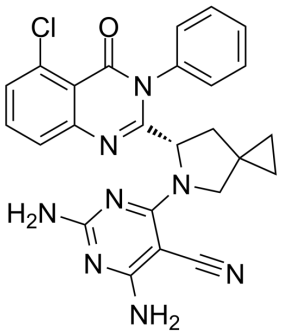
PI3Kδ/γ-IN-2

Cat. No.:	HY-146789
CAS No.:	2412195-89-0
Molecular Formula:	$C_{25}H_{21}ClN_8O$
Molecular Weight:	484.94
Target:	PI3K
Pathway:	PI3K/Akt/mTOR
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

PI3Kδ/γ-IN-2 is a potent PI3Kδ and PI3Kγ dual inhibitor with IC_{50}s of 1 nM and 4.3 nM, respectively. PI3Kδ/γ-IN-2 has favorable oral bioavailability. PI3Kδ/γ-IN-2 has potential for battling B-cell malignancies[1].

IC_{50} & Target

PI3Kδ	PI3Kγ
1 nM (IC_{50})	4.3 nM (IC_{50})

In Vitro

PI3Kδ/γ-IN-2 (compound 26) (0-5 μM; 72 hours) exhibits remarkable anti-proliferative activity against SU-DHL-6 cell line[1].
PI3Kδ/γ-IN-2 (10-100 nM; 2 hours) down-regulates both phos-Akt (Ser473) and phos-S6K1 (Thr389), and decreases the phosphoration of Akt and S6K1 at 30 nM[1].

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

Cell Proliferation Assay

Cell Line:	SU-DHL-6[1]
Concentration:	0-5 μM
Incubation Time:	72 hours
Result:	Exhibited remarkable anti-proliferative activity against SU-DHL-6 cell line with GI_{50} value of 33 nM.

Western Blot Analysis

Cell Line:	SU-DHL-6[1]
Concentration:	10, 30 and 100 nM
Incubation Time:	2 hours
Result:	Down-regulated both phos-Akt (Ser473) and phos-S6K1 (Thr389) in a dose-dependent manner, and exhibited a more significant decrease in the phosphoration of Akt and S6K1 at 30 nM.

In Vivo

PI3Kδ/γ-IN-2 (5 mg/kg; PO or IV; single) exhibits a high plasma exposure, an attractive oral bioavailability, and an acceptable clearance[1].

Pharmacokinetic Parameters of PI3Kδ/γ-IN-2 in male Sprague-Dawley rats[1].

	IV (5 mg/kg)	PO (5 mg/kg)
$T_{1/2}$ (h)	3.0 ± 0.3	14.3 ± 4.4
AUC_{0-t} (h·μg/L)	5576 ± 606	4878 ± 694
V_{SS} (L/kg)	3.9 ± 0.6	
CL (L/h/kg)	0.9 ± 0.1	
F (%)		87.5 ± 12.5

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

Animal Model:	Male Sprague-Dawley rats[1]
Dosage:	5 mg/kg
Administration:	PO or IV; single (Pharmacokinetics Analysis)
Result:	Exhibited a high plasma exposure (AUC_{0-t} = 4878 ± 694 h μg/L), an attractive oral bioavailability (F% = 87.5 ± 12.5), and an acceptable clearance (CL = 0.9 ± 0.1 L/h/kg).

REFERENCES

[1]. Tao Q, et al. Structurally novel PI3Kδ/γ dual inhibitors characterized by a seven-membered spirocyclic spacer: The SARs investigation and PK evaluation. Eur J Med Chem. 2020;191:112143.

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