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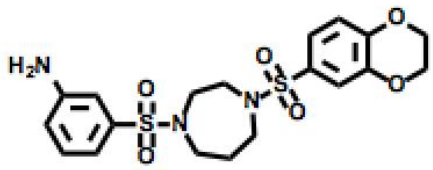
Pyruvate Kinase M2 (PKM2) Activator – DASA-58 (ML203)

Chemical Name: 3-((4-((2,3-dihydrobenzo[b][1,4]dioxin-6-yl)sulfonyl)-1,4-diazepan-1-yl)sulfonyl)aniline



Molecular Weight:	453.53
Formula:	$C_{19}H_{23}N_3O_6S_2$
Purity:	≥98%
CAS#:	1203494-49-8
Solubility:	DMSO up to 100 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

DASA-58 (ML203) is a potent and selective Pyruvate kinase M2 (PKM2) activator with EC_{50} ~38 nM. 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. DASA-58 inhibits LPS-induced Hif-1α and IL-1β, as well as the expression of a range of other Hif-1α-dependent genes. In PC3 cells, DASA-58 impairs stromal-induced EMT program by restoring PK activity and abrogating the nuclear translocation of PKM2, as well as its association with HIF-1α. It also dramatically reduces (~6-fold) CAFs-induced lung metastases formation in PC3 cells.

How to Use:

In vitro: DASA-58 was used at 1-10 μM final concentration in various assays.

In vivo: DASA-58 (40 μM) treated cells are injected into male SCID-bg/bg mice bearing PC3 tumors by IV.

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.