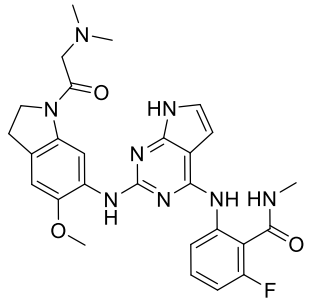
Product data sheet

MedKoo Cat#: 401475 Name: GSK1838705A CAS#: 1116235-97-2 Chemical Formula: $C_{27}H_{29}FN_8O_3$ Exact Mass: 532.23467 Molecular Weight: 532.57	
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:

GSK1838705A is a small-molecule kinase inhibitor that inhibits IGF-IR and IR (insulin receptor) with IC50s of 2.0 and 1.6 nM, respectively . GSK1838705A blocks the in vitro proliferation of cell lines derived from solid and hematologic malignancies, including multiple myeloma and Ewing's sarcoma, and retards the growth of human tumor xenografts in vivo. Despite the inhibitory effect of GSK1838705A on insulin receptor, minimal effects on glucose homeostasis were observed at efficacious doses. GSK1838705A also inhibits the anaplastic lymphoma kinase (ALK), which drives the aberrant growth of anaplastic large-cell lymphomas, some neuroblastomas, and a subset of non-small cell lung cancers. GSK1838705A inhibits ALK, with an IC(50) of 0.5 nmol/L, and causes complete regression of ALK-dependent tumors in vivo at well-tolerated doses. GSK1838705A is therefore a promising antitumor agent for therapeutic use in human cancers. (source: Mol Cancer Ther. 2009 Oct;8(10):2811-20).

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	73.32	137.67
DMSO:PBS (pH 7.2) (1:3)	0.25	0.47
DMF	25.0	46.94
Ethanol	2.0	3.76

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.88 mL	9.39 mL	18.78 mL
5 mM	0.38 mL	1.88 mL	3.76 mL
10 mM	0.19 mL	0.94 mL	1.88 mL
50 mM	0.04 mL	0.19 mL	0.38 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. Zhou F, Chen X, Fan S, Tai S, Jiang C, Zhang Y, Hao Z, Zhou J, Shi H, Zhang L, Liang C. GSK1838705A, an insulin-like growth factor-1 receptor/insulin receptor inhibitor, induces apoptosis and reduces viability of docetaxel-resistant prostate cancer cells both in vitro and in vivo. Onco Targets Ther. 2015 Apr 10;8:753-60. doi: 10.2147/OTT.S79105. PMID: 25926740; PMCID: PMC4403692.
2. Sabbatini P, Korenchuk S, Rowand JL, Groy A, Liu Q, Leperi D, Atkins C, Dumble M, Yang J, Anderson K, Kruger RG, Gontarek RR, Maksimchuk KR, Suravajjala S, Lapierre RR, Shotwell JB, Wilson JW, Chamberlain SD, Rabindran SK, Kumar R. GSK1838705A inhibits the insulin-like growth factor-1 receptor and anaplastic lymphoma kinase and shows antitumor activity in

experimental models of human cancers. Mol Cancer Ther. 2009 Oct;8(10):2811-20. doi: 10.1158/1535-7163.MCT-09-0423. PMID: 19825801.

In vivo study

1. Zhou X, Shen F, Ma P, Hui H, Pei S, Chen M, Wang Z, Zhou W, Jin B. GSK1838705A, an IGF-1R inhibitor, inhibits glioma cell proliferation and suppresses tumor growth in vivo. Mol Med Rep. 2015 Oct;12(4):5641-6. doi: 10.3892/mmr.2015.4129. Epub 2015 Jul 28. PMID: 26238593; PMCID: PMC4581800.
2. Zhou F, Chen X, Fan S, Tai S, Jiang C, Zhang Y, Hao Z, Zhou J, Shi H, Zhang L, Liang C. GSK1838705A, an insulin-like growth factor-1 receptor/insulin receptor inhibitor, induces apoptosis and reduces viability of docetaxel-resistant prostate cancer cells both in vitro and in vivo. Onco Targets Ther. 2015 Apr 10;8:753-60. doi: 10.2147/OTT.S79105. PMID: 25926740; PMCID: PMC4403692.

7. Bioactivity

Biological target:

GSK1838705A is a reversible IGF-IR and insulin receptor inhibitor with IC50s of 2.0 and 1.6 nM, respectively.

In vitro activity

As shown in Figure 2A and B, the subG1 DNA content in PC-3R cells significantly increased after treatment with GSK1838705A when compared with the control group ($P<0.01$). This study also observed the nuclear morphology in PC-3R cells after treatment with GSK1838705A. After treatment with GSK1838705A, the PC-3R cell nuclei showed consistent morphological changes, including chromatin condensation and nuclear fragmentation, both of which are indicators of cell apoptosis (Figure 2C and D). GSK1838705A-induced cell apoptosis was also confirmed by TUNEL staining assay (Figure 2C). These structural alterations indicate that treatment with GSK1838705A generated apoptosis in docetaxel-resistant PC-3R cells. Further, Western blot analysis showed that treatment with GSK1838705A significantly increased levels of cleaved caspase-3 in resistant cells (Figure 2E), further confirming GSK1838705A-induced apoptosis in resistant cells.

Reference: Onco Targets Ther. 2015; 8: 753–760. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4403692/

In vivo activity

GSK1838705A significantly inhibited the growth of the tumor mass. Treatment with GSK1838705A at 4 or 8 mg/kg resulted in reductions of ~45 and 85% in tumor volume, respectively, 11 days after the first administration (Fig. 4A). No significant weight loss was observed in either treatment group during the course of treatment, indicating that the concentrations of GSK1838705A used were well tolerated by the recipient mice, and no significant cytotoxicity accompanied the GSK1838705A treatment (Fig. 4B). Consistent with the results of the in vitro investigations, GSK1838705A induced significant apoptosis in the tumor cells. Following treatment of tumors with 8 mg/kg GSK1838705A, significant DNA fragmentation was detected using a TUNEL assay and nuclear staining (Fig. 4C). Taken together, these results provided clear evidence indicating that GSK1838705A effectively suppressed the growth of the tumor in vivo by inducing apoptosis of the tumor cells.

Reference: Mol Med Rep. 2015 Oct; 12(4): 5641–5646. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4581800/

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.