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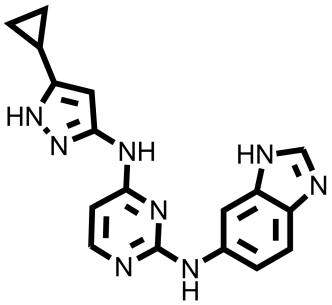
IRE1a Modulator – APY29

Chemical Name: N2-(1H-benzo[d]imidazol-6-yl)-N4-(5-cyclopropyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine



Molecular Weight:	332.36
Formula:	$C_{17}H_{16}N_8$
Purity:	≥98%
CAS#:	1216665-49-4
Solubility:	DMSO up to 100 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

APY29 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, APY29 occupies IRE1α's kinase ATP-binding site to activate RNase-mediated XBP1 mRNA splicing even without upstream endoplasmic reticulum stress. It dose-dependently reduces IRE1α kinase autophosphorylation in vitro with IC_{50}~0.28 μM. As dysregulation of the UPR has been implicated in a variety of cell degenerative and neoplastic disorders, small molecule modulators of IRE1α, such as APY29, 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: APY29 was used at 2-20 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.
2. Korennykh AV, et al. The unfolded protein response signals through high-order assembly of Ire1. (2009) Nature. 457(7230):687-93.