

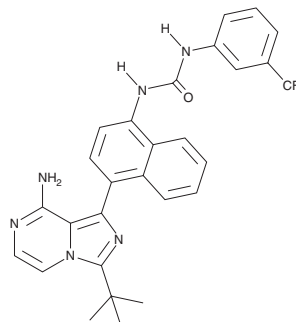
PRODUCT INFORMATION



KIRA6

Item No. 19151

CAS Registry No.: 1589527-65-0
Formal Name: N-[4-[8-amino-3-(1,1-dimethylethyl)imidazo[1,5-a]pyrazin-1-yl]-1-naphthalenyl]-N'-[3-(trifluoromethyl)phenyl]-urea
Synonyms: IRE1 Inhibitor IV, IRE1 α Kinase Inhibiting RNase Attenuator
MF: C₂₈H₂₅F₃N₆O
FW: 518.5
Purity: \geq 98%
UV/Vis.: λ_{max} : 228, 292, 330 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: As supplied, 2 years from the QC date provided on the Certificate of Analysis, when stored properly



Laboratory Procedures

KIRA6 is supplied as a crystalline solid. A stock solution may be made by dissolving the KIRA6 in the solvent of choice. KIRA6 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of KIRA6 in these solvents is approximately 5, 20, and 15 mg/ml, respectively.

KIRA6 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, KIRA6 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. KIRA6 has a solubility of approximately 0.3 mg/ml in a 1:2 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

The IRE1 pathway is a component of the unfolded protein response that senses unfolded proteins *via* an ER luminal domain that becomes oligomerized during stress. It is associated with promoting cell survival through the activity of the IRE1 α RNase, whose activity upregulates proteins that enhance ER protein folding and quality control. However, under high ER stress, the IRE1 α RNase becomes hyperactive and is less discriminant in its substrate specificity, endonucleolytically cleaving many additional mRNAs that localize to the ER membrane, leading to cell proliferation blocks, inflammation, and apoptosis. KIRA6 is an ATP-competitive IRE1 α kinase inhibiting RNase attenuator (KIRA) that allosterically inhibits IRE1 α RNase kinase activity (IC₅₀ = 0.6 μ M) and prevents oligomerization.¹ It has been shown to inhibit IRE1 α *in vivo* and to promote cell survival under ER stress.¹ At 20 μ g/ml, KIRA6 is reported to preserve photoreceptor functional viability in rat models of ER stress-induced retinal degeneration.¹ At 5 mg/kg, it has also been shown to preserve pancreatic β cells, increase insulin, and reduce hyperglycemia in Akita diabetic mice.¹

Reference

1. Ghosh, R., Likun, W., Wang, E.S., *et al.* Allosteric inhibition of the IRE1 α RNase preserves cell viability and function during endoplasmic reticulum stress. *Cell* **158**(3), 534-548 (2014).

WARNING
THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA
This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

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