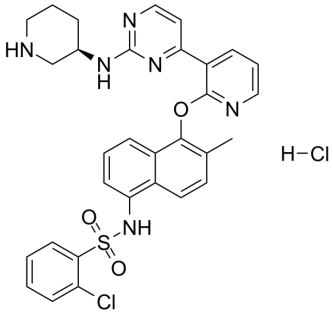
Kira8 Hydrochloride

Cat. No.:	HY-114368A
CAS No.:	2250019-92-0
Molecular Formula:	$C_{31}H_{30}Cl_2N_6O_3S$
Molecular Weight:	637.58
Target:	IRE1
Pathway:	Cell Cycle/DNA Damage
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Kira8 Hydrochloride (AMG-18 Hydrochloride) 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

- Am J Physiol Lung Cell Mol Physiol. 2021 Jul 28.
- bioRxiv. 2020 Apr.

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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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