

244 IRE1 α /IRE1 β Inhibitor

► Asset Overview

Product Type	Small molecule
Indication	Oncology, Immunology, Metabolic diseases etc.
Current Stage	Preclinical
Target(MoA)	IRE1 α /IRE1 β inhibitor
Brief Description	<ul style="list-style-type: none"> • Since activation of the unfolded protein response (UPR) via IRE1α and/or IRE1β kinase promotes key cellular response to endoplasmic reticulum (ER) stress, inhibition of IRE1α/IRE1β activity has critical therapeutic implications in various UPR related and cell-degenerative diseases such as diabetes, cancer, fibrosis, asthma, and retinitis pigmentosa.. • A novel series of compounds for selectively regulating IRE1α or IRE1β activity were identified. • Potent, selective and orally bioavailable IRE1α/IRE1β inhibitors.
Organization	University of California, San Francisco

► Differentiation

□ IRE1 α /IRE1 β kinase inhibitor with good druggability

- IRE1 α /IRE1 β inhibitors: poor oral bioavailability, solubility, and physiochemical characteristics
- These compounds have the following advantages: equipotent and selective to existing IRE1 α /IRE1 β kinase inhibitors, increased oral bioavailability, increased solubility, permeability and absorption, metabolically stable series of compounds

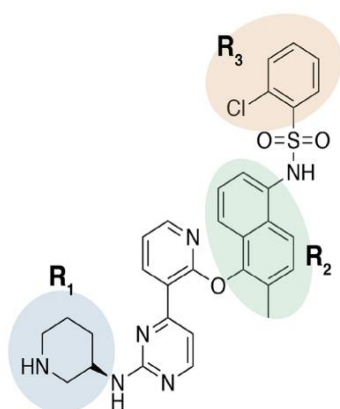
□ IRE1 α inhibitors are developed for cancers

- The dual kinase endoribonuclease IRE1 is a master regulator of cell fate decisions in cells experiencing endoplasmic reticulum (ER) stress
- In mammalian cells, there are two paralogs of IRE1: IRE1 α and IRE1 β . While IRE1 α has been extensively studied, much less is understood about IRE1 β and its role in signaling
- IRE1 α , a central enzyme in the ER stress-response signaling pathway activates the normally dormant XBP1 protein. Persistent IRE1 α -XBP1 signaling in innate immune cells in the tumor microenvironment has been shown to disrupt the immune system's ability to fight cancer in several ways: Disabling DCs' ability to activate cancer-fighting T cells / Causing macrophages to promote tumor cell metastases / Increasing regulatory T cells that suppress the immune system
- IRE1 α inhibitor (Quentis therapeutics): small molecule, preclinical for cancer (planned to initiate phase I in 2019)
- MCK-8866 (MannKind): IRE1 α inhibitor, small molecule, preclinical for TNBC

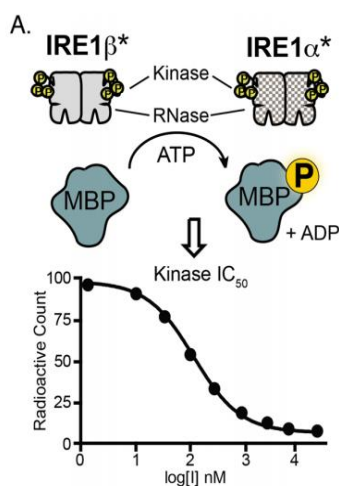
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► Key Data

IRE1 RNase & kinase inhibition by KIRA-1



1	IRE1 α *	IRE1 β *	IRE1 α Selectivity
RNase IC ₅₀	5.0 ± 2.3 nM	55 ± 5 nM	11-fold



244 IRE1 α /IRE1 β Inhibitor

► Intellectual Property

Patent No.	
Application Date	
Status	
Country	

► Contact Information

Contact Person	Priya Ramu
Email	priya.ramu@ucsf.edu
URL	https://techtransfer.universityofcalifornia.edu/NCD/29893.html