

Product Data Sheet

Product Name: KRCA 0008

Cat. No.: GC13902

Chemical Properties

Cas. No. 1472795-20-2

Chemical Name (E)-1-(4-(4-((2-((4-(4-acetylpiperazin-1-yl)-2-methoxyphenyl)amino)-5-chloropyrimidin-4(3H)-ylidene)amino)-3-methoxyphenyl)piperazin-1-yl)ethanone

SMILES CC(N1CCN(C2=CC(OC)=C(/N=C(N3)\C(Cl)=CN=C3NC4=C(OC)C=C(N5CCN(C(C)=O)CC5)C=C4)C=C2)CC1)=O

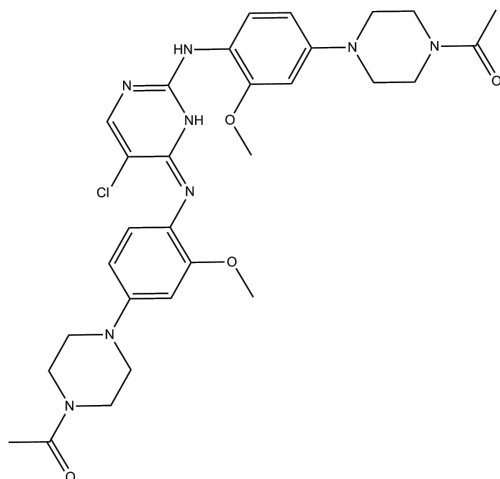
Formula $C_{30}H_{37}ClN_8O_4$ M.Wt 609.12

Solubility Soluble in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Background

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

Caution: Product has not been fully validated for medical applications. For research use only.

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(93% in rat) and low brain exposure ($C_{\text{brain}}/C_{\text{plasma}} = \sim 0.02$). 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 $\text{IC}_{50} = 30$ μM) and is negative on Ames test (1000 $\mu\text{g}/\text{plate}$), 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.

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.

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