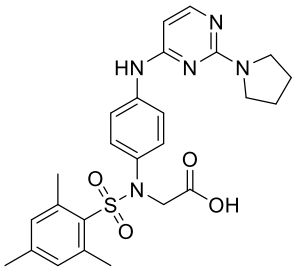
Product data sheet

MedKoo Cat#: 408066 Name: DDO-5936 CAS#: 2355377-13-6 (free acid) Chemical Formula: $C_{25}H_{29}N_5O_4S$ Exact Mass: 495.194 Molecular Weight: 495.598	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

DDO-5936 is a potent PPI inhibitor targeting Hsp90-Cdc37 protein-protein interaction (PPI) as Orally Active Inhibitors for the Treatment of Colorectal Cancer. DDO-5936 disrupted the Hsp90-Cdc37 PPI both in vitro and in vivo via binding to a previously unknown site on Hsp90 involving Glu47, one of the binding determinants for the Hsp90-Cdc37 PPI, leading to selective down-regulation of Hsp90 kinase clients in HCT116 cells. In addition, inhibition of Hsp90-Cdc37 complex formation by DDO-5936 resulted in a remarkable cyclin-dependent kinase 4 decrease and consequent inhibition of cell proliferation through Cdc37-dependent cell cycle arrest.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.02 mL	10.09 mL	20.18 mL
5 mM	0.40 mL	2.02 mL	4.04 mL
10 mM	0.20 mL	1.01 mL	2.02 mL
50 mM	0.04 mL	0.20 mL	0.40 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

Wang L, Jiang J, Zhang L, Zhang Q, Zhou J, Li L, Xu X, You Q. Discovery and Optimization of Small Molecules Targeting the Protein-Protein Interaction of Heat Shock Protein 90 (Hsp90) and Cell Division Cycle 37 as Orally Active Inhibitors for the Treatment of Colorectal Cancer. J Med Chem. 2020 Feb 13;63(3):1281-1297. doi: 10.1021/acs.jmedchem.9b01659. Epub 2020 Jan 24. PMID: 31935086.

In vivo study

Wang L, Zhang L, Li L, Jiang J, Zheng Z, Shang J, Wang C, Chen W, Bao Q, Xu X, Jiang Z, Zhang J, You Q. Small-molecule inhibitor targeting the Hsp90-Cdc37 protein-protein interaction in colorectal cancer. Sci Adv. 2019 Sep 18;5(9):eaax2277. doi: 10.1126/sciadv.aax2277. PMID: 31555737; PMCID: PMC6750927.

7. Bioactivity

Biological target:

Hsp90-Cdc37 protein-protein interaction.

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In vitro activity

Based on a first specific small-molecule inhibitor targeting Hsp90-Cdc37 PPI (DDO-5936), which was previously reported by this group, a preliminary investigation of the structure-activity relationships and pharmacodynamic evaluations was conducted to improve the potency and drug-like properties. Here, efforts resulted in the currently best inhibitor 18h with improved binding affinity (Kd = 0.5 μM) and cellular inhibitory activity (IC50 = 1.73 μM). Both in vitro and in vivo assays revealed that 18h could efficiently block the Hsp90-Cdc37 interaction to specifically inhibit kinase clients of Hsp90. Furthermore, 18h showed ideal physiochemical properties with favorable stability, leading to an oral efficacy in vivo.

Reference: Wang L, Jiang J, Zhang L, Zhang Q, Zhou J, Li L, Xu X, You Q. Discovery and Optimization of Small Molecules Targeting the Protein-Protein Interaction of Heat Shock Protein 90 (Hsp90) and Cell Division Cycle 37 as Orally Active Inhibitors for the Treatment of Colorectal Cancer. J Med Chem. 2020 Feb 13;63(3):1281-1297. doi: 10.1021/acs.jmedchem.9b01659. Epub 2020 Jan 24. PMID: 31935086.

In vivo activity

Here, DDO-5936 as a small-molecule inhibitor of the Hsp90-Cdc37 protein-protein interaction (PPI) was indenitified in colorectal cancer. DDO-5936 disrupted the Hsp90-Cdc37 PPI both in vitro and in vivo via binding to a previously unknown site on Hsp90 involving Glu47, one of the binding determinants for the Hsp90-Cdc37 PPI, leading to selective down-regulation of Hsp90 kinase clients in HCT116 cells. In addition, inhibition of Hsp90-Cdc37 complex formation by DDO-5936 resulted in a remarkable cyclin-dependent kinase 4 decrease and consequent inhibition of cell proliferation through Cdc37-dependent cell cycle arrest. Together, results demonstrated DDO-5936 as an identified specific small-molecule inhibitor of the Hsp90-Cdc37 PPI that could be used to comprehensively investigate alternative approaches targeting Hsp90 chaperone cycles for cancer therapy.

Reference: Wang L, Zhang L, Li L, Jiang J, Zheng Z, Shang J, Wang C, Chen W, Bao Q, Xu X, Jiang Z, Zhang J, You Q. Small-molecule inhibitor targeting the Hsp90-Cdc37 protein-protein interaction in colorectal cancer. Sci Adv. 2019 Sep 18;5(9):eaax2277. doi: 10.1126/sciadv.aax2277. PMID: 31555737; PMCID: PMC6750927.