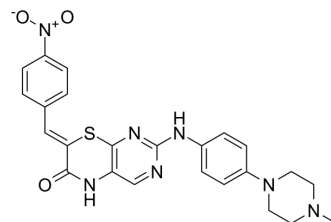


ON 146040

Cat. No.:	HY-12338
CAS No.:	1404231-34-0
Molecular Formula:	C ₂₄ H ₂₃ N ₇ O ₃ S
Molecular Weight:	489.55
Target:	PI3K; Bcr-Abl
Pathway:	PI3K/Akt/mTOR; Protein Tyrosine Kinase/RTK
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (51.07 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent		1 mg	5 mg	10 mg
	Concentration	Mass			
	1 mM		2.0427 mL	10.2135 mL	20.4269 mL
	5 mM		0.4085 mL	2.0427 mL	4.0854 mL
	10 mM		0.2043 mL	1.0213 mL	2.0427 mL

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

BIOLOGICAL ACTIVITY

Description

ON 146040 is a potent PI3K α and PI3K δ (IC₅₀~14 and 20 nM, respectively) inhibitor. ON 146040 also inhibits Abl1 (IC₅₀<150 nM).

IC₅₀ & Target

PI3K α 14 nM (IC ₅₀)	PI3K δ 20 nM (IC ₅₀)	PI3K γ 1 μ M (IC ₅₀)	PI3K β 3 μ M (IC ₅₀)
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In Vitro

In biochemical testing, ON 146040 inhibits PI3K α / PI3K δ isoforms (IC₅₀~14 and 20 nM, respectively) without having a major effect on PI3K β / PI3K γ isoforms (IC₅₀~3 and 1 μ M, respectively). ON 146040 is also found to inhibit Abl1 and several mutant versions of this kinase (IC₅₀<150 nM), although ON 146040 is not found to be active against the T315I mutant. ON 146040 represents the first dual PI3K and BCR-ABL inhibitor that targets the STAT3 and STAT5 pathways. ON 146040 disrupts the oncogenic activity of both STAT3 and STAT5 by targeting upstream activators, including PI3K α and δ isoforms as well as wild type and mutant BCR-ABL. ON 146040 is highly potent in killing hematologic tumor cells with IC₅₀ values in the 150 to 1,000 nM range. Following treatment with ON 146040, STAT3 and STAT5 phosphorylation are down-regulated in leukemia and myeloma cells^[1].

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

REFERENCES

[1]. Targeting oncogenic STAT3 and STAT5 signaling with on 146040, a small molecule inhibitor of PI3K α/δ and BCR-ABL.

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

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