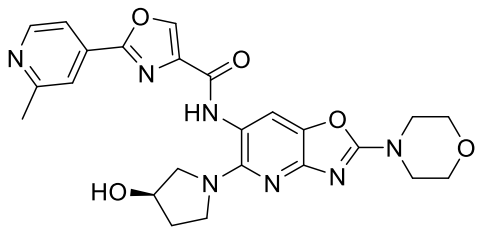
Product data sheet

MedKoo Cat#: 462493 Name: Emavusertib CAS#: 1801344-14-8 Chemical Formula: $C_{24}H_{25}N_7O_5$ Exact Mass: 491.1917 Molecular Weight: 491.508	
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:
Emavusertib, also known as CA-4948 is a potent IRAK4/FLT3 inhibitor with anti-tumor activity. CA-4948 demonstrated good cellular activity in ABC DLBCL and AML cell lines. CA-4948 demonstrated moderate to high selectivity in a panel of 329 kinases as well as exhibited desirable ADME and PK profiles including good oral bioavailability in mice, rat, and dog and showed >90% tumor growth inhibition in relevant tumor models with excellent correlation with in vivo PD modulation.

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
DMSO	38.39	78.11
Ethanol	2.0	4.07

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.03 mL	10.17 mL	20.35 mL
5 mM	0.41 mL	2.03 mL	4.07 mL
10 mM	0.20 mL	1.02 mL	2.03 mL
50 mM	0.04 mL	0.20 mL	0.41 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

1. Gummadi VR, Boruah A, Ainan BR, Vare BR, Manda S, Gondle HP, Kumar SN, Mukherjee S, Gore ST, Krishnamurthy NR, Marappan S, Nayak SS, Nellore K, Balasubramanian WR, Bhumireddy A, Giri S, Gopinath S, Samiulla DS, Daginakatte G, Basavaraju A, Chelur S, Eswarappa R, Belliappa C, Subramanya HS, Booher RN, Ramachandra M, Samajdar S. Discovery of CA-4948, an Orally Bioavailable IRAK4 Inhibitor for Treatment of Hematologic Malignancies. ACS Med Chem Lett. 2020 Oct 14;11(12):2374-2381. doi: 10.1021/acsmedchemlett.0c00255. PMID: 33335659; PMCID: PMC7734642.
2. Zhang Y, Chen X, Wang H, Gordon-Mitchell S, Sahu S, Bhagat TD, Choudhary G, Aluri S, Pradhan K, Sahu P, Carbajal M, Zhang H, Agarwal B, Shastri A, Martell R, Starczynowski D, Steidl U, Maitra A, Verma A. Innate immune mediator, Interleukin-1 receptor accessory protein (IL1RAP), is expressed and pro-tumorigenic in pancreatic cancer. J Hematol Oncol. 2022 May 23;15(1):70. doi: 10.1186/s13045-022-01286-4. PMID: 35606824.

In vivo study

1. Gummadi VR, Boruah A, Ainan BR, Vare BR, Manda S, Gondle HP, Kumar SN, Mukherjee S, Gore ST, Krishnamurthy NR, Marappan S, Nayak SS, Nellore K, Balasubramanian WR, Bhumireddy A, Giri S, Gopinath S, Samiulla DS, Daginakatte G, Basavaraju A, Chelur S, Eswarappa R, Belliappa C, Subramanya HS, Booher RN, Ramachandra M, Samajdar S. Discovery of CA-

Product data sheet

4948, an Orally Bioavailable IRAK4 Inhibitor for Treatment of Hematologic Malignancies. ACS Med Chem Lett. 2020 Oct 14;11(12):2374-2381. doi: 10.1021/acsmedchemlett.0c00255. PMID: 33335659; PMCID: PMC7734642.
2. Xu J, Qian Q, Xia M, Wang X, Wang H. Trichlorocarban induces developmental and immune toxicity to zebrafish (Danio rerio) by targeting TLR4/MyD88/NF-κB signaling pathway. Environ Pollut. 2021 Jan 10;273:116479. doi: 10.1016/j.envpol.2021.116479. Epub ahead of print. PMID: 33460871.

7. Bioactivity

Biological target:

CA-4948 is a potent IRAK4/FLT3 inhibtor.

In vitro activity

In CA-4948 in vitro experiments, pIRAK1 modulation was observed only at later time points. CA-4948 also exhibited good CYP inhibition profile (IC50 > 50 μM in CYP2C19 and <5% inhibition at 1 μM across CYP3A4, 2D6, 2C9, 2C8, 2B6, and 1A2). CA-4948 was not genotoxic in the in vitro bacterial mutagenesis assay and did not produce any biologically relevant clastogenicity changes in the in vivo micronucleus test in mice.

Reference: ACS Med Chem Lett. 2020 Oct 14;11(12):2374-2381. https://pubmed.ncbi.nlm.nih.gov/33335659/

In vivo activity

In vivo efficacy of CA-4948 was evaluated in an OCI-Ly3 xenograft model through oral route of administration in a once daily dosing regimen. A dose of 200 mg/kg q.d. showed partial tumor regression and a 100 mg/kg q.d. dose showed >90% tumor growth inhibition. The compound was well-tolerated, and there were no overt toxicities at these efficacious doses. Drug concentrations from plasma and tumors were determined at 2 h post final dose administration on day 15. CA-4948 treatment resulted in dose proportional increase in plasma and tumor exposures.

Reference: ACS Med Chem Lett. 2020 Oct 14;11(12):2374-2381. https://pubmed.ncbi.nlm.nih.gov/33335659/