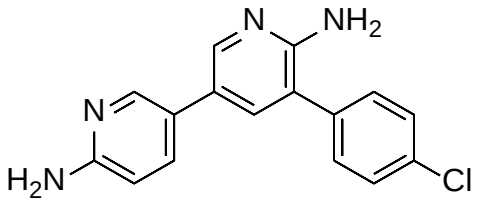
Product data sheet

MedKoo Cat#: 527680 Name: PF-06260933 CAS: 1811510-56-1 (free base) Chemical Formula: $C_{16}H_{13}ClN_4$ Exact Mass: 296.0829 Molecular Weight: 296.758	
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-06260933 is a potent and highly selective inhibitor of MAP4K4.

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	1.0	3.37
DMSO	30.0	101.09
Ethanol	2.0	6.74

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	3.37 mL	16.85 mL	33.70 mL
5 mM	0.67 mL	3.37 mL	6.74 mL
10 mM	0.34 mL	1.69 mL	3.37 mL
50 mM	0.07 mL	0.34 mL	0.67 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. Ammirati M, Bagley SW, Bhattacharya SK, Buckbinder L, Carlo AA, Conrad R, Cortes C, Dow RL, Dowling MS, El-Kattan A, Ford K, Guimarães CR, Hepworth D, Jiao W, LaPerle J, Liu S, Londregan A, Loria PM, Mathiowetz AM, Munchhof M, Orr ST, Petersen DN, Price DA, Skoura A, Smith AC, Wang J. Discovery of an in Vivo Tool to Establish Proof-of-Concept for MAP4K4-Based Antidiabetic Treatment. ACS Med Chem Lett. 2015 Oct 6;6(11):1128-33. doi: 10.1021/acsmedchemlett.5b00215. PMID: 26617966; PMCID: PMC4645242.

In vivo study

1. Zou Z, Dong YS, Liu DD, Li G, Hao GZ, Gao X, Pan PY, Liang GB. MAP4K4 induces early blood-brain barrier damage in a murine subarachnoid hemorrhage model. Neural Regen Res. 2021 Feb;16(2):325-332. doi: 10.4103/1673-5374.290904. PMID: 32859792; PMCID: PMC7896238.
2. Ammirati M, Bagley SW, Bhattacharya SK, Buckbinder L, Carlo AA, Conrad R, Cortes C, Dow RL, Dowling MS, El-Kattan A, Ford K, Guimarães CR, Hepworth D, Jiao W, LaPerle J, Liu S, Londregan A, Loria PM, Mathiowetz AM, Munchhof M, Orr ST, Petersen DN, Price DA, Skoura A, Smith AC, Wang J. Discovery of an in Vivo Tool to Establish Proof-of-Concept for MAP4K4-Based Antidiabetic Treatment. ACS Med Chem Lett. 2015 Oct 6;6(11):1128-33. doi: 10.1021/acsmedchemlett.5b00215. PMID: 26617966; PMCID: PMC4645242.

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7. Bioactivity

Biological target:

PF-06260933 is an orally active and highly selective inhibitor of MAP4K4 with IC50s of 3.7 and 160 nM for kinase and cell.

In vitro activity

To optimize the hydrogen bond with Asp115, compound 16 (PF-06260933) was prepared, as modeling indicated that the NH2 group of the newly introduced aminopyridine group interacts with Asp115 in a similar fashion as the phenol OH in 13. Compound 16 (PF-6260933) was very potent against the enzyme with a very good ligand efficiency (LE = 0.57) and was the most potent analogue in the cell assay. Indeed, compound 16 showed a kinase activity IC50 (tested at Km) of 15 and 8 nM for TNIK and MINK, respectively.

Reference: ACS Med Chem Lett. 2015 Oct 6;6(11):1128-33. https://pubmed.ncbi.nlm.nih.gov/26617966/

In vivo activity

The model mice were assigned to four groups: MAP4K4 recombinant protein, scramble small interfering RNA, and MAP4K4 small interfering RNA were delivered by intracerebroventricular injection, while PF-06260933, a small-molecule inhibitor of MAP4K4, was administrated orally. Furthermore, administration of the MAP4K4 inhibitor PF-06260933 reduced blood-brain barrier damage in mice, promoted the recovery of neurological function, and reduced p-p65 and MMP9 protein expression.

Reference: Neural Regen Res. 2021 Feb;16(2):325-332. https://pubmed.ncbi.nlm.nih.gov/32859792/