

PRN1371

Chemical Properties

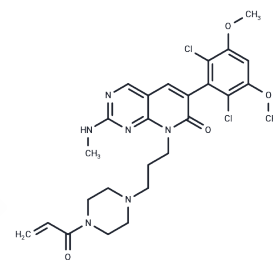
CAS No. : 1802929-43-6

Formula: C₂₆H₃₀Cl₂N₆O₄

Molecular Weight: 561.46

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Actual storage temperature shall be subject to the COA.



Biological Description

Description	PRN1371 is a specific and potent FGFR1-4 and CSF1R inhibitor (IC ₅₀ s: 0.6/1.3/4.1/19.3/8.1 nM for FGFR1/2/3/4 and CSF1R).
Targets(IC ₅₀)	c-Fms,FGFR,CSF-1R
In vitro	PRN1371 exhibits high biochemical and cellular potency (FGFR1 IC ₅₀ : 0.6 nM, SNU16 IC ₅₀ : 2.6 nM), sustained target engagement (FGFR1 occupancy 24 h = 96%), less than 30% hERG inhibition at 1 μM, and favorable predicted ADME stability with BME reactivity K _d > 100 μM.
In vivo	In PK studies of rat, dog, and cynomolgus monkey, PRN1371 show rapid iv clearance in all species. PRN1371 shows rapid clearance (Cl=160 mL per min per kg), yet dosing p.o (20 mg/kg) demonstrates high oral exposure (AUC=4348 h·ng/mL) and a reasonable half-life (t _{1/2} =3.8 h). Low levels of pFGFR2 confirm the ability of PRN1371 to block FGFR2 activity in tumor tissue. PRN1371 induces a dose-dependent reduction in tumor volume and up to 68% tumor growth inhibition at the highest dose of 10 mg/kg b.i.d. following 27 days of treatment. All doses are well tolerated with no significant bodyweight loss.

Solubility Information

Solubility	DMSO: 12 mg/mL (21.37 mM),Sonication and heating are recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.56 mM),Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.7811 mL	8.9054 mL	17.8107 mL
5 mM	0.3562 mL	1.7811 mL	3.5621 mL
10 mM	0.1781 mL	0.8905 mL	1.7811 mL
50 mM	0.0356 mL	0.1781 mL	0.3562 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Brameld KA, et al. Discovery of the Irreversible Covalent FGFR Inhibitor 8-(3-(4-Acryloylpiperazin-1-yl)propyl)-6-(2,6-dichloro-3,5-dimethoxyphenyl)-2-(methylamino)pyrido[2,3-d]pyrimidin-7(8H)-one (PRN1371) for the Treatment of Solid Tumors. *J Med Chem.* 2017 Aug 10;60(15):6516-6527.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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