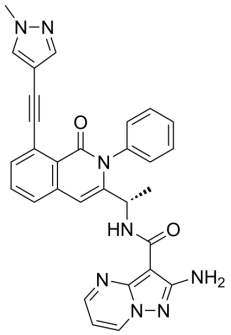
Eganelisib

Cat. No.:	HY-100716
CAS No.:	1693758-51-8
Molecular Formula:	$C_{30}H_{24}N_8O_2$
Molecular Weight:	528.56
Target:	PI3K
Pathway:	PI3K/Akt/mTOR

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (47.30 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8919 mL	9.4597 mL	18.9193 mL
	5 mM	0.3784 mL	1.8919 mL	3.7839 mL
	10 mM	0.1892 mL	0.9460 mL	1.8919 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: ≥ 2.5 mg/mL (4.73 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.73 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Eganelisib (IPI549) is a potent and selective PI3Kγ inhibitor with an IC_{50} of 16 nM. Eganelisib shows >100-fold selectivity over other lipid and protein kinases[1].

IC_{50} & Target

PI3Kγ	PI3Kα	PI3Kβ
16 nM (IC_{50})	3.2 μM (IC_{50})	3.5 μM (IC_{50})

In Vitro

Eganelisib (IPI549) inhibits PI3Kγ with IC_{50} of 16 nM, with >100-fold selectivity over other lipid and protein kinases (PI3Kα IC_{50}=3.2 μM, PI3Kβ IC_{50}=3.5 μM, PI3Kδ IC_{50}>8.4 μM). Eganelisib is evaluated for activity across all Class I PI3K isoforms. The binding affinity of Eganelisib for PI3K-γ is determined by measuring the individual rates constants and for PI3K-α, β and δ using equilibrium fluorescent titration. Eganelisib is a remarkably tight binder to PI3Kγ with a K_d of 290 pM and >58-fold

	weaker affinity for other Class I PI3K isoforms (PI3Kα K_d=17 nM, PI3Kβ K_d=82 nM, PI3Kδ K_d=23 M). In PI3K-α, -β, -γ, and -δ dependent cellular phospho-AKT assays, Eganelisib demonstrates excellent PI3K-γ potency (IC_{50}=1.2 nM) and selectivity against other Class I PI3K isoforms (>146-fold). Cellular IC_{50}s for Class I PI3Kα (250 nM), PI3Kβ (240 nM), PI3Kγ (1.2 nM), PI3Kδ (180 nM) are determined in SKOV-3, 786-O, RAW 264.7, and RAJI cells, respectively, by monitoring inhibition of pAKT S473 by ELISA. Furthermore, Eganelisib dose dependently inhibits PI3Kγ dependent bone marrow-derived macrophage (BMDM) migration. Eganelisib is selective against a panel of 80 GPCRs, ion channels, and transporters at 10 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Eganelisib (IPI549) demonstrates favorable pharmacokinetic properties and robust inhibition of PI3K-γ mediated neutrophil migration. In vivo (mice, rats, dog, and monkeys), Eganelisib has excellent oral bioavailability, low clearance, and distributed into tissues with a mean volume of distribution of 1.2 L/kg. Overall, Eganelisib has a favorable pharmacokinetic profile to allow potent and selective inhibition of PI3K-γ in vivo. The $t_{1/2}$ of IPI-549 for mouse, rat, dog and monkey is 3.2, 4.4, 6.7 and 4.3 h, respectively. Eganelisib significantly reduces neutrophil migration in a dose dependent manner in this model when administered orally at all of the tested doses[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	C57BL/6J and Balb/c mice (6 to 8 weeks old) are used in this study. On day 0 of the experiments, tumor cells are injected intradermally (i.d.) in the right flank. Eganelisib is administered by oral gavage once a day at 15 mg/kg. Treatment is initiated on day 7 ending on day 21 post tumor implant. Control groups receive vehicle (5% NMP, 95% PEG). Tumors are measured every second or third day with a caliper, and the volume (length×width×height) is calculated. Animals are euthanized for signs of distress or when the total tumor volume reaches 2500 mm^3. Finally, Tumors are isolated, and frozen until needed[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2022 Oct;610(7931):366-372.
- Cancer Cell. 2021 Sep 1;S1535-6108(21)00445-1.
- ACS Nano. 2021 Dec 9.
- Nat Commun. 2022 May 20;13(1):2834.
- Nat Commun. 2019 Sep 25;10(1):4364.

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REFERENCES

[1]. Evans CA, et al. Discovery of a Selective Phosphoinositide-3-Kinase (PI3K)-γ Inhibitor (IPI-549) as an Immuno-Oncology Clinical Candidate. ACS Med Chem Lett. 2016 Jul 22;7(9):862-7.

[2]. De Henau O, et al. Overcoming resistance to checkpoint blockade therapy by targeting PI3Kγ in myeloid cells. Nature. 2016 Nov 17;539(7629):443-447.

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

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