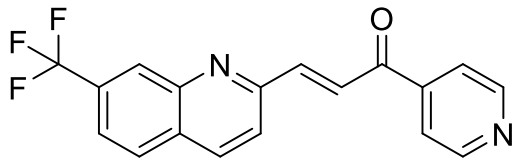
Product data sheet

MedKoo Cat#: 206166 Name: PFK-158 CAS#: 1462249-75-7 Chemical Formula: $C_{18}H_{11}F_3N_2O$ Exact Mass: 328.08235 Molecular Weight: 328.29	
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:

PFK-158, also known as ACT-PFK-158, is an inhibitor of 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatases (PFK-2/FBPase) isoform 3 (PFKFB3) with potential antineoplastic activity. Upon administration, PFKFB3 inhibitor PFK-158 binds to and inhibits the activity of PFKFB3, which leads to the inhibition of both the glycolytic pathway in and glucose uptake by cancer cells. This prevents the production of macromolecules and energy that causes the enhanced cellular proliferation in cancer cells as compared to that of normal, healthy cells. Depriving cancer cells of nutrients and energy leads to the inhibition of cancer cell growth.

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	14.0	42.6

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.05 mL	15.23 mL	30.46 mL
5 mM	0.61 mL	3.05 mL	6.09 mL
10 mM	0.30 mL	1.52 mL	3.05 mL
50 mM	0.06 mL	0.30 mL	0.61 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. Mondal S, Roy D, Sarkar Bhattacharya S, Jin L, Jung D, Zhang S, Kalogera E, Staub J, Wang Y, Xuyang W, Khurana A, Chien J, Telang S, Chesney J, Tapolsky G, Petras D, Shridhar V. Therapeutic targeting of PFKFB3 with a novel glycolytic inhibitor PFK158 promotes lipophagy and chemosensitivity in gynecologic cancers. Int J Cancer. 2019 Jan 1;144(1):178-189. doi: 10.1002/ijc.31868. Epub 2018 Oct 30. Erratum in: Int J Cancer. 2019 Jul 15;145(2):E13. PMID: 30226266; PMCID: PMC6261695.
2. Sarkar Bhattacharya S, Thirusangu P, Jin L, Roy D, Jung D, Xiao Y, Staub J, Roy B, Molina JR, Shridhar V. PFKFB3 inhibition reprograms malignant pleural mesothelioma to nutrient stress-induced macropinocytosis and ER stress as independent binary adaptive responses. Cell Death Dis. 2019 Sep 27;10(10):725. doi: 10.1038/s41419-019-1916-3. PMID: 31562297; PMCID: PMC6764980.

In vivo study

1. Mondal S, Roy D, Sarkar Bhattacharya S, Jin L, Jung D, Zhang S, Kalogera E, Staub J, Wang Y, Xuyang W, Khurana A, Chien J, Telang S, Chesney J, Tapolsky G, Petras D, Shridhar V. Therapeutic targeting of PFKFB3 with a novel glycolytic inhibitor PFK158 promotes lipophagy and chemosensitivity in gynecologic cancers. Int J Cancer. 2019 Jan 1;144(1):178-189. doi: 10.1002/ijc.31868. Epub 2018 Oct 30. Erratum in: Int J Cancer. 2019 Jul 15;145(2):E13. PMID: 30226266; PMCID: PMC6261695.

Product data sheet

2. Sarkar Bhattacharya S, Thirusangu P, Jin L, Roy D, Jung D, Xiao Y, Staub J, Roy B, Molina JR, Shridhar V. PFKFB3 inhibition reprograms malignant pleural mesothelioma to nutrient stress-induced macropinocytosis and ER stress as independent binary adaptive responses. Cell Death Dis. 2019 Sep 27;10(10):725. doi: 10.1038/s41419-019-1916-3. PMID: 31562297; PMCID: PMC6764980.

7. Bioactivity

Biological target:

PFK-158 is a potent and selective PFKFB3 inhibitor that reduces glucose uptake, ATP production, lactate release, and induces apoptosis and autophagy in cancer cells. PFK-158 has an IC50 value of 137 nM.

In vitro activity

Since elevated glucose utilization in cancer supports lipogenesis at multiple levels13 and considering that it could be another contributing factor toward chemoresistance, it was checked whether PFK158 treatment could modulate lipid pathways. Results showed that the C13 and HeyA8MDR cells had more LDs compared to the chemosensitive cells (Fig.4 a and b) and PFK158 treatment significantly reduced the number of LDs in these cells (Fig4 c and d). Of interest, genetic downregulation of PFKFB3 in C13 and HeyA8MDR cells (Fig.4 e and g) also resulted in a reduction of LDs. The data indicates that PFK158 has synergistic anti‐proliferative effects in vitro when combined with cisplatin in C13 and HeyA8MDR cells compared to OV2008 and HeyA8, respectively (Fig. S3A‐C and E‐G, Supporting Information). PFK158 treatment induces lipophagy and also sensitizes chemoresistant cells to chemotherapy‐induced cytotoxicity both in vitro and in vivo. Importantly, this data also showed that inhibiting autophagy with BafA reverses the PFK158‐induced chemosensitivity to carboplatin more in the resistant than the sensitive cells. In conclusion, this is one of the first studies to show that PFK158, a specific inhibitor of PFKFB3, simultaneously targets both the glycolytic and lipogenic pathways, two pathways that are very active in cancer, and promotes lipophagy to inhibit tumor growth.

Int J Cancer. 2019 Jan 1;144(1):178-189. https://pubmed.ncbi.nlm.nih.gov/30226266/

In vivo activity

PFK158 (Fig.1b) obtained on an MTA from Gossamer Bio (San Diego, CA) was dissolved in 40% solution of Captisol in ddH2O for in vivo studies. To further investigate the activity of PFK158 alone and/or in combination with carboplatin (CBP) in an MPM xenograft nude mouse model, EMMeso cells were implanted subcutaneously in nude mice (Fig. S9A). A noticeable reduction in tumor burden (Fig. S9B and Fig.7a), tumor growth (Fig.7b), tumor volume (Fig.7c), and tumor weight (Fig.7d) were observed in both in PFK158 alone and in combination treatment. It was also observed that the tumor burden in PFK158-treated mice was significantly ($P < 0.0002$) less than the one in the vehicle-treated controls. However, the data also showed that the PFK158 alone was profoundly effective as it was in combination with CBP treatment in reducing pleural mesothelioma progression compared to CBP single treatment group Together the in vivo data revealed that PFK158-mediated inhibition of tumorigenesis occurs through methuosis and ER stress to reduce the tumor burden. Finally, PFK158 alone and in combination with carboplatin-inhibited tumorigenesis of EMMeso xenografts in vivo. Since most cancer cells exhibit an increased glycolytic rate, these results provide evidence for PFK158, in combination with standard chemotherapy, may have a potential in the treatment of MPM. This is the first study to establish that inhibition of PFKFB3 with a small molecule antagonist, PFK158; can introduce glycolytic assault which simultaneously triggers ER stress and methuosis and eventually suppress MPM cell growth both in vitro and in vivo (Fig.88).

Cell Death Dis. 2019 Oct; 10(10): 725. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6764980/

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.