PF-AKT400

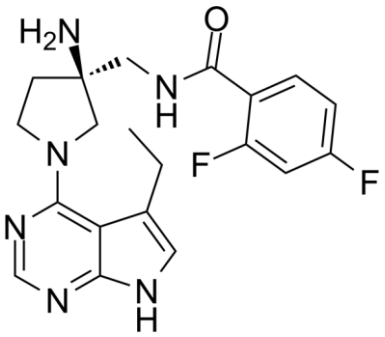
Product Code: F002697

CAS No.: 1004990-28-6

Mol. Weight: C20H22F2N6O

Mol. Formula: 400.43

Storage Temp: Powder: -20℃, 36 months; 4℃, 24 months
In solvent: -80℃, 24 months; -20℃, 12 months



Synonyms: AKT protein kinase inhibitor

Target: Akt

Pathway: PI3K/Akt/mTOR

Biological Activity

制备储备液:

质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg
1 mM	2.4973 mL	12.4866 mL	24.9732 mL
5 mM	0.4995 mL	2.4973 mL	4.9946 mL
10 mM	0.2497 mL	1.2487 mL	2.4973 mL

Bioactive: PF-AKT400 is a broadly selective, potent, ATP-competitive Akt inhibitor, displays 900-fold greater selectivity for PKBα (IC50=0.5 nM) than PKA (IC50=450 nM).

In Vivo: PF-AKT400 is subsequently evaluated for modulation of Akt in tumors and in multiple in vivo mouse models of antitumor efficacy. It is active in a PC3 prostate carcinoma xenograft experiment, with 75% TGI observed at 100 mg/kg b.i.d. dosing for 10 days. In a colorectal carcinoma (Colo205) xenograft study, PF-AKT400 produces 60% TGI at 150 mg/kg b.i.d. after 10 days. Most intriguingly, in combination with Rapamycin (10 mg/kg, ip), 75

mg/kg b.i.d. (10 days) of PF-AKT400 results in 98% TGI in an additional PC3 prostate carcinoma xenograft study compared to 56% TGI and 66% TGI with PF-AKT400 and Rapamycin as single agents. To define the in vivo potency of PF-AKT400 (Compound 42) in the PC3 xenograft model, oral administration of 25, 75, and 100 mg/kg PF-AKT400 is performed with blood and tumor sampling over time. Immunoblot analysis of detergent-soluble extracts derived from PC3 tumors shows a significant reduction of S6 phosphorylation, and hyperphosphorylation of Akt upon treatment at doses that produced significant tumor growth inhibition. Plasma drug concentrations peak rapidly after oral administration of doses between 25-100 mg/kg (Tmax=0.5 h). Peak PD responses of phospho-S6 and phospho-Akt are observed at approximately 2-4h and 1h post-administration of PF-AKT400, respectively. The time-course of PD marker response is well described by a PK/PD model at doses that ranged from no efficacy (25 mg/kg) to maximal efficacy (100 mg/kg).

In Vitro: PF-AKT400 (Compound 42) provides significantly enhanced selectivity for Akt relative to earlier leads such as spiroindoline 2. Free IC50 and EC50 values are estimated for phospho-S6 reduction (110 nM) and Akt hyperphosphorylation (216 nM), respectively. These values corresponded well to the cellular IC50 for PF-AKT400 in U87 cells measuring p-GSK-3α (310 nM).