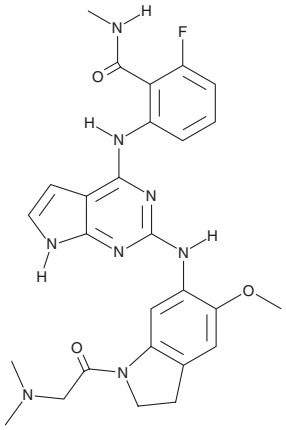
PRODUCT INFORMATION

GSK1838705A

Item No. 24904



CAS Registry No.:	1116235-97-2
Formal Name:	2-[[2-[[1-[2-(dimethylamino)acetyl]-2,3-dihydro-5-methoxy-1H-indol-6-yl]amino]-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amino]-6-fluoro-N-methyl-benzamide
MF:	$C_{27}H_{29}FN_8O_3$
FW:	532.6
Purity:	≥95%
UV/Vis.:	λ_{max}: 286, 327 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

GSK1838705A is supplied as a crystalline solid. A stock solution may be made by dissolving the GSK1838705A in the solvent of choice. GSK1838705A is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of GSK1838705A in these solvents is approximately 2, 33, and 25 mg/ml, respectively.

GSK1838705A is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, GSK1838705A should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. GSK1838705A has a solubility of approximately 0.25 mg/ml in a 1:3 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

GSK1838705A is an inhibitor of the insulin-like growth factor-1 receptor (IGF-1R) and the insulin receptor (IR; IC_{50}s = 2 and 1.6 nM, respectively).[1] It is selective for IGF-1R and IR over a panel of 47 kinases (IC_{50}s = >1,600 nM), however, it also inhibits anaplastic lymphoma kinase (ALK; IC_{50} = 0.5 nM). GSK1838705A inhibits IGF-1 and insulin-induced phosphorylation of IGF-1R and IR in a concentration-dependent manner as well as phosphorylation of the downstream signaling markers Akt, IRS-1, and ERK in MCF-7 breast carcinoma cells. It inhibits growth in a panel of cancer cell lines (EC_{50}s = 24-8,378 nM) with the IGF-1R signaling-dependent multiple myeloma and Ewing's sarcoma cell lines being the most sensitive. *In vivo*, GSK1838705A completely inhibits IGF-1-induced phosphorylation of IGF-1R, Akt, and IRS-1 as well as reduces tumor growth in the COLO 205 and NIH-3T2/LISN mouse xenograft models when administered at doses of ≥1 and ≥10 mg/kg, respectively. It also induces tumor cell apoptosis and reduces tumor growth in U87MG glioma and PC3R prostate cancer mouse xenograft models.[3,4]

References

1. Sabbatini, P., Korenchuk, S., Rowand, J.L., *et al.* 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.* **8(10)**, 2811-2820 (2009).
2. Zhou, X., Shen, F., Ma, P., *et al.* GSK1838705A, an IGF-1R inhibitor, inhibits glioma cell proliferation and suppresses tumor growth *in vivo*. *Mol. Med. Rep.* **12(4)**, 5641-5646 (2015).
3. Zhou, F., Chen, X., Fan, S., *et al.* 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)8**, 753-760 (2015).

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