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p21-Activated Kinase Inhibitor II, PF-3758309 - CAS 898044-15-0 - Calbiochem

Art. ID SAF-5006130001

Unit EA

Description

A cell-permeable pyrrolopyrazole that acts as a potent inhibitor against p21-activated kinases (Ki in nM/[ATP] in &#181,M = 13.7/200, 18.7/40, 18.1/80. 17.1/72, respectively, in PAK1, PAK4, PAK5, PAK6 kinase assays, IC50 = 190 and 99 nM against PAK1 and PAK3, respectively) by directly targeting the kinase ATP-binding site in a reversible manner (Kd = 4.5 nM using rhPAK4300-591 kinase domain). Inhibits PAK4-dependent cellular signaling (IC50 = 24.2 nM against TNFalpha-stimulated NF-kappaB activity in HEK293T) and proliferation (IC50 = 0.24 and 27 nM, respectively, against HCT116 and A549 colonies formation) in vitro and the growth of human tumors in nude mice in vivo (10 to 25 mg/kg, b.i.d. p.o).Please note that the molecular weight for this compound is batch-specific due to variable water content. Please refer to the vial label or the certificate of analysis for the batch-specific molecular weight. The molecular weight provided represents the baseline molecular weight without water., A cell-permeable pyrrolopyrazole that acts as a potent inhibitor against p21-activated kinases (Ki in nM/[ATP] in &#181,M = 13.7/200, 18.7/40, 18.1/80. 17.1/72, respectively, in PAK1, PAK4, PAK5, PAK6 in vitro kinase assays, IC50 = 190 and 99 nM against PAK1 and PAK3, respectively) and potently inhibits cellular PAK4-mediated GEF-H1 Ser810 phosphoryation (IC50 = 1.3 nM using HEK293-derived TR-293-KDG cells) by directly targeting the kinase ATP-binding site in a reversible manner (Kd = 4.5 nM, koff = 0.010/s, t1/2 = 68 s, by SPR using rhPAK4300-591 kinase domain). PF-3758309 is expected to inhibit cellular AMPK and RSK2 activity only at much higher concentrations (estimated IC50 = 40 nM and 171 nM, respectively, assuming cellular [ATP] = 2 mM) and exhibit even less potency toward 144 other cellular kinases when administered at effective concentration range for cellular PAK1/4/5/6 inhibition. In addition to inhibiting PAK4-dependent cellular signaling (IC50 = 24.2 nM against 20 ng/mL TNFalpha-stimulated NF-kappaB reporter transcription in HEK293T) and proliferation (IC50 = 0.24 and 27 nM, respectively, against HCT116 and A549 colonies formation) in cultures in vitro, PF-3758309 is also reported to effectively inhibit human tumor growth in nude mice in vivo (% inhibition/tumor/BID p.o. dosage in mg/kg = 97%/HCT116/20, 106%/Colo205/20, 89%/MDA-MB231/20, 71%/A549/10, 85%/M24met/25).

Text/Information	Analyte/Parameter	CAS number	Concentration/Value	Unit	Method	Source
	PF-3758309	[898044-15-0]				