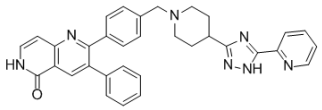
Akt1 and Akt2-IN-1

Cat. No.:	HY-50862
CAS No.:	893422-47-4
Molecular Formula:	$C_{33}H_{29}N_7O$
Molecular Weight:	539.63
Target:	Akt
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 : ≥ 35 mg/mL (64.86 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8531 mL	9.2656 mL	18.5312 mL
5 mM	0.3706 mL	1.8531 mL	3.7062 mL
10 mM	0.1853 mL	0.9266 mL	1.8531 mL

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

BIOLOGICAL ACTIVITY

Description

Akt1 and Akt2-IN-1 is an allosteric inhibitor of Akt1 (IC_{50}=3.5 nM) and Akt2 (IC_{50}=42 nM), with potent and balanced activity.

IC_{50} & Target

Akt1	Akt2
3.5 nM (IC_{50})	42 nM (IC_{50})

In Vitro

Consistent with the allosteric mode of inhibition, Akt1 and Akt2-IN-1 (Compound 17) is dependent on the PH-domain for Akt inhibition, is selective for Akt1/2 over Akt3 (IC_{50}= 1900 nM), and is highly selective over other members of the AGC family of kinases (>50 μM vs PKA, PKC, SGK). Akt1 and Akt2-IN-1 (Compound 17) has moderate activity in an hERG binding assay (IC_{50}= 5610 nM) and is a substrate for human P-glycoprotein[1].

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

In Vivo

Akt1 and Akt2-IN-1 (Compound 17) is well tolerated in at exposures that provide high levels of Akt1 and 2 inhibition in vivo. Akt1 and Akt2-IN-1 (Compound 17) has also been shown to inhibit the growth of A2780 tumors in vivo when used as monotherapy. Akt1 and Akt2-IN-1 (Compound 17) has potent inhibitory activity against Akt1 and 2 in vivo in a mouse lung

and efficacy in a tumor xenograft model. Akt1 and Akt2-IN-1 (Compound 17) shows good pharmacokinetics in rat with a low clearance of 4.6 mL/min/kg and a half-life of 3.8 h. Due to the improved cell potency, physical properties, and rodent pharmacokinetics of Akt1 and Akt2-IN-1 (Compound 17), tolerability and Akt inhibition are assessed in mice. Using an acute dosing schedule (IP dosing of 50 mg/kg at times 0, 3, and 8 h), administration of Akt1 and Akt2-IN-1 (Compound 17) is well tolerated in mice and shows high levels of Akt inhibition in mouse lung[1].

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

REFERENCES

[1]. Bilodeau MT, Allosteric inhibitors of Akt1 and Akt2: a naphthyridinone with efficacy in an A2780 tumor xenograft model. Bioorg Med Chem Lett. 2008 Jun 1;18(11):3178-82.

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