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Zuschläge

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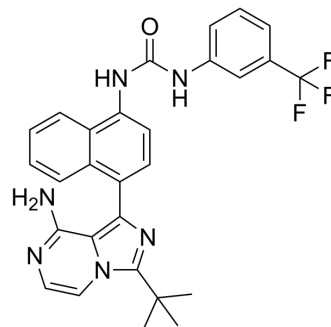
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KIRA6

Cat. No.:	HY-19708
CAS No.:	1589527-65-0
Molecular Formula:	C ₂₈ H ₂₅ F ₃ N ₆ O
Molecular Weight:	518.53
Target:	IRE1
Pathway:	Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months



SOLVENT & SOLUBILITY

In Vitro	DMSO : 25 mg/mL (48.21 mM; Need ultrasonic)				
	Preparing Stock Solutions	Solvent Concentration Mass	1 mg	5 mg	10 mg
		1 mM	1.9285 mL	9.6426 mL	19.2853 mL
		5 mM	0.3857 mL	1.9285 mL	3.8571 mL
		10 mM	0.1929 mL	0.9643 mL	1.9285 mL
Please refer to the solubility information to select the appropriate solvent.					
In Vivo	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 0.5 mg/mL (0.96 mM); Clear solution				
	2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 0.5 mg/mL (0.96 mM); Clear solution				
	3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 0.5 mg/mL (0.96 mM); Clear solution				

BIOLOGICAL ACTIVITY

Description	KIRA6 is an advanced small-molecule IRE1α RNase kinase inhibitor with an IC ₅₀ of 0.6 μM ^[2] . KIRA6 can trigger an apoptotic response ^[1] .
IC ₅₀ & Target	IC ₅₀ : 0.6 μM (IRE1α RNase kinase) ^[2]
In Vitro	KIRA6 (1nM-100μM) binds to the cytoplasmic domain of KIT with a K_d value of 10.8 μM^[1]. KIRA6 (10-1000 nM; 72 hours) strongly compromises the viability of the KIT-dependent cell line HMC-1.1 at the low nM

concentration, in a manner that coincided with KIT blockade^[1].

KIRA6 (10-1000 nM; 1 hour) reduces signaling output of KIT, including the phosphorylation of KIT as well as its downstream signaling modules, PSTAT5 and phosphorylated ERK1/2^[1].

KIRA6 (1 μ M; 0-48 hours) inhibits Ins1 mRNA decay from IRE1 α hyperactivation at a dose-dependent manner^[2].

KIRA6 (0.1-10 μ M; 72 hours) dose-dependently reduces 1NM-PP1 potentiation of Ins1 apoptosis during ER stress in a dose-dependent manner^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay^[1]

Cell Line:	HMC-1.1 cells
Concentration:	10 nM, 30 nM, 100 nM, 300 nM, 1000 nM
Incubation Time:	72 hours
Result:	Inhibited cell viability from 30 nM.

Western Blot Analysis^[1]

Cell Line:	HMC-1.1 cells
Concentration:	10 nM, 30 nM, 100 nM, 300 nM, 1000 nM
Incubation Time:	1 hours
Result:	Reduced expression of phosphorylated KIT, STAT5 and ERK1/2.

RT-PCR^[2]

Cell Line:	INS-1 IRE1 α (WT) cells
Concentration:	1 μ M
Incubation Time:	0 hour, 12 hours, 24 hours, 48 hours
Result:	Inhibited Ins1 mRNA expression.

Apoptosis Analysis^[2]

Cell Line:	INS-1 IRE1 α (WT) cells
Concentration:	1-10 μ M
Incubation Time:	72 hours
Result:	Reduced 1NM-PP1 potentiation of Ins1 apoptosis during ER stress.

In Vivo

KIRA6 (intraperitoneal injection; 5 mg/kg; 37 days) shows significant amelioration of random glucose levels over several weeks compared to vehicle, both fed ad lib^[2].

KIRA6 (intraperitoneal injection; 5 mg/kg; 21 or 18 days postinjections) increases both plasma insulin and C-peptide levels, remains insulin-positive islet areas at high level after stopping injections in the Akita Mouse^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Ins2+/Akita mice ^[2]
Dosage:	5 mg/kg

Administration:	Intraperitoneal injection; 5 mg/kg; 21 or 18 days postinjections
Result:	Attenuates b cell functional loss, increased insulin levels.

CUSTOMER VALIDATION

- Science. 2019 Jul 19;365(6450):eaau6499.
- ACS Cent Sci. 2020 Jan 22;6(1):76-82.
- Nano Today. April 2022, 101416.
- ACS Nano. 2021 Aug 20.
- Nat Commun. 2024 Jan 2;15(1):72.

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REFERENCES

- [1]. Mahameed M, et al. The unfolded protein response modulators GSK2606414 and KIRA6 are potent KIT inhibitors. Cell Death Dis. 2019 Apr 1;10(4):300.
- [2]. 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.

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

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