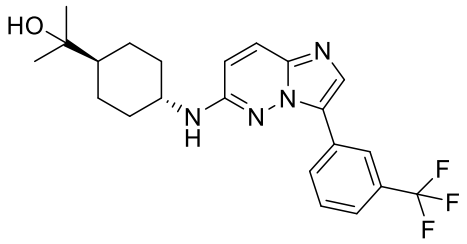
Product data sheet

MedKoo Cat#: 527505 Name: TP-3654 CAS#: 1361951-15-6 Chemical Formula: $C_{22}H_{25}F_3N_4O$ Exact Mass: 418.198 Molecular Weight: 418.4642	
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:
TP-3654 is a Pim-1 and Pim-3 kinase inhibitor potentially for the treatment of prostate cancer, acute myeloid leukemia, multiple sclerosis and psoriasis. TP-3654 displays favorable human ether-à-go-go-related gene and cytochrome P450 inhibition profiles compared with the first-generation PIM inhibitor, SGI-1776, and exhibits oral bioavailability.

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	86	200.74
Ethanol	6	14.34

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.39 mL	11.95 mL	23.90 mL
5 mM	0.48 mL	2.39 mL	4.78 mL
10 mM	0.24 mL	1.19 mL	2.39 mL
50 mM	0.05 mL	0.24 mL	0.48 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. Foulks JM, Carpenter KJ, Luo B, Xu Y, Senina A, Nix R, Chan A, Clifford A, Wilkes M, Vollmer D, Brenning B, Merx S, Lai S, McCullar MV, Ho KK, Albertson DJ, Call LT, Bearss JJ, Tripp S, Liu T, Stephens BJ, Mollard A, Warner SL, Bearss DJ, Kanner SB. A small-molecule inhibitor of PIM kinases as a potential treatment for urothelial carcinomas. Neoplasia. 2014 May;16(5):403-12. doi: 10.1016/j.neo.2014.05.004. Epub 2014 Jun 18. PMID: 24953177; PMCID: PMC4198696.

2. Whillock AL, Mambetsariev N, Lin WW, Stunz LL, Bishop GA. TRAF3 regulates the oncogenic proteins Pim2 and c-Myc to restrain survival in normal and malignant B cells. Sci Rep. 2019 Sep 9;9(1):12884. doi: 10.1038/s41598-019-49390-9. Erratum in: Sci Rep. 2019 Nov 20;9(1):17502. PMID: 31501481; PMCID: PMC6733949.

In vivo study

1. Foulks JM, Carpenter KJ, Luo B, Xu Y, Senina A, Nix R, Chan A, Clifford A, Wilkes M, Vollmer D, Brenning B, Merx S, Lai S, McCullar MV, Ho KK, Albertson DJ, Call LT, Bearss JJ, Tripp S, Liu T, Stephens BJ, Mollard A, Warner SL, Bearss DJ, Kanner SB. A small-molecule inhibitor of PIM kinases as a potential treatment for urothelial carcinomas. Neoplasia. 2014 May;16(5):403-12. doi: 10.1016/j.neo.2014.05.004. Epub 2014 Jun 18. PMID: 24953177; PMCID: PMC4198696.

2. Lampron MC, Vitry G, Nadeau V, Grobs Y, Paradis R, Samson N, Tremblay È, Boucherat O, Meloche J, Bonnet S, Provencher S, Potus F, Paulin R. PIM1 (Moloney Murine Leukemia Provirus Integration Site) Inhibition Decreases the Nonhomologous End-Joining DNA Damage Repair Signaling Pathway in Pulmonary Hypertension. Arterioscler Thromb Vasc Biol. 2020 Mar;40(3):783-801. doi: 10.1161/ATVBAHA.119.313763. Epub 2020 Jan 23. PMID: 31969012.

7. Bioactivity

Biological target:

TP-3654 is a second-generation Pim kinase inhibitor with Ki values of 5 and 42 nM for Pim-1 and Pim-3, respectively.

In vitro activity

The cellular potency of TP-3654 was determined by measuring its effect on baseline phosphorylation of BAD, a known substrate of PIM, on serine 112 by overexpression of PIM-1 and BAD in HEK-293 cells. Overexpression of the catalytically inactive mutant PIM-1 (K67M) did not increase phosphorylation of BAD compared to BAD transfection alone (Figure 2A) and was used as a negative control to subtract BAD phosphorylation by cellular kinases other than PIM-1. TP-3654 demonstrated potent PIM-1 specific cellular activity in the PIM-1/BAD overexpression system with an average EC50 = 67 nM (Figure 1C). In addition, TP-3654 treatment reduced levels of phospho-BAD in vitro using the bladder cancer cell line UM-UC-3 (Figure 2B). To exclude the possibility that this phospho-BAD decrease was due to off-target activity, we measured levels of phospho-4EBP1 in parallel with phospho-BAD. There was no appreciable difference in levels of phospho-4EBP1 in TP-3654–treated cells (Figure 2B), providing further evidence that PIM inhibition was the primary mechanism for the phospho-BAD decrease observed in TP-3654–treated cells and not activity of the compound inhibiting AKT, another known kinase that can phosphorylate BAD.

Reference: Neoplasia. 2014 May;16(5):403-12. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24953177/

In vivo activity

It was tested whether TP-3654 could inhibit the growth of established mouse xenograft tumors using the UM-UC-3 and PC-3 solid tumor cell lines. Oral dosing of 200 mg/kg TP-3654 significantly reduced both UM-UC-3 and PC-3 tumor growth measured by volume (caliper) and by final tumor weight, with no significant changes in body weight or gross adverse toxicity (Figure 5).

Reference: Neoplasia. 2014 May;16(5):403-12. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24953177/

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.