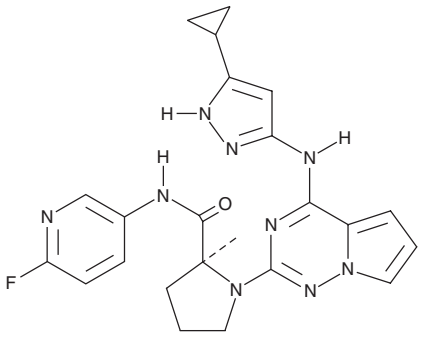
PRODUCT INFORMATION

BMS 754807

Item No. 17505

CAS Registry No.: 1001350-96-4
Formal Name: 1-[4-[(5-cyclopropyl-1H-pyrazol-3-yl) amino]pyrrolo[2,1-f][1,2,4]triazin-2-yl]-N-(6-fluoro-3-pyridinyl)-2-methyl-(2S)-2-pyrrolidinecarboxamide
MF: $C_{23}H_{24}FN_9O$
FW: 461.5
Purity: ≥98%
UV/Vis.: λ_{max}: 244, 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

BMS 754807 is supplied as a crystalline solid. A stock solution may be made by dissolving the BMS 754807 in the solvent of choice, which should be purged with an inert gas. BMS 754807 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of BMS 754807 in these solvents is approximately 30 mg/ml.

BMS 754807 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, BMS 754807 should first be dissolved in ethanol and then diluted with the aqueous buffer of choice. BMS 754807 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of ethanol:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

BMS 754807 is a reversible, orally bioavailable dual inhibitor of insulin-like growth factor 1 receptor (IGF-1R) and insulin receptor (InsR) tyrosine kinases (IC_{50}s = 1.8 and 1.7 nM, respectively).[1,2] It has minimal effect against an array of other tyrosine and serine/threonine kinases.[1] BMS 754807 inhibits cell proliferation or induces apoptosis in a variety of cancer cells *in vitro*.[2] It inhibits the growth of tumor xenografts in mice and this effect is often enhanced by combination therapy with other chemotherapeutics.[2-4] Predictive biomarkers, including elevated IGF-1R expression, for effectiveness of BMS 754807 have been delineated.[5]

References

1. Wittman, M.D., Carboni, J.M., Yang, Z., *et al.* Discovery of a 2,4-disubstituted pyrrolo-[1,2-f][1,2,4]triazine inhibitor (BMS-754807) of insulin-like growth factor receptor (IGF-1R) kinase in clinical development. *J. Med. Chem.* **52(23)**, 7630-7363 (2009).
2. Carboni, J.M., Wittman, M., Yang, Z., *et al.* BMS-754807, a small molecule inhibitor of insulin-like growth factor-1R/IR. *Mol. Cancer Ther.* **8(12)**, 3341-3349 (2009).
3. Awasthi, N., Zhang, C., Ruan, W., *et al.* BMS-754807, a small-molecule inhibitor of insulin-like growth factor-1 receptor/insulin receptor, enhances gemcitabine response in pancreatic cancer. *Mol. Cancer Ther.* **11(12)**, 2644-2653 (2012).
4. Dayyani, F., Parikh, N.U., Varkaris, A.S., *et al.* Combined inhibition of IGF-1R/IR and Src family kinases enhances antitumor effects in prostate cancer by decreasing activated survival pathways. *PLoS One* **7(12)**, e51189 (2012).
5. Huang, F., Chang, H., Greer, A., *et al.* IRS2 copy number gain, KRAS and BRAF mutation status as predictive biomarkers for response to the IGF-1R/IR inhibitor BMS-754807 in colorectal cancer cell lines. *Mol. Cancer Ther.* **14(2)**, 620-630 (2014).

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