



# SZABO SCANDIC

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## Produktinformation



Forschungsprodukte & Biochemikalien



Zellkultur & Verbrauchsmaterial



Diagnostik & molekulare Diagnostik



Laborgeräte & Service

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### Lieferung & Zahlungsart

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### Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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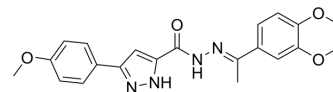
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## SKI-178

Cat. No.:	HY-12892
CAS No.:	1259484-97-3
Molecular Formula:	C <sub>21</sub> H <sub>22</sub> N <sub>4</sub> O <sub>4</sub>
Molecular Weight:	394.42
Target:	SphK; Apoptosis
Pathway:	Immunology/Inflammation; Apoptosis
Storage:	Powder    -20°C    3 years In solvent   -80°C    6 months -20°C    1 month



### SOLVENT & SOLUBILITY

In Vitro	DMSO : 50 mg/mL (126.77 mM; Need ultrasonic)					
	Preparing Stock Solutions	<div><div>Solvent</div><div>Concentration</div></div>	Mass	1 mg	5 mg	10 mg
		1 mM	2.5354 mL	12.6768 mL	25.3537 mL	
		5 mM	0.5071 mL	2.5354 mL	5.0707 mL	
		10 mM	0.2535 mL	1.2677 mL	2.5354 mL	
Please refer to the solubility information to select the appropriate solvent.						
In Vivo	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: 2.5 mg/mL (6.34 mM); Suspended solution; Need ultrasonic					
	2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (6.34 mM); Clear solution					

### BIOLOGICAL ACTIVITY

Description	SKI-178 is a potent sphingosine kinase-1 (SphK1) and SphK2 inhibitor. SKI-178 is cytotoxic at IC <sub>50</sub> concentrations ranging from 1.8 to 0.1 μM in both agent sensitive and multi-agent resistant cancer cell lines (i.e., MTR3, NCI-ADR and HL60/VCR cells). SKI-178 induces apoptosis in a CDK1-dependent manner in human acute myeloid leukemia cell lines <sup>[1][2]</sup> .	
IC <sub>50</sub> & Target	SphK1	SphK2
In Vitro	SKI-178 (5 μM; 24 hours)-induced apoptotic cell death correlates with prolonged Bcl-2 phosphorylation <sup>[1]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only. Apoptosis Analysis <sup>[1]</sup>	

	Cell Line:	HL-60 cells
	Concentration:	5 $\mu$ M
	Incubation Time:	24 hours
	Result:	JNK activity (indicated by phosphorylation at Thr183/Tyr185) increased in a time-dependent manner starting as early as 2 hours continued to increase for at least 24 hours. There was a concomitant increase in apoptotic cell death indicated by the cleavage of caspase-7. Bcl-2 phosphorylation at Ser70 increased with time in response to SKI-178 treatment, reaching maximal levels at 8 hours, which was consistent with the timing of caspase-7 activation.
In Vivo	SKI-178 (20 mg/kg; retro-orbital injection under isoflurane anesthesia) inhibits leukemic progression in the MLL-AF9 model <sup>[3]</sup> .	
	MCE has not independently confirmed the accuracy of these methods. They are for reference only.	
	Animal Model:	MLL-AF9 mouse model (leukemic mice) <sup>[3]</sup>
	Dosage:	20 mg/kg
	Administration:	Retro-orbital injection under isoflurane anesthesia; three times per week for 1 and 3 weeks
	Result:	White blood cell (WBC) counts decreased from their initial 104 cells/ $\mu$ L levels and continued to decline after 3 weeks of treatment until they reached normal levels ( $\sim 4 \times 10^3$ cells/ $\mu$ L).

## REFERENCES

- [1]. Hengst JA, et al. SKI-178: A Multitargeted Inhibitor of Sphingosine Kinase and Microtubule Dynamics Demonstrating Therapeutic Efficacy in Acute Myeloid Leukemia Models. *Cancer Transl Med.* 2017;3(4):109-121.
- [2]. Hengst JA, et al. Development of a sphingosine kinase 1 specific small-molecule inhibitor. *Bioorg Med Chem Lett.* 2010;20(24):7498-7502.
- [3]. Dick TE, et al. The apoptotic mechanism of action of the sphingosine kinase 1 selective inhibitor SKI-178 in human acute myeloid leukemia cell lines. *J Pharmacol Exp Ther.* 2015;352(3):494-508.

**Caution: Product has not been fully validated for medical applications. For research use only.**

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