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产品名称：KRCA-0008
产品别名：KRCA-0008

生物活性：	
Description	KRCA-0008 is a potent and selective ALK/Ack1 inhibitor with IC50 of 12 nM/4 nM for ALK and Ack1 respectively; displays drug-like properties without hERG liability. IC50 value: 12 nM/4 nM(ALK/Ack1) [1] Target: ALK/Ack1 inhibitor KRCA-0008 retains good drug-like properties: good water-solubility (54 μM in 5% DMSO–water, 150 μM in 5% DMSO–PBS buffer) with moderate plasma protein binding (93% in rat) and low brain exposure (Cbrain/Cplasma = ～0.02). It has good liver microsomal stability (% remaining after 30 min: 52% in mouse, 89% in rat, 72% in human) and little to no CYP inhibition (1A2, 2C9, 2D6, 3A4 @ 10 μM). It does not appear to cause hERG blockade (patch clamp IC50 = 30 μM) and is negative on Ames test (1000 μg/plate), chromosomal aberration assay and micronucleus assay. KRCA-0008 also shows promising pharmacokinetic parameters in both mice and rat (oral bioavailability = 66–94.5%). KRCA-0008 shows a modest tumor growth inhibition in vivo activity in H3122 human lung cancer bearing mice model comparable to Crizotinib without significant body weight change. It is important to mention the KRCA-0008 25 mpk and 50 mpk groups did not show dose-dependent tumor growth inhibition.
Solvent&Solubility	***In Vitro:*** **H_2O : < 0.1 mg/mL** (insoluble)
References	[1]. Park CH, et al. Novel bis-ortho-alkoxy-para-piperazinesubstituted-2,4-dianilinopyrimidines (KRCA-0008) as potent and selective ALK inhibitors for anticancer treatment. Bioorg Med Chem Lett. 2013 Nov 15;23(22):6192-6.