

Product Data Sheet

Product Name: KIRA6
Cat. No.: GC19212

Chemical Properties

Cas. No. 1589527-65-0

SMILES O=C(NC1=CC=CC(C(F)(F)F)=C1)NC2=C3C=CC=CC3=C(C4=C5C(N)=NC=CN5C(C(C)(C)C)=N4)C=C2

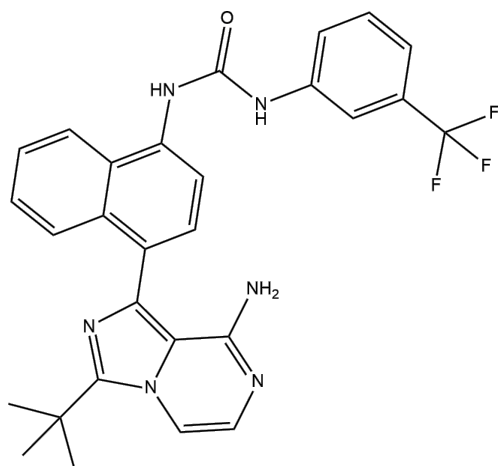
Formula C28H25F3N6O M.Wt 518.53

Solubility DMSO : ≥ 5 mg/mL (9.64 mM); Ethanol : 2 mg/mL (3.86 mM) 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

KIRA6 allosterically inhibits IRE1α RNase kinase activity with an IC₅₀ of 0.6 μM.

KIRA6 dose-dependently inhibits IRE1α (WT) kinase activity, XBP1 RNA cleavage, Ins2 RNA cleavage and oligomerization. KIRA6 strongly inhibits JNK phosphorylation from IRE1α hyperactivation or ER stress. Also, KIRA6 dose-dependently inhibits Ins1 mRNA decay, proinsulin depletion, and apoptosis from IRE1α hyperactivation. In INS-1 cells, KIRA6 inhibits IRE1α auto-

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

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phosphorylation by Tg and XBP1 mRNA splicing by Tm in a dose-dependent manner. KIRA6 reduces ER stress-induced death of cultured cells and in pancreatic islet explants[1].

KIRA6 has negligible toxicity up to 10 μ M, providing a favorable therapeutic index to test cytoprotection. KIRA6 in BALB/c mice intraperitoneally (i.p.) dosed at 10 mg/kg shows good drug plasma AUC levels with moderate clearance (22.4 mL/min/kg). Drug half-life is 3.90 hours, Cmax is 3.3 μ M, and plasma levels at 4 and 8hr are 1.2 μ M and 0.33 μ M, respectively. Intravitreal co-injection of KIRA6 with Tm significantly reduces XBP1 splicing, TXNIP induction, and decay of the ER-localized photoreceptor-specific Rhodopsin mRNA. KIRA6 dose-dependently inhibits Rhodopsin RNA cleavage by IRE1 α . Concomitant with blockage of Terminal UPR outputs, co-injection of KIRA6 in the Tm model reduces photoreceptor loss by Optical Coherence Tomography (OCT) and histology. KIRA6 substantially protects against loss of ERG responsiveness, significantly preserving both a- and b-wave amplitudes[1].

References:

[1]. Ghosh R, et al. Allosteric inhibition of the IRE1 α RNase preserves cell viability and function during endoplasmic reticulum stress. *Cell*. 2014 Jul 31;158(3):534-48.

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