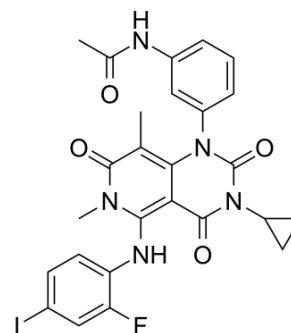


## Trametinib

<b>Cat. No.:</b>	HY-10999		
<b>CAS No.:</b>	871700-17-3		
<b>Molecular Formula:</b>	C <sub>26</sub> H <sub>23</sub> FIN <sub>5</sub> O <sub>4</sub>		
<b>Molecular Weight:</b>	615.39		
<b>Target:</b>	MEK; Autophagy; Apoptosis		
<b>Pathway:</b>	MAPK/ERK Pathway; Autophagy; Apoptosis		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

<b>In Vitro</b>	DMSO : 33.33 mg/mL (54.16 mM; Need ultrasonic)					
		Solvent Concentration	Mass	1 mg	5 mg	10 mg
	<b>Preparing Stock Solutions</b>	1 mM		1.6250 mL	8.1249 mL	16.2499 mL
		5 mM		0.3250 mL	1.6250 mL	3.2500 mL
10 mM			0.1625 mL	0.8125 mL	1.6250 mL	
Please refer to the solubility information to select the appropriate solvent.						
<b>In Vivo</b>	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.5 mg/mL (4.06 mM); Clear solution  2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (4.06 mM); Clear solution					

### BIOLOGICAL ACTIVITY

<b>Description</b>	Trametinib (GSK1120212; JTP-74057) is an orally active MEK inhibitor that inhibits MEK1 and MEK2 with IC <sub>50</sub> s of about 2 nM. Trametinib activates autophagy and induces apoptosis <sup>[1][2]</sup> .	
<b>IC<sub>50</sub> &amp; Target</b>	MEK1 2 nM (IC <sub>50</sub> )	MEK2 2 nM (IC <sub>50</sub> )
<b>In Vitro</b>	Trametinib (GSK1120212; JTP-74057) (0.1-100 nM) blocks tumor necrosis factor- $\alpha$ and interleukin-6 production from peripheral blood mononuclear cells (PBMCs). Trametinib (JTP-74057) inhibits the growth of 9 out of 10 human colorectal cancer cell lines, and they shows cell-cycle arrest at the G1 phase after drug treatment <sup>[1]</sup> . The combination of GSK2118436 and Trametinib (GSK1120212) effectively inhibits cell growth, decreases ERK	

phosphorylation, decreases cyclin D1 protein, and increases p27(kip1) protein in the resistant clones<sup>[2]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### In Vivo

Adjuvant-induced arthritis (AIA) and type II collagen-induced arthritis (CIA) development are suppressed almost completely by 0.1 mg/kg of Trametinib (GSK1120212; JTP-74057) or 10 mg/kg of HWA486<sup>[1]</sup>.  
Trametinib (0.3 mg/kg, 1 mg/kg, p.o.) is effective in inhibiting the HT-29 xenograft growth in a nude mouse xenograft model<sup>[2]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

#### Kinase Assay<sup>[2]</sup>

The nonphosphorylated myelin basic protein (MBP) is coated onto an ELISA plate, and the active form of B-Raf/c-Raf is mixed with unphosphorylated MEK1/MEK2 and ERK2 in 10  $\mu$ M ATP and 12.5 mM MgCl<sub>2</sub> containing MOPS buffer in the presence of various concentrations of Trametinib (JTP-74057). The phosphorylation of MBP is detected by the anti-phosphoMBP antibody. Kinase inhibitory activities against a total of 99 kinases are tested at 10  $\mu$ M ATP<sup>[2]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### Cell Assay<sup>[2]</sup>

Cells are treated with various concentrations of Trametinib (JTP-74057) in 100 mm dishes for 3 or 4 days. Both floating and adherent cells are collected and fixed with 70% ethanol. After washing with PBS, the cells are suspended in 100  $\mu$ L/mL RNase and 25  $\mu$ L/mL Propidium iodide (PI) and incubated at 37°C for 30 min in the dark. The DNA content of each single cell is determined using the flow cytometer Cytomics FC500 or Guava EasyCyte plus<sup>[2]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### Animal Administration<sup>[2]</sup>

Mice<sup>[2]</sup>  
Female BALB/c-nu/nu mice are used. On day 0, HT-29 cells or COLO205 cells suspended in ice-cold HBSS (-) are inoculated subcutaneously into the right flank of the mice at  $5 \times 10^6$  cells/100  $\mu$ L/site or  $1 \times 10^6$  cells/100  $\mu$ L/site, respectively. The acetic acid-solvated form of Trametinib (JTP-74057, 0.3 mg/kg, 1 mg/kg) is dissolved in 10% Cremophor EL-10% PEG400 and is administered orally once daily for 14 days from the day when the mean tumor volume reached 100 mm<sup>3</sup>. The tumor length [L(mm)] and width [W(mm)] are measured using a microgauge twice a week after commencement of dosing, and the tumor volume is calculated using the following formula: tumor volume (mm<sup>3</sup>)=L×W×W/2.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Cell. 2018 Aug 9;174(4):843-855.e19.
- Cancer Discov. 2020 Aug;10(8):1226-1239.
- Cancer Discov. 2018 Mar;8(3):354-369.
- Cancer Discov. 2015 Sep;5(9):960-71.
- Cancer Discov. 2012 Oct;2(10):934-47.

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## REFERENCES

[1]. Yamaguchi T, et al. Suppressive effect of an orally active MEK1/2 inhibitor in two different animal models for rheumatoid arthritis: a comparison with HWA486. *Inflamm Res*, 2012, 61(5), 445-454.

[2]. Yamaguchi T, et al. Antitumor activities of JTP-74057 (GSK1120212), a novel MEK1/2 inhibitor, on colorectal cancer cell lines in vitro and in vivo. *Int J Oncol*, 2011, 39(1),

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23-31.

[3]. Abe H, et al. Discovery of a Highly Potent and Selective MEK Inhibitor: GSK1120212 (JTP-74057 DMSO Solvate). ACS Med Chem Lett. 2011 Feb 28;2(4):320-4.

[4]. Liu H, et al. Identifying and Targeting Sporadic Oncogenic Genetic Aberrations in Mouse Models of Triple Negative Breast Cancer. Cancer Discov. 2018 Mar;8(3):354-369.

[5]. Lai J, et al. Elimination of melanoma by sortase A-generated TCR-like antibody-drug conjugates (TL-ADCs) targeting intracellular melanoma antigen MART-1. Biomaterials. 2018 Sep;178:158-169.

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**Caution: Product has not been fully validated for medical applications. For research use only.**

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