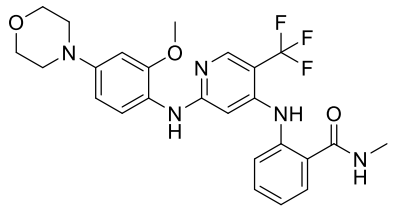
Product data sheet

MedKoo Cat#: 406262 Name: PND-1186 CAS#: 1061353-68-1 Chemical Formula: $C_{25}H_{26}F_3N_5O_3$ Exact Mass: 501.19877 Molecular Weight: 501.5	
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:

PND-1186, also known as SR-2156 and VS-4718, is a potent FAK inhibitor with a 50% inhibitory concentration (IC50) of 1.5 nM in vitro. PND-1186 has an IC50 of ~100 nM in breast carcinoma cells. Notably, 1.0 ÂµM PND-1186 (>5-fold above IC50) had limited effects on cell proliferation. However, under non-adherent conditions as spheroids and as colonies in soft agar, 0.1 ÂµM PND-1186 blocked FAK and p130Cas tyrosine phosphorylation, promoted caspase-3 activation, and triggered cell apoptosis. PND-1186 inhibited 4T1 breast carcinoma subcutaneous tumor growth correlated with elevated tumor cell apoptosis and caspase 3 activation.

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	30.0	59.8
Ethanol	30.0	59.8

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.99 mL	9.97 mL	19.94 mL
5 mM	9.40 mL	1.99 mL	3.99 mL
10 mM	0.20 mL	1.00 mL	1.99 mL
50 mM	0.04 mL	0.20 mL	0.40 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. Gnani D, Romito I, Artuso S, Chierici M, De Stefanis C, Panera N, Crudele A, Ceccarelli S, Carcarino E, D'Oria V, Porru M, Giorda E, Ferrari K, Miele L, Villa E, Balsano C, Pasini D, Furlanello C, Locatelli F, Nobili V, Rota R, Leonetti C, Alisi A. Focal adhesion kinase depletion reduces human hepatocellular carcinoma growth by repressing enhancer of zeste homolog 2. Cell Death Differ. 2017 May;24(5):889-902. doi: 10.1038/cdd.2017.34. Epub 2017 Mar 24. PMID: 28338656; PMCID: PMC5423113.
2. Serrels A, Lund T, Serrels B, Byron A, McPherson RC, von Kriegsheim A, Gómez-Cuadrado L, Canel M, Muir M, Ring JE, Maniati E, Sims AH, Pachter JA, Brunton VG, Gilbert N, Anderton SM, Nibbs RJ, Frame MC. Nuclear FAK controls chemokine transcription, Tregs, and evasion of anti-tumor immunity. Cell. 2015 Sep 24;163(1):160-73. doi: 10.1016/j.cell.2015.09.001. PMID: 26406376; PMCID: PMC4597190.

In vivo study

1. Kurmasheva RT, Gorlick R, Kolb EA, Keir ST, Maris JM, Lock RB, Carol H, Kang M, Reynolds CP, Wu J, Houghton PJ, Smith MA. Initial testing of VS-4718, a novel inhibitor of focal adhesion kinase (FAK), against pediatric tumor models by the Pediatric

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Preclinical Testing Program. Pediatr Blood Cancer. 2017 Apr;64(4):10.1002/pbc.26304. doi: 10.1002/pbc.26304. Epub 2016 Oct 27. PMID: 27786412; PMCID: PMC5578428.
2. Walsh C, Tanjoni I, Uryu S, Tomar A, Nam JO, Luo H, Phillips A, Patel N, Kwok C, McMahon G, Stupack DG, Schlaepfer DD. Oral delivery of PND-1186 FAK inhibitor decreases tumor growth and spontaneous breast to lung metastasis in pre-clinical models. Cancer Biol Ther. 2010 May 15;9(10):778-90. doi: 10.4161/cbt.9.10.11433. PMID: 20234193; PMCID: PMC2933309.

7. Bioactivity

Biological target:

PND-1186 (VS-4718) is a potent, highly-specific and reversible inhibitor of FAK with an IC50 of 1.5 nM.

In vitro activity

HCC cells were exposed to 0.5 μM and 1 μM of PND-1186. The treatment with PND-1186 decreased cell proliferation rate (Supplementary Figure S8a) by significantly inducing G0/G1 phase arrest and apoptosis at 48 h (Supplementary Figure S8b, Figure 8a). Accordingly, PND-1186 treatment caused downregulation of FAK Tyr-397 phosphorylation and cyclin D1 amount (Supplementary Figures S8c and d) and increased the expression of both p21 and cleaved caspase-3 at 48 h (Figure 8b). As expected, 1 μM PND-1186 significantly downregulated EZH2 mRNA and upregulated NOTCH2 expression (Figure 8c).

Reference: Cell Death Differ. 2017 May; 24(5): 889–902. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5423113/

In vivo activity

VS-4718 induced significant differences in EFS distribution compared to control in 18 of 36 (50%) of the evaluable solid tumor mice xenografts and in 0 of 8 (0%) of the evaluable ALL xenografts, including the Ph+ ALL xenograft, ALL-4 (Table 2). Significant differences in EFS distribution were most commonly observed for the osteosarcoma panel (6 of 6), the rhabdomyosarcoma panel (4 of 6), and the neuroblastoma panel (4 of 6). VS-4718 did not induce tumor growth inhibition meeting criteria for intermediate EFS T/C(>2) activity in either the solid tumor or ALL xenografts. Only 3 models met criteria for PD2 responses (one Ewing, rhabdomyosarcoma, and neuroblastoma xenograft each). Objective responses were not observed for the solid tumor or ALL xenografts.

Reference: Pediatr Blood Cancer. 2017 Apr; 64(4): 10.1002/pbc.26304. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5578428/