



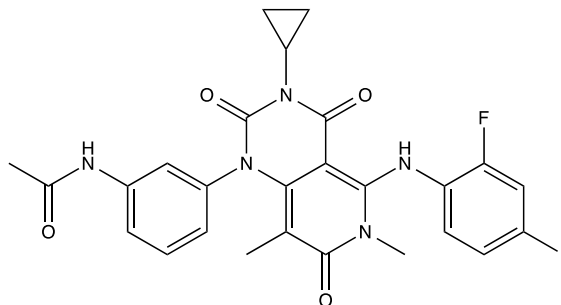
## Catalog # 10-4759

### 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 # FBS2035



Trametinib is a highly potent ( $IC_{50}$  uMEK1 = 0.7 nM, pp-MEK1 = 14.9 nM)<sup>1</sup> 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)<sup>2</sup>. 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<sup>+</sup> T cells.<sup>3,4</sup> Enhanced the efficacy of immunomodulatory therapy in a CT26 model.<sup>5</sup> Trametinib also displays potent anti-arthritis effects.<sup>6</sup>

- 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) Allegranza *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<sub>26</sub>H<sub>23</sub>FIN<sub>5</sub>O<sub>4</sub>  
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.

**Materials provided by Focus Biomolecules are for laboratory research use only and are not intended for human or veterinary applications.**

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