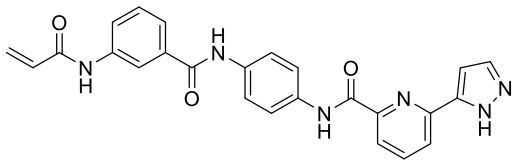
Product data sheet

MedKoo Cat#: 535214 Name: JH-X-119-01 CAS#: 2227368-54-7 (free base) Chemical Formula: $C_{25}H_{20}N_6O_3$ Exact Mass: 452.1597 Molecular Weight: 452.474	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.



1. Product description:
Jh-X-119-01 is a novel potent and selective interleukin-1 receptor-associated kinases 1 (IRAK1) inhibitor. JH-X-119-01 irreversibly labels IRAK1 at C302. This compound exhibited cytotoxic activity at single digit micromolar concentrations in a panel of WM, DLBCL, and lymphoma cell lines expressing MYD88. Cotreatment of JH-X-119-01 with the BTK inhibitor ibrutinib resulted in synergistic killing effects in these systems.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.21 mL	11.05 mL	22.10 mL
5 mM	0.44 mL	2.21 mL	4.42 mL
10 mM	0.22 mL	1.11 mL	2.21 mL
50 mM	0.04 mL	0.22 mL	0.44 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

Hatcher JM, Yang G, Wang L, Ficarro SB, Buhrlage S, Wu H, Marto JA, Treon SP, Gray NS. Discovery of a Selective, Covalent IRAK1 Inhibitor with Antiproliferative Activity in MYD88 Mutated B-Cell Lymphoma. ACS Med Chem Lett. 2020 Oct 9;11(11):2238-2243. doi: 10.1021/acsmedchemlett.0c00378. PMID: 33214835; PMCID: PMC7667833.

In vivo study

Pan B, Gao J, Chen W, Liu C, Shang L, Xu M, Fu C, Zhu S, Niu M, Xu K. Selective inhibition of interleukin-1 receptor-associated kinase 1 ameliorates lipopolysaccharide-induced sepsis in mice. Int Immunopharmacol. 2020 Aug;85:106597. doi: 10.1016/j.intimp.2020.106597. Epub 2020 May 13. PMID: 32422509.

7. Bioactivity
Biological target:

IRAK1

Product data sheet

In vitro activity

The discovery of a highly potent and selective covalent inhibitor of IRAK1, JH-X-119-01 was reported. Intact protein MS labeling studies confirmed that JH-X-119-01 irreversibly labels IRAK1 at C302. This compound exhibited cytotoxic activity at single digit micromolar concentrations in a panel of WM, DLBCL, and lymphoma cell lines expressing MYD88. Cotreatment of JH-X-119-01 with the BTK inhibitor ibrutinib resulted in synergistic killing effects in these systems. Taken together, JH-X-119-01 represents a highly selective probe of IRAK1 for further development.

Reference: Hatcher JM, Yang G, Wang L, Ficarro SB, Buhrlage S, Wu H, Marto JA, Treon SP, Gray NS. Discovery of a Selective, Covalent IRAK1 Inhibitor with Antiproliferative Activity in MYD88 Mutated B-Cell Lymphoma. ACS Med Chem Lett. 2020 Oct 9;11(11):2238-2243. doi: 10.1021/acsmedchemlett.0c00378. PMID: 33214835; PMCID: PMC7667833.

In vivo activity

Jh-X-119-01 selectively inhibited IRAK1 phosphorylation comparing with a non-selective IRAK1/4 inhibitor which simultaneously inhibited phosphorylation of IRAK1 and IRAK4. Both Jh-X-119-01 and IRAK1/4 inhibitor increased survival of septic mice, but Jh-X-119-01-treated mice had higher blood CD11b+ cell counts than IRAK1/4 inhibitor-treated ones [24 h: (1.18 ± 0.26) × 106/ml vs. (0.79 ± 0.20) × 106/ml, p = 0.001; 48 h: (1.00 ± 0.30) × 106/ml vs. (0.67 ± 0.23) × 106/ml, p = 0.042]. IRAK1/4 inhibitor induced more apoptosis of macrophages than Jh-X-119-01 did in vitro. IRAK1/4 inhibitor decreased protein levels of anti-apoptotic BCL-2 and MCL-1 in RAW 264.7 and THP-1 cells, an effect not seen in Jh-X-119-01-treated cells. In conclusion, Jh-X-119-01 selectively inhibited activation of IRAK1 and protected mice from LPS-induced sepsis. Jh-X-119-01 showed less toxicity on macrophages comparing with a non-selective IRAK1/4 inhibitor.

Reference: Pan B, Gao J, Chen W, Liu C, Shang L, Xu M, Fu C, Zhu S, Niu M, Xu K. Selective inhibition of interleukin-1 receptor-associated kinase 1 ameliorates lipopolysaccharide-induced sepsis in mice. Int Immunopharmacol. 2020 Aug;85:106597. doi: 10.1016/j.intimp.2020.106597. Epub 2020 May 13. PMID: 32422509.

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.