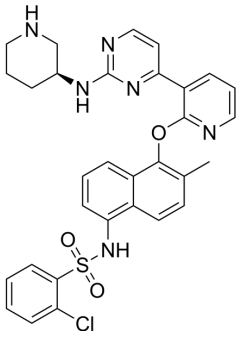
Kira8

Cat. No.:	HY-114368
CAS No.:	1630086-20-2
Molecular Formula:	$C_{31}H_{29}ClN_6O_3S$
Molecular Weight:	601.12
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

Ethanol : 76.92 mg/mL (127.96 mM; ultrasonic and adjust pH to 5 with HCl)

DMSO : 65 mg/mL (108.13 mM; Need ultrasonic)

H_2O : 30 mg/mL (49.91 mM; ultrasonic and warming and adjust pH to 2 with HCl and heat to 60°C)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.6636 mL	8.3178 mL	16.6356 mL
5 mM	0.3327 mL	1.6636 mL	3.3271 mL
10 mM	0.1664 mL	0.8318 mL	1.6636 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 4 mg/mL (6.65 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 3% ethanol, 7% Tween-80, and 90% normal saline
   Solubility: ≥ 2.31 mg/mL (3.84 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.17 mg/mL (3.61 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.17 mg/mL (3.61 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Kira8 (AMG-18) is a mono-selective IRE1α inhibitor that allosterically attenuates IRE1α RNase activity with an IC_{50} of 5.9 nM[1].

IC_{50} & Target	IRE1α[1] IC50: 5.9 nM (IRE1α RNase)[1]
In Vitro	Kira8 blocks IRE1α oligomerization, and potently inhibits IRE1α RNase activity against XBP1 and Ins2 RNAs. Kira8 more potently reduces IRE1α-driven apoptosis in INS-1 cells than KIRA6 and also reverses XBP1 splicing promoted by GNF-2[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Male $Ins2^{+/Akita}$ mice are injected i.p. with KIRA8 (50 mg/kg; daily; for 35 days), significant reduction of hyperglycemia become apparent over several weeks[1]. ?One week treatment of pre-diabetic NODs mice with Kira8 (50 mg/kg; i.p.; once a day) leads to significant reductions in islet XBP1 splicing and TXNIP mRNAs, and preserves Ins1/Ins2, BiP and MANF mRNAs[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male $Ins2^{+/Akita}$ mice[1]
Dosage:	50 mg/kg
Administration:	Injected i.p.; daily; for 35 days
Result:	Significant reduction of hyperglycemia became apparent over several weeks.

CUSTOMER VALIDATION

- Nucleic Acids Res. 2023 Feb 11;gkad077.
- NPJ Parkinsons Dis. 2023 Mar 7;9(1):35.
- Int J Mol Sci. 2022, 23(16), 9000.
- Am J Physiol Lung Cell Mol Physiol. 2021 Jul 28.
- Arch Biochem Biophys. 2023 Feb 22;109552.

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REFERENCES

[1]. Morita S, et al. Targeting ABL-IRE1α Signaling Spares ER-Stressed Pancreatic β Cells to Reverse Autoimmune Diabetes. Cell Metab. 2017 Apr 4;25(4):883-897.e8.

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