IPN60090

Cat. No.: HY-103671

CAS No.: 1853164-83-6

Molecular Formula: $C_{24}H_{27}F_3N_8O_3$

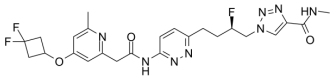
Molecular Weight: 532.52

Target: Glutaminase

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 31.43 mg/mL (59.02 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8779 mL	9.3893 mL	18.7786 mL
	5 mM	0.3756 mL	1.8779 mL	3.7557 mL
	10 mM	0.1878 mL	0.9389 mL	1.8779 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3.14 mg/mL (5.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

IPN-60090 is an orally active and highly selective inhibitor of glutaminase 1 (GLS1; IC_{50}=31 nM), with no activity observed against GLS-2. IPN-60090 exhibits excellent physicochemical and pharmacokinetic properties in vivo. IPN-60090 can be used for solid tumors research, such as lung and ovarian cancers[1][2].

IC_{50} & Target

IC50: 31 nM (GLS1)[2]

In Vitro

There are two known isoforms of glutaminase: GLS-1 (also called kidney-type or KGA), and GLS-2 (also called liver-type or LGA). GLS-1 is ubiquitous and GLS-2 expression appears limited primarily to the liver.
In a dual-coupled enzyme assay, IPN60090 inhibits purified recombinant human GLS-1 (GAC isoform) with an IC_{50} of 31 nM, and has no activity against GLS-2, with an IC_{50} of >50000 nM[2].
IPN60090 inhibits the proliferation of A549 cells with an IC_{50} of 26 nM[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

IPN60090 (3 mg/kg for i.v.; 10 mg/kg for p.o.) has excellent pharmacokinetic properties, with CL=4.1 mL/min/kg, $t_{1/2}$=1 hour, C_{max}=19 μM, F%=89%[2].

IPN-60090 (oral administration; 100 mg/kg; twice daily; 30 days) shows similar efficacy and target engagement to CB-839 (HY-12248) dosed orally at 250 mg/kg twice daily. And the 100 mg/kg BID dose of IPN-60090 is a tolerated dose for the following model study[2].

IPN-60090 (oral administration; 100 mg/kg; twice daily; 30 days; monotherapy or in combination with TAK228 (HY-13328)) causes tumor growth inhibition. IPN-60090 alone demonstrates robust in vivo target engagement in a dose-dependent manner. The glutamate/glutamine ratios and the free plasma concentrations of IPN-60090 at 4 hours post-dose on both day 4 and day 28 are all decreased[2]. Furthermore, IPN-60090 in combination with TAK228 strongly causes an 85% tumor growth inhibition, IPN-60090 alone causes a 28% tumor growth inhibition in vivo[2].

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

Animal Model:	Female CD-1 mice[2]
Dosage:	3 mg/kg for i.v.; 10 mg/kg for p.o. (Pharmacokinetic Analysis)
Administration:	Intravenous injection and oral administration
Result:	CL (4.1 mL/min/kg), $t_{1/2}$ (1 hour) for i.v.; C_{max} (19 μM), F% (89%) for p.o..

Animal Model:	Ru337 non-small cell lung cancer patient-derived xenograft (PDX) subcutaneous mouse model as monotherapy or in combination[2]
Dosage:	100 mg/kg
Administration:	Oral administration; 100 mg/kg; twice daily; 30 days; monotherapy or in combination with TAK228
Result:	Exhibited an improvement in the combination regimen group over either single agent.

REFERENCES

[1]. Maria Emilia Di Francesco, et al. Gls1 inhibitors for treating disease. WO2016004404A2.

[2]. Michael J Soth, et al. Discovery of IPN60090, a Clinical Stage Selective Glutaminase-1 (GLS-1) Inhibitor with Excellent Pharmacokinetic and Physicochemical Properties. J Med Chem. 2020 Nov 12;63(21):12957-12977.

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