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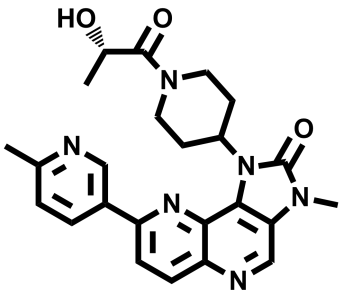
PI3K/mTOR Dual Inhibitor - PF-04979064

Chemical Name: (S)-1-(1-(2-hydroxypropanoyl)piperidin-4-yl)-3-methyl-8-(6-methylpyridin-3-yl)-1H-imidazo[4,5-c][1,5]naphthyridin-2(3H)-one



Molecular Weight:	446.50
Formula:	$C_{24}H_{26}N_6O_3$
Purity:	≥98%
CAS#:	1220699-06-8
Solubility:	DMSO up to 100 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 month -20 °C 1 year

Biological Activity:

PF-04979064 is a highly potent and orally bioavailable PI3K/mTOR dual inhibitor developed through structure-based drug design. It inhibited mTOR, PI3Kα, β, δ and γ isoforms and AKT phosphorylation with IC_{50} as 2.64 nM, 0.395 nM, 0.111 nM, 0.122 nM and 28.3 nM, respectively. PF-04979064 exhibited cellular potency with an IC_{50} of 9.1 nM in a BT20 cell assay. PF-04979064 exhibited excellent in vitro potency, very good solubility, high LipE, excellent kinome selectivity, robust PK/PD correlation and tumor growth inhibition (TGI) in a U87MG mouse xenograft model, and acceptable predicted human clearance after incorporating both CYP- and AO-mediated metabolism. PF-04979064 is the back-up candidate to PF-04691502 which is in Phase I/II clinical trials for treating solid tumors.

How to Use:

In vitro: PF-04979064 was used at 1-10 μM in vitro and in cellular assays.

In vivo: PF-04979064 was orally dosed to mice at 15-40 mg/kg once per day for two weeks.

Reference:

1. Hengmiao Cheng, et al. Discovery of the Highly Potent PI3K/mTOR Dual Inhibitor PF-04979064 through Structure-Based Drug Design. (2013) ACS Med. Chem. Lett., 4 (1), pp91-97.