ inhibitor with IC_{50} of 2 nM. PI3Kδ-IN-10 robustly suppresses the downstream AKT pathway to induce subsequent apoptosis in hepatocellular carcinoma models[1].
IC_{50} & Target	PI3Kδ 2 nM (IC_{50})
In Vitro	PI3Kδ-IN-10 (compound 9x) (0-10 μM; 72 hours) has cell proliferation inhibitory effects in HCC cell lines with IC_{50} of 0.53 - 1.36 μM[1]. PI3Kδ-IN-10 (0-50 μM; 24 hours) markedly enhances expression level of cleaved PARP and cleaved caspase-3, also reduces the level of Akt phosphorylation at Ser473 and Thr308 in a dose-dependent manner[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay

Cell Line:	Bel-7402, HepG2, Hep3B[1]
Concentration:	0-10 μM
Incubation Time:	72 hours
Result:	Showed cell proliferation inhibitory effects in HCC cell lines with IC_{50} of 0.53 - 1.36 μM.

Western Blot Analysis

Cell Line:	Bel-7402, HepG2[1]
Concentration:	0 μM, 1.56 μM, 3.12 μM, 6.25 μM, 12.5 μM, 50 μM
Incubation Time:	24 hours
Result:	Markedly enhanced expression level of cleaved PARP and cleaved caspase-3, also reduced the level of Akt phosphorylation at Ser473 and Thr308 in a dose-dependent manner.

In Vivo	PI3Kδ-IN-10 (5 mg/kg for PO, 1 mg/kg for IV, single) exhibits an acceptable half-life ($T_{1/2}$), a moderate distribution volume, and acceptable oral bioavailability[1]. PI3Kδ-IN-10 (40 and 20 mg/kg; IV, for 12 days) effectively suppress the growth of live cancer xenografts with inhibition ratios

of 76.02% and 59.15% at 40 mg/kg and 20 mg/kg[1].

Pharmacokinetic Parameters of PI3Kδ-IN-10 in female Balb/c (nu/nu) mice[1].

	PO (5 mg/kg)	IV (1 mg/kg)
$T_{1/2}$ (h)	2.502	1.131
AUC (h·μg/L)	3067.94	2791.37
Vz/F (L/kg)	6.15	0.587
T_{max} (h)	3	0.083
F (%)	22.0	

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female Balb/c (nu/nu) mice[1]
Dosage:	5 mg/kg or 1 mg/kg
Administration:	PO and IV, single (Pharmacokinetic Analysis)
Result:	Exhibited an acceptable half-life ($T_{1/2}$), a moderate distribution volume, and acceptable oral bioavailability.

Animal Model:	Female Balb/c (nu/nu) mice (6 weeks)[1]
Dosage:	40 and 20 mg/kg
Administration:	IV, for 12 days
Result:	Effectively suppressed the growth of live cancer xenografts with inhibition ratios of 76.02% and 59.15% at 40 mg/kg and 20 mg/kg.

REFERENCES

[1]. Qi J, Wang W, Tang Y, et al. Discovery of Novel Indazoles as Potent and Selective PI3Kδ Inhibitors with High Efficacy for Treatment of Hepatocellular Carcinoma. J Med Chem. 2022;65(5):3849-3865.

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