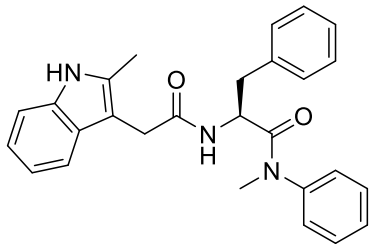
Product data sheet

MedKoo Cat#: 555391 Name: PF3450074 CAS#: 1352879-65-2 Chemical Formula: $C_{27}H_{27}N_3O_2$ Exact Mass: 425.2103 Molecular Weight: 425.532	
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:

PF-3450074, also known as PF74, is a HIV-1 inhibitor that targets HIV capsid protein. PF74 binds specifically to HIV-1 particles and triggers premature HIV-1 uncoating in target cells. PF74 Inhibits HIV-1 Integration by Altering the Composition of the Preintegration Complex. PF74 Reinforces the HIV-1 Capsid To Impair Reverse Transcription-Induced Uncoating.

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	250.0	587.52

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.35 mL	11.75 mL	23.50 mL
5 mM	0.47 mL	2.35 mL	4.70 mL
10 mM	0.23 mL	1.17 mL	2.35 mL
50 mM	0.05 mL	0.23 mL	0.47 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. Matreyek KA, Yücel SS, Li X, Engelman A. Nucleoporin NUP153 phenylalanine-glycine motifs engage a common binding pocket within the HIV-1 capsid protein to mediate lentiviral infectivity. PLoS Pathog. 2013;9(10):e1003693. doi: 10.1371/journal.ppat.1003693. Epub 2013 Oct 10. PMID: 24130490; PMCID: PMC3795039.
2. Zhou J, Price AJ, Halambage UD, James LC, Aiken C. HIV-1 Resistance to the Capsid-Targeting Inhibitor PF74 Results in Altered Dependence on Host Factors Required for Virus Nuclear Entry. J Virol. 2015 Sep;89(17):9068-79. doi: 10.1128/JVI.00340-15. Epub 2015 Jun 24. PMID: 26109731; PMCID: PMC4524096.

In vivo study

1. Zhou J, Price AJ, Halambage UD, James LC, Aiken C. HIV-1 Resistance to the Capsid-Targeting Inhibitor PF74 Results in Altered Dependence on Host Factors Required for Virus Nuclear Entry. J Virol. 2015 Sep;89(17):9068-79. doi: 10.1128/JVI.00340-15. Epub 2015 Jun 24. PMID: 26109731; PMCID: PMC4524096.

7. Bioactivity

Biological target:

PF-3450074 (PF-74) is a specifical inhibitor of HIV-1 capsid protein (CA) and displays a broad-spectrum inhibition of HIV isolates with submicromolar potency (EC50=8-640 nM).

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In vitro activity

It was assessed whether PF74 could additionally antagonize NUP153C engagement by CA in the context of HIV-1 infection, given the caveat that one could not unambiguously correlate data from protein binding assays with effects from PF74-induced capsid destabilization in cells. PF74 exhibited dose-dependent inhibition of WT HIV-1 and N74D CA mutant viral infection, but had no effect on CA mutant T54A/N57A, which lacks the critical Asn57 side-chain necessary for PF74 binding. WT virus was noticeably less sensitive to PF74 in Trim-NUP153C expressing cells, with an EC90 of 5.65 μM as opposed to 0.65 μM in control cells. The competing effect of PF74 on Trim-NUP153C inhibition seemingly occurred between the concentrations of 0.1 and 1 μM, as the inhibition curves within the two cell lines were nearly superimposable outside of these concentrations. N74D CA mutant virus also exhibited a shift in the PF74 EC90 concentration in Trim-NUP153C cells, though this occurred at higher PF74 concentrations than with the WT virus.

Reference: PLoS Pathog. 2013;9(10):e1003693. https://pubmed.ncbi.nlm.nih.gov/24130490/

In vivo activity

The altered dependence of 4Mut and 5Mut infection on expression of TNPO3 and RanBP2 prompted examination of the fitness of 4Mut in primary targets of HIV-1 replication in vivo—i.e., CD4+ T cells and macrophages. Activated primary CD4+ T cells supported robust replication of wild-type X4- and R5-tropic HIV-1 (Fig. 9A). In contrast, and as observed with the CEM T cell line, 4Mut was markedly attenuated, as was 5Mut. Addition of PF74 or BI-2 promoted 4Mut replication in the cells. In macrophages, in contrast, replication of the 4Mut virus (rendered CCR5 dependent by replacement of the NL4-3 env by that of HIV-1.BaL) was severely impaired and was not stimulated by PF74 or BI-2. Surprisingly, replication of the N74D mutant, which we had included as a control, was markedly stimulated by PF74 and BI-2 in macrophages at drug concentrations that were only moderately inhibitory toward the wild-type virus. We conclude that the 4Mut virus, while exhibiting features of the N74D mutant in terms of host factor requirement, responds differently to capsid-targeting inhibitors in macrophages.

Reference: J Virol. 2015 Sep;89(17):9068-79. https://pubmed.ncbi.nlm.nih.gov/26109731/