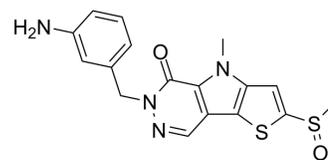


## TEPP-46

<b>Cat. No.:</b>	HY-18657		
<b>CAS No.:</b>	1221186-53-3		
<b>Molecular Formula:</b>	C <sub>17</sub> H <sub>16</sub> N <sub>4</sub> O <sub>2</sub> S <sub>2</sub>		
<b>Molecular Weight:</b>	372.46		
<b>Target:</b>	Pyruvate Kinase		
<b>Pathway:</b>	Metabolic Enzyme/Protease		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : 50 mg/mL (134.24 mM; Need ultrasonic)

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.6849 mL	13.4243 mL	26.8485 mL
	5 mM	0.5370 mL	2.6849 mL	5.3697 mL
	10 mM	0.2685 mL	1.3424 mL	2.6849 mL

Please refer to the solubility information to select the appropriate solvent.

#### In Vivo

- Add each solvent one by one: 50% PEG300 >> 50% saline  
Solubility: 10 mg/mL (26.85 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 0.5% CMC-Na/saline water  
Solubility: 5 mg/mL (13.42 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline  
Solubility: ≥ 2.87 mg/mL (7.71 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 2.5 mg/mL (6.71 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: 2.5 mg/mL (6.71 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.08 mg/mL (5.58 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

TEPP-46 (ML-265) is a potent and selective pyruvate kinase M2 (PKM2) activator with an AC<sub>50</sub> of 92 nM, showing little or no

	effect on PKM1, PKL and PKR <sup>[1]</sup> .
<b>In Vitro</b>	TEPP-46 and DASA-58 activate PKM2 by a mechanism similar to that of the endogenous activator FBP. Pre-treatment of cells with TEPP-46 or DASA-58 prevents pervanadate-induced inhibition of PKM2 activity. TEPP-46 also induces a decrease in the intracellular levels of acetyl-coA, lactate, ribose phosphate and serine <sup>[1]</sup> . TEPP-46 inhibits LPS-induced Hif-1 $\alpha$ and IL-1 $\beta$ , as well as the expression of a range of other Hif-1 $\alpha$ -dependent genes. TEPP-46 treatment significantly downregulates the expression of the M1 markers Il12p40 and Cxcl-10. Activation of PKM2 using TEPP-46 significantly inhibits FSL-1 and CpG-induced Il1b mRNA expression. TEPP-46 inhibits Mtb-induced Il1b mRNA levels, boosts Mtb-induced levels of Il10 mRNA, and has no effect on levels of Tnf <sup>[2]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
<b>In Vivo</b>	TEPP-46 exhibits good oral bioavailability with relatively low clearance, long half-life, and good volume of distribution-parameters that predict for drug exposure in tumor tissues. TEPP-46 at 150 mg/kg readily achieves maximal PKM2 activation measured in A549 xenograft tumors <sup>[1]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

<b>Cell Assay</b> <sup>[1]</sup>	2,000 cells are seeded in 96-well plates 24 h prior to treatment start. CellTiter96 <sup>®</sup> AQueous is used to assess cell viability following oxidant and PKM2 activator combination treatments. MTS: (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium). MCE has not independently confirmed the accuracy of these methods. They are for reference only.
<b>Animal Administration</b> <sup>[1]</sup>	H1299 parental and H1299 cells with constitutive expression of a mouse PKM1 cDNA (H1299-PKM1 cells) are propagated in RPMI supplemented with 10% fetal bovine serum, 2 mM glutamine, and hygromycin for transgene selection. Cells are harvested, resuspended in sterile PBS, and 5 $\times$ 10 <sup>5</sup> cells are injected subcutaneously into nu/nu mice. Tumor growth is monitored by caliper measurement, the mice are sacrificed and tumors harvested after the time indicated. Tumors are weighed, divided and either flash-frozen in liquid nitrogen or fixed in formalin for later analysis. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Kidney Int. 2023 Jan 30;S0085-2538(23)00052-2.
- Sci Transl Med. 2019 Feb 6;11(478):eaau8866.
- Nat Commun. 2022 May 16;13(1):2698.
- Neuro Oncol. 2023 Jun 5;noad103.
- Sci Adv. 2022 Sep 23;8(38):eabo0987.

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## REFERENCES

- [1]. Anastasiou D, et al. Pyruvate kinase M2 activators promote tetramer formation and suppress tumorigenesis. Nat Chem Biol. 2012 Oct;8(10):839-847.
- [2]. Palsson-McDermott EM, et al. Pyruvate kinase M2 regulates Hif-1 $\alpha$  activity and IL-1 $\beta$  induction and is a critical determinant of the warburg effect in LPS-activated macrophages. Cell Metab. 2015 Jan 6;21(1):65-80.

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

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