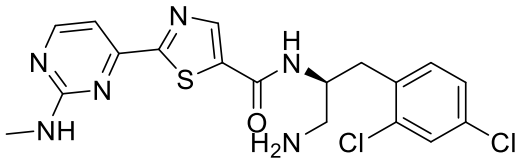
Product data sheet

MedKoo Cat#: 205737 Name: Debio-0932 (CUDC305) CAS#: 1061318-81-7 Chemical Formula: $C_{22}H_{30}N_6O_2S$ Exact Mass: 442.21509 Molecular Weight: 442.58	
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:

Debio 0932, also known as CUDC-305, is a novel heat shock protein 90 (HSP90) inhibitor with strong affinity for HSP90 alpha/beta, high oral bioavailability and potent anti-proliferative activity against a broad range of cancer cell lines (with a mean IC50 of 220 nmol/L), including many non-small cell lung cancer (NSCLC) cell lines which are resistant to standard-of-care (SOC) agents. Debio 0932 potently inhibits tumour growth in subcutaneous xenograft models of a number of solid and haematological malignancies, including models of NSCLC which harbour mutations conferring acquired or primary erlotinib resistance.

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
DMSO	33	74.56

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.26 mL	11.30 mL	22.59 mL
5 mM	0.45 mL	2.26 mL	4.52 mL
10 mM	0.23 mL	1.13 mL	2.26 mL
50 mM	0.05 mL	0.23 mL	0.45 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

1. Bao R, Lai CJ, Qu H, Wang D, Yin L, Zifcak B, Atoyan R, Wang J, Samson M, Forrester J, DellaRocca S, Xu GX, Tao X, Zhai HX, Cai X, Qian C. CUDC-305, a novel synthetic HSP90 inhibitor with unique pharmacologic properties for cancer therapy. Clin Cancer Res. 2009 Jun 15;15(12):4046-57. doi: 10.1158/1078-0432.CCR-09-0152. Epub 2009 Jun 9. PMID: 19509149.

2. Bao R, Lai CJ, Wang DG, Qu H, Yin L, Zifcak B, Tao X, Wang J, Atoyan R, Samson M, Forrester J, Xu GX, DellaRocca S, Borek M, Zhai HX, Cai X, Qian C. Targeting heat shock protein 90 with CUDC-305 overcomes erlotinib resistance in non-small cell lung cancer. Mol Cancer Ther. 2009 Dec;8(12):3296-306. doi: 10.1158/1535-7163.MCT-09-0538. PMID: 19952121.

In vivo study

1. Bao R, Lai CJ, Qu H, Wang D, Yin L, Zifcak B, Atoyan R, Wang J, Samson M, Forrester J, DellaRocca S, Xu GX, Tao X, Zhai HX, Cai X, Qian C. CUDC-305, a novel synthetic HSP90 inhibitor with unique pharmacologic properties for cancer therapy. Clin Cancer Res. 2009 Jun 15;15(12):4046-57. doi: 10.1158/1078-0432.CCR-09-0152. Epub 2009 Jun 9. PMID: 19509149.

2. Bao R, Lai CJ, Wang DG, Qu H, Yin L, Zifcak B, Tao X, Wang J, Atoyan R, Samson M, Forrester J, Xu GX, DellaRocca S, Borek M, Zhai HX, Cai X, Qian C. Targeting heat shock protein 90 with CUDC-305 overcomes erlotinib resistance in non-small cell lung cancer. Mol Cancer Ther. 2009 Dec;8(12):3296-306. doi: 10.1158/1535-7163.MCT-09-0538. PMID: 19952121.

7. Bioactivity

Biological target:

Debio 0932 (CUDC-305) is an orally active HSP90 inhibitor, with IC50s of 100 and 103 nM for HSP90α and HSP90β, respectively.

In vitro activity

Whether HSP90 inhibition by CUDC-305 can induce degradation of oncoproteins was examined. In the HER2 overexpressing BT-474 breast cancer cells, CUDC-305 treatment reduced the levels of HER2/phosphorylated HER2 and phosphorylated HER3 and suppressed downstream AKT and RAF/MEK/ERK signaling. CUDC-305 also down-regulated survivin and cyclin D1, further supporting its proapoptotic and antiproliferative roles in cancer cells (Fig. 1B). The reduction of HSP90 client proteins was concurrent with an increase of HSP70, a marker of HSP90 inhibition. These results suggest that CUDC-305 specifically targets HSP90 and suppresses receptor tyrosine kinase signaling. To confirm its anticancer activity, the growth inhibitory effects of CUDC-305 was tested against a total of 40 human cancer cell lines, including 34 solid and 6 hematologic tumor–derived lines (Table 1). CUDC-305 inhibited the proliferation of these cancer cell lines with an IC50, ranging from 40 to 900 nmol/L (mean IC50, 220 nmol/L).

Reference: Clin Cancer Res. 2009 Jun 15;15(12):4046-57.
http://clincancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=19509149

In vivo activity

Given the therapeutically relevant exposure of CUDC-305 in brain tissue, the efficacy of the compound in the U87MG glioblastoma tumor models was tested. A single-dose PD study was first conducted to evaluate the duration of its biological effects in tumor xenografts implanted s.c. After a single oral dosing of CUDC-305 at 160 mg/kg, U87MG tumors were collected at various time points over a 48-hour period and subjected to Western blot analysis. As shown in Fig. 2B, HSP70 was induced from 3 to 48 hours after compound administration, correlating with our earlier findings of extended tumor exposure (9.4 μmol/L at 48 hours, 20-fold above IC50 in U87MG cells) after a single oral dosing of CUDC-305 at 160 mg/kg. Therefore, an every-other-day (q2d) dosing regimen was adopted for most efficacy studies. HSP90 client proteins, including p-AKT, and c-RAF were shown to be down-regulated, along with the induction of apoptosis as measured by poly(ADP-ribose) polymerase cleavage (Fig. 2B). Note that although minimal or no inhibition was observed for c-MET or total AKT in this single-dose PD study, inhibition of these HSP90 client proteins was achieved after multiple oral doses, as shown in our subsequent efficacy-PD study in the same tumor model.

Reference: Clin Cancer Res. 2009 Jun 15;15(12):4046-57.
http://clincancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=19509149