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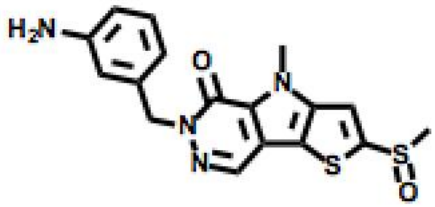
Pyruvate Kinase M2 (PKM2) Activator – TEPP-46 (ML265)

Chemical Name: 6-(3-aminobenzyl)-4-methyl-2-(methylsulfinyl)-4,6-dihydro-5H-thieno[2',3':4,5]pyrrolo[2,3-d]pyridazin-5-one



Molecular Weight:	372.46
Formula:	$C_{17}H_{16}N_4O_2S_2$
Purity:	≥98%
CAS#:	1221186-53-3
Solubility:	DMSO up to 100 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

TEPP-46 (ML265) is a potent and selective Pyruvate kinase M2 (PKM2) activator with EC_{50} ~92 nM. It demonstrates >100-fold selectivity for PKM2 over the related PKM1, PKR, and PKL isoforms. It can stabilize pyruvate kinase subunit interactions, promote PKM2 tetramer formation and prevent inhibition by phosphotyrosine signaling. It can alter metabolism in cultured cells, and inhibit xenograft tumor growth in vivo. TEPP-46 inhibits LPS-induced Hif-1α and IL-1β, as well as the expression of a range of other Hif-1α-dependent genes.

How to Use:

In vitro: TEPP-46 was used at 1-10 μM final concentration in various assays.

In vivo: TEPP-46 was dosed to mice orally at 50 mg/Kg twice per day.

Reference:

1. Anastasiou D, et al. Pyruvate kinase M2 activators promote tetramer formation and suppress tumorigenesis. (2012) Nat Chem Biol. 8(10):839-47.
2. Palsson-McDermott EM, et al. Pyruvate kinase M2 regulates Hif-1α activity and IL-1β induction and is a critical determinant of the warburg effect in LPS-activated macrophages. (2015) Cell Metab. 21(1):65-80.
3. Giannoni E, et al. Targeting stromal-induced pyruvate kinase M2 nuclear translocation impairs oxphos and prostate cancer metastatic spread. (2015) Oncotarget. 6(27):24061-74.
4. Walsh MJ, et al. ML265: A potent PKM2 activator induces tetramerization and reduces tumor formation and size in a mouse xenograft model. Probe Reports from the NIH Molecular Libraries Program.