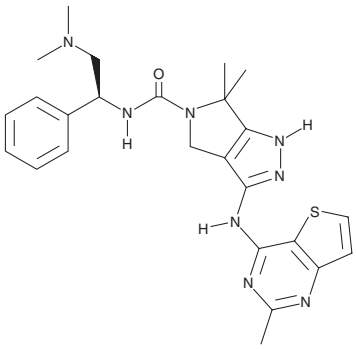
PRODUCT INFORMATION

PF-3758309

Item No. 19186

CAS Registry No.:	898044-15-0
Formal Name:	N-[(1S)-2-(dimethylamino)-1-phenylethyl]-4,6-dihydro-6,6-dimethyl-3-[(2-methylthieno[3,2-d]pyrimidin-4-yl)amino]-pyrrolo[3,4-c]pyrazole-5(1H)-carboxamide
Synonym:	PF-309
MF:	$C_{25}H_{30}N_8OS$
FW:	490.6
Purity:	≥98%
UV/Vis.:	λ_{max}: 266, 312 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

PF-3758309 is supplied as a crystalline solid. A stock solution may be made by dissolving the PF-3758309 in the solvent of choice, which should be purged with an inert gas. PF-3758309 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of PF-3758309 in ethanol is approximately 5 mg/ml and approximately 10 mg/ml in DMSO and DMF.

PF-3758309 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, PF-3758309 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. PF-3758309 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

p21-Activated kinases (PAKs) are STE20 serine/threonine kinases that are vital to normal cell function. Binding of various upstream partners to PAKs results in release of an autoinhibitory domain that blocks activity of the kinase domain.[1] PAKs are upregulated in several human cancers and are potential therapeutic targets for cancer intervention.[1] PF-3758309 is an ATP-competitive inhibitor of PAK4, preventing the phosphorylation of the PAK4 substrate GEF-H1 (IC_{50} = 1.3 nM) and blocking anchorage-independent growth of a panel of tumor cell lines (IC_{50} = 4.7 nM).[2] It also inhibits the ability of kinase domains from other PAKs to phosphorylate peptide substrates (K_is = 18.1, 17.1, 13.7, 190, and 99 nM for PAKs 5, 6, 1, 2, and 3, respectively).[2] PF-3758309 blocks the growth of multiple human tumor xenografts.[2]

References

1. Kumar, R., Gururaj, A.E., and Barnes, C.J. p21-Activated kinases in cancer. *Nat. Rev. Cancer.* **6(6)**, 459-471 (2006).
2. Murray, B.W., Guo, C., Piraino, J., *et al.* Small-molecule p21-activated kinase inhibitor PF-3758309 is a potent inhibitor of oncogenic signaling and tumor growth. *Proc. Natl. Acad. Sci. USA* **107(20)**, 9446-9451 (2010).

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