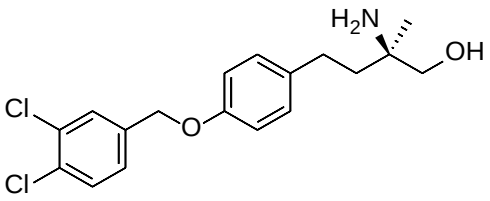
Product data sheet

MedKoo Cat#: 463756 Name: P053 CAS: 2748196-63-4 Chemical Formula: $C_{18}H_{21}Cl_2NO_2$ Exact Mass: 353.0949 Molecular Weight: 354.271	
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:
P053 is a the first isoform-specific ceramide synthase inhibitor.

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	30.0	84.68
DMSO	65.0	183.48
Ethanol	30.0	84.68

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.82 mL	14.11 mL	28.23 mL
5 mM	0.56 mL	2.82 mL	5.65 mL
10 mM	0.28 mL	1.41 mL	2.82 mL
50 mM	0.06 mL	0.28 mL	0.56 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

Turner N, Lim XY, Toop HD, Osborne B, Brandon AE, Taylor EN, Fiveash CE, Govindaraju H, Teo JD, McEwen HP, Couttas TA, Butler SM, Das A, Kowalski GM, Bruce CR, Hoehn KL, Fath T, Schmitz-Peiffer C, Cooney GJ, Montgomery MK, Morris JC, Don AS. A selective inhibitor of ceramide synthase 1 reveals a novel role in fat metabolism. Nat Commun. 2018 Aug 21;9(1):3165. doi: 10.1038/s41467-018-05613-7. PMID: 30131496; PMCID: PMC6104039.

In vivo study

Turner N, Lim XY, Toop HD, Osborne B, Brandon AE, Taylor EN, Fiveash CE, Govindaraju H, Teo JD, McEwen HP, Couttas TA, Butler SM, Das A, Kowalski GM, Bruce CR, Hoehn KL, Fath T, Schmitz-Peiffer C, Cooney GJ, Montgomery MK, Morris JC, Don AS. A selective inhibitor of ceramide synthase 1 reveals a novel role in fat metabolism. Nat Commun. 2018 Aug 21;9(1):3165. doi: 10.1038/s41467-018-05613-7. PMID: 30131496; PMCID: PMC6104039.

7. Bioactivity
Biological target:

P053 is a potent, non-competitive and selective ceramide synthase 1 (CerS1) inhibitor wirh an IC_{50} of 0.5 μM.

In vitro activity

Product data sheet

In a live-cell ceramide synthase assay using cortical neuron cultures, a two hour pre-treatment with P053 resulted in dose-dependent inhibition of de novo C18:0 ceramide synthesis from deuterated dihydrosphingosine (Fig. 2a), confirming that the drug is cell permeable and inhibits CerS1 activity in living cells.

Reference: Nat Commun. 2018 Aug 21;9(1):3165. https://pubmed.ncbi.nlm.nih.gov/30131496/

In vivo activity

As C18 is the dominant ceramide in SkM, P053 treatment reduced total ceramide content in this organ (Fig. 3f; $P = 0.73$ for effect of diet, $P < 0.001$ for effect of P053 by 2-way ANOVA). Very long chain ceramides (C22:0, C24:0 and C24:1) were significantly increased by P053 treatment in the HFD group (Fig. 3d, e), as was 42:2 SM, which is assumed to be the 18:1/24:1 (C24:1) form (Fig. 3g). Mean levels of 36:1 SM, which is derived from C18:0 ceramide, were 13% lower in P053-treated compared to vehicle-treated mice on both diets (Fig. 3g), however this effect was not statistically significant.

Reference: Nat Commun. 2018 Aug 21;9(1):3165. https://pubmed.ncbi.nlm.nih.gov/30131496/