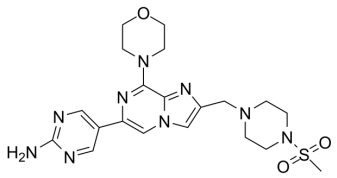
ETP-46321

Cat. No.:	HY-12340
CAS No.:	1252594-99-2
Molecular Formula:	$C_{20}H_{27}N_9O_3S$
Molecular Weight:	473.55
Target:	PI3K
Pathway:	PI3K/Akt/mTOR

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 : ≥ 33 mg/mL (69.69 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.1117 mL	10.5585 mL	21.1171 mL
5 mM	0.4223 mL	2.1117 mL	4.2234 mL
10 mM	0.2112 mL	1.0559 mL	2.1117 mL

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

BIOLOGICAL ACTIVITY

Description

ETP-46321 is a potent and orally bioavailable PI3Kα and PI3Kδ inhibitor with K_{iapp}s of 2.3 and 14.2 nM, respectively.

IC_{50} & Target

p110α 2.3 nM (Ki)	PI3Kα-E545K 1.77 nM (Ki)	PI3Kα-E542K 1.89 nM (Ki)	PI3Kα-H1047R 2.33 nM (Ki)
p110δ 14.2 nM (Ki)	p110β 170 nM (Ki)	p110γ 179 nM (Ki)	

In Vitro

ETP-46321 is selected to be screened against other PI3K isoforms. ETP-46321 is more potent against isoform α (K_{iapp}=2.3 nM). ETP-4632, has been profiled and shown to be a potent PI3K α and δ inhibitor, highly selective versus mTOR and 288 representative kinases. ETP-46321 is also tested against three of the p110α mutant enzymes detected in human cancers (E542K, E545K and H1047R), being equipotent against these mutants when compared to the wild type protein (K_{iapp}=2.33, 1.77 and 1.89 nM for PI3Kα-H1047R, PI3Kα-E545K and PI3Kα-E542K, respectively). ETP-46321 inhibits the phosphorilation of AKT in U2OS cell line with an IC_{50} of 8.3 nM[1].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ETP-46321, is selected for in vivo studies based on its appealing pharmacokinetic profile in BALB-C mice, low in vivo Clearance (0.6 L/h/Kg) and good oral bioavailability (90%). ETP-46321 demonstrates a good pharmacokinetic profile in mice and is selected for preliminary in vivo evaluation in a lung tumor mouse model driven by a K-RasG12V oncogenic mutation, showing significant tumor growth inhibition, and reduction of the tumor metabolic activity as measured by positron emission tomography (PET) techniques[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice[1] BALB/C mice are treated daily with ETP-46321 (50 mg/kg, p.o.) for three weeks. Tumor volumes of four mice in each treatment group are measured and compared to the starting volume at the beginning of the treatment. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Martínez González S, et al. Identification of ETP-46321, a potent and orally bioavailable PI3K α, δ inhibitor. Bioorg Med Chem Lett. 2012 May 15;22(10):3460-6.

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