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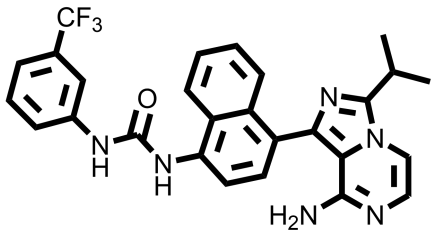
# IRE-3 --- IRE1a Modulator

**Chemical Name:** 1-(4-(8-amino-3-isopropylimidazo[1,5-a]pyrazin-1-yl)naphthalen-1-yl)-3-(3-(trifluoromethyl)phenyl)urea



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|---|---|
| Molecular Weight: | 504.51 |
| Formula: | $C_{27}H_{23}F_3N_6O$ |
| Purity: | ≥98% |
| CAS#: | 1414938-21-8 |
| Solubility: | DMSO up to 50 mM |
| Storage | Powder: 4 °C 1 year<br>DMSO: 4 °C 3 months<br>-20 °C 1 year |

**Biological Activity:**

IRE-3 is a highly potent and selective small molecule modulator of IRE1α. Under endoplasmic reticulum stress, unfolded protein accumulation leads to activation of the endoplasmic reticulum transmembrane kinase/endoRNase (RNase) IRE1α. IRE1α oligomerizes, autophosphorylates and initiates splicing of XBP1 mRNA, thus triggering the unfolded protein response (UPR). Interestingly, IRE-3 inhibits the XBP1 mRNA splicing through binding to the IRE1α ATP-binding site, even under endoplasmic reticulum stress. It shows dose-dependent reduction of IRE1α kinase autophosphorylation in vitro with $IC_{50}$ ~3.12 μM. IRE-3 can also block enzymatic activities of IRE1α in INS-1 rat insulinoma cell lines. As dysregulation of the UPR has been implicated in a variety of cell degenerative and neoplastic disorders, small molecule modulators of IRE1α, such as IRE-3 and APY-29, serve as useful tools to understand the UPR's role in pathophysiology and to develop drugs for endoplasmic reticulum stress-related diseases.

**How to Use:**

**In vitro:** IRE-3 was used at 10-20 μM in vitro and in cellular assays.

**In vivo:**

**Reference:**

1. Wang L, et al. Divergent allosteric control of the IRE1α endoribonuclease using kinase inhibitors. (2012) Nat Chem Biol. 8(12):982-9.