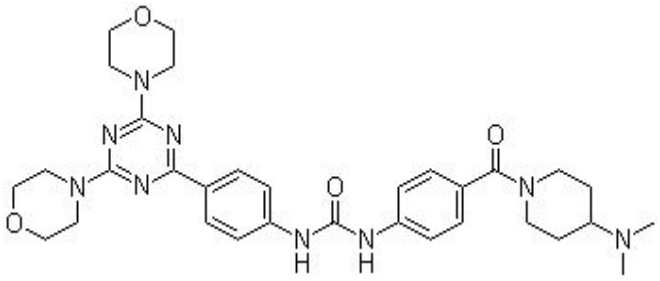
Product Introduction

PF-05212384 (PKI-587)

PKI-587 is a highly potent dual inhibitor of **PI3Kα**, PI3Kγ and mTOR with **IC50** of 0.4 nM, 5.4 nM and 1.6 nM, respectively. Phase 2.

Technical Data:

Molecular Weight (MW):	615.73	
Formula:	C32H41N9O4	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 2 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	1197160-78-3	

Biological Activity

PKI-587 shows potent inhibitory activity against PI3K-α, PI3K-γ and mTOR with IC50 of 0.4 nM, 5.4 nM and 1.6 nM, respectively. Furthermore, PKI-587 also exhibits its potency against the most frequently occurring mutant forms of PI3Kα, notably the H1047R and E545K with IC50 of 0.6 nM and 0.6 nM, respectively. [1] Correlated with suppression of phosphorylation of PI3K/mTOR signaling pathway proteins, PKI-587 causes tumor cell growth inhibition in MDA-361 and PC3-MM2 cell lines with IC50 of 4 nM and 13.1 nM, respectively. [1]

In nude mice, PKI-587 treatment at 25 mg/kg iv leads to low plasma clearance (7 (mL/min)/kg), high volume of distribution (7.2 L/kg), and long half-life, (14.4 hours). In the MDA-361 xenograft model, PKI-587 produces potent antitumor efficacy with the minimum efficacious dose (MED) of 3 mg/kg against MDA-361 tumors and maximum tolerated single dose (MTD) of 30 mg/kg. While in the H1975 (non-small-cell lung carcinoma, mutant EGFR [L858R, T790M]) xenograft model, PKI-587 at 25 mg/kg for 7 weeks results in 90% survival of the group treated. [1]

References

[1] Venkatesan AM, et al. J Med Chem. 2010, 53(6), 2636-2645.
[2] Gedaly R, et al. J Surg Res. 2011, doi.org/10.1016/j.jss.2011.10.045.

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