# **Product data sheet**



MedKoo Cat#: 407121				
Name: SMI-4a				
CAS#: 438190-29-5				
Chemical Formula: C <sub>11</sub> H <sub>6</sub> F <sub>3</sub> NO <sub>2</sub> S				
Exact Mass: 273.0071				
Molecular Weight: 273.23				
Product supplied as:	Powder			
Purity (by HPLC):	$\geq$ 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:

SMI-4a is a potent and selective Pim protein kinase inhibitor, which blocks the growth of precursor T-cell lymphoblastic leukemia/lymphoma. SMI-4a was found to induce phosphorylation of extracellular signal-related kinase1/2 (ERK1/2), and the combination of SMI-4a and a mitogen-activated protein kinase kinase 1/2 (MEK1/2) inhibitor was highly synergistic in killing pre-T-LBL cells. SMI-4a may be developed as a therapeutic strategy for the treatment of pre-T-LBL.

#### 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
DMF	30	109.80
DMSO	30	109.80
Ethanol	30	109.80

#### 4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.66 mL	18.30 mL	36.60 mL
5 mM	0.73 mL	3.66 mL	7.32 mL
10 mM	0.37 mL	1.83 mL	3.66 mL
50 mM	0.07 mL	0.37 mL	0.73 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

- Fan RF, Lu Y, Fang ZG, Guo XY, Chen YX, Xu YC, Lei YM, Liu KF, Lin DJ, Liu LL, Liu XF. PIM-1 kinase inhibitor SMI-4a exerts antitumor effects in chronic myeloid leukemia cells by enhancing the activity of glycogen synthase kinase 3β. Mol Med Rep. 2017 Oct;16(4):4603-4612. doi: 10.3892/mmr.2017.7215. Epub 2017 Aug 10. PMID: 28849186; PMCID: PMC5647015.
- Xia Z, Knaak C, Ma J, Beharry ZM, McInnes C, Wang W, Kraft AS, Smith CD. Synthesis and evaluation of novel inhibitors of Pim-1 and Pim-2 protein kinases. J Med Chem. 2009 Jan 8;52(1):74-86. doi: 10.1021/jm800937p. PMID: 19072652; PMCID: PMC5404933.

#### In vivo study

1. Zhang Z, Xie S, Qian J, Gao F, Jin W, Wang L, Yan L, Chen H, Yao W, Li M, Wang X, Zhu L. Targeting macrophagic PIM-1 alleviates osteoarthritis by inhibiting NLRP3 inflammasome activation via suppressing mitochondrial ROS/Cl- efflux signaling pathway. J Transl Med. 2023 Jul 8;21(1):452. doi: 10.1186/s12967-023-04313-1. PMID: 37422640; PMCID: PMC10329339.

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 Wang J, Cao Y, Liu Y, Zhang X, Ji F, Li J, Zou Y. PIM1 inhibitor SMI-4a attenuated lipopolysaccharide-induced acute lung injury through suppressing macrophage inflammatory responses via modulating p65 phosphorylation. Int Immunopharmacol. 2019 Aug;73:568-574. doi: 10.1016/j.intimp.2019.05.040. Epub 2019 Jun 13. PMID: 31203114.

## 7. Bioactivity

#### Biological target:

SMI-4a is a Pim-1 inhibitor (IC50 =  $24\mu$ M and Ki =  $0.6\mu$ M). SMI-4a also inhibits Pim-2 (IC50 =  $100\mu$ M), and does not significantly inhibit the other serine/threonine- or tyrosine-kinases. SIM-4a kills a wide range of both myeloid and lymphoid cell lines (IC50s = 0.8 to  $40\mu$ M).

#### In vitro activity

SMI-4a shows promise in treating chronic myeloid leukemia (CML), especially in combination with existing chemotherapeutics, for imatinib-resistant CML. It inhibits cell proliferation, induces apoptosis, and reduces colony formation in K562 and imatinib-resistant K562 cell lines. SMI-4a impacts key signaling pathways, decreasing p-Ser9-GSK3 $\beta$ , inhibiting  $\beta$ -catenin translocation, and modulating gene expression related to apoptosis.

Reference: Mol Med Rep. 2017 Oct;16(4):4603-4612. https://pubmed.ncbi.nlm.nih.gov/28849186/

#### In vivo activity

SMI-4a could be a promising therapy for LPS-induced acute lung injury (ALI)by reducing cytokine production through inhibiting p65 activities. In an LPS-induced ALI murine model, SMI-4a improved survival rates, reduced lung edema severity, and decreased inflammatory cell counts. It also suppressed cytokine production in cells and lung fluid. SMI-4a mitigated nuclear p65 and phosphorylated p65 levels.

Reference: Int Immunopharmacol. 2019 Aug;73:568-574. https://pubmed.ncbi.nlm.nih.gov/31203114/

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.