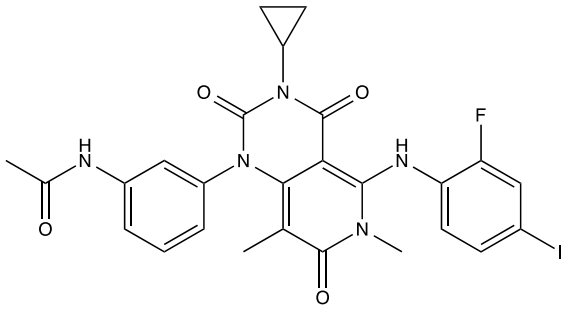
Catalog # 10-4759
Trametinib

CAS# 871700-17-3

N-{3-[3-cyclopropyl-5-(2-fluoro-4-iodophenylamino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydro-2H-pyrido[4,3-d]pyrimidin-1-yl]phenyl}acetamide; GSK1120212

Lot # FBS2163



Trametinib is a highly potent (IC_{50} uMEK1 = 0.7 nM, pp-MEK1 = 14.9 nM)[1] and selective MEK inhibitor displaying selective inhibition of proliferation in various BRAF mutant cancer cell lines (IC_{50} ACHN = 9.8 nM; IC_{50} HT-29 = 0.57 nM)[2]. It is approved for use against unresectable or metastatic BRAF-mutant melanoma alone or in combination with Dabrafenib. Trametinib can limit outgrowth of tumors without directly inhibiting tumor cell proliferation *via* abrogation of cytokine-driven expansion of monocytic myeloid-derived suppressor cells (mMDSC) through a mechanism involving $CD8^+$ T cells.[3,4] Enhanced the efficacy of immunomodulatory therapy in a CT26 model.[5] Trametinib also displays potent anti-arthritic effects.[6]

1) Gilmartin *et al.* (2011), *GSK1120212 (JTP-74057) is an Inhibitor of MEK Activity and Activation with Favorable Pharmacokinetic Properties for Sustained In Vivo Pathway Inhibition;* Clin.Cancer Res. **17** 989
2) Abe *et al*. (2011), *Discovery of a Highly Potent and Selective MEK Inhibitor: GSK1120212 (JTP-74057 DMSO solvate)*; ACS Med. Chem. Lett. **2** 320
3) Allegrezza *et al*. (2016), *Trametinib Drives T-cell-Dependent Control of KRAS Tumors by Inhibiting Pathological Myelopoiesis*; Cancer Res. **76** 6253
4) Vella *et al.* (2014), *MEK inhibition, alone or in combination with BRAF inhibition, affects multiple functions of isolated normal human lymphocytes and dendritic cells;* Cancer Immunol. Res. **2** 351
5) Liu, *et al.* (2015), *The BRAF and MEK Inhibitors Dabrafenib and Trametinib: Effects on Immune Function and in Combination with Immunomodulatory Antibodies Targeting PD-1, PD-L1, and CTLA-4;* Clin. Cancer Res. **21** 1639
6) Yamaguchi *et al.* (2012), *Suppressive effect of an orally active MEK1/2 inhibitor in two different animal models for rheumatoid arthritis: a comparison with leflunomide*; Inflamm. Res. **61** 445

PHYSICAL DATA

Molecular Weight:	615.39
Molecular Formula:	$C_{26}H_{23}FIN_5O_4$
Purity:	>98% by HPLC NMR: Conforms
Solubility:	DMSO (20 mg/mL)
Physical Description:	White solid
Storage and Stability:	Store as supplied at -20°C for up to 1 year from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 2 months.

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