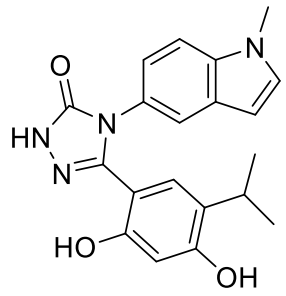
Product data sheet

MedKoo Cat#: 202703 Name: Ganetespib (STA-9090) CAS#: 888216-25-9 Chemical Formula: $C_{20}H_{20}N_4O_3$ Exact Mass: 364.15354 Molecular Weight: 364.4	
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:
Ganetespib, also known as STA-9090, is a synthetic small-molecule inhibitor of heat shock protein 90 (Hsp90) with potential antineoplastic activity. Hsp90 inhibitor STA-9090 binds to and inhibits Hsp90, resulting in the proteasomal degradation of oncogenic client proteins, the inhibition of cell proliferation and the elevation of heat shock protein 72 (Hsp72); it may inhibit the activity of multiple kinases, such as c-Kit, EGFR, and Bcr-Abl, which as client proteins depend on functional HsP90 for maintenance.

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	32	87.82

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.74 mL	13.72 mL	27.44 mL
5 mM	0.55 mL	2.74 mL	5.49 mL
10 mM	0.27 mL	1.37 mL	2.74 mL
50 mM	0.05 mL	0.27 mL	0.55 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. Proia DA, Foley KP, Korbut T, Sang J, Smith D, Bates RC, Liu Y, Rosenberg AF, Zhou D, Koya K, Barsoum J, Blackman RK. Multifaceted intervention by the Hsp90 inhibitor ganetespib (STA-9090) in cancer cells with activated JAK/STAT signaling. PLoS One. 2011 Apr 14;6(4):e18552. doi: 10.1371/journal.pone.0018552. PMID: 21533169; PMCID: PMC3077378.

2. Shimamura T, Perera SA, Foley KP, Sang J, Rodig SJ, Inoue T, Chen L, Li D, Carretero J, Li YC, Sinha P, Carey CD, Borgman CL, Jimenez JP, Meyerson M, Ying W, Barsoum J, Wong KK, Shapiro GI. Ganetespib (STA-9090), a nongeldanamycin HSP90 inhibitor, has potent antitumor activity in in vitro and in vivo models of non-small cell lung cancer. Clin Cancer Res. 2012 Sep 15;18(18):4973-85. doi: 10.1158/1078-0432.CCR-11-2967. Epub 2012 Jul 17. PMID: 22806877; PMCID: PMC3477583.

In vivo study

1. Shimamura T, Perera SA, Foley KP, Sang J, Rodig SJ, Inoue T, Chen L, Li D, Carretero J, Li YC, Sinha P, Carey CD, Borgman CL, Jimenez JP, Meyerson M, Ying W, Barsoum J, Wong KK, Shapiro GI. Ganetespib (STA-9090), a nongeldanamycin HSP90 inhibitor, has potent antitumor activity in in vitro and in vivo models of non-small cell lung cancer. Clin Cancer Res. 2012 Sep 15;18(18):4973-85. doi: 10.1158/1078-0432.CCR-11-2967. Epub 2012 Jul 17. PMID: 22806877; PMCID: PMC3477583.

2. Ying W, Du Z, Sun L, Foley KP, Proia DA, Blackman RK, Zhou D, Inoue T, Tatsuta N, Sang J, Ye S, Acquaviva J, Ogawa LS, Wada Y, Barsoum J, Koya K. Ganetespib, a unique triazolone-containing Hsp90 inhibitor, exhibits potent antitumor activity and a superior safety profile for cancer therapy. Mol Cancer Ther. 2012 Feb;11(2):475-84. doi: 10.1158/1535-7163.MCT-11-0755. Epub 2011 Dec 5. PMID: 22144665.

7. Bioactivity

Biological target:

Ganetespib (STA-9090) is an HSP90 inhibitor with IC50 of 4 nM in OSA 8 cells, induces apoptosis of OSA cells while normal osteoblasts are not affected; active metabolite of STA-1474.

In vitro activity

JAK kinases are established Hsp90 client proteins and here we show that the novel small molecule Hsp90 inhibitor ganetespib (formerly STA-9090) exhibits potent in vitro activity in a range of solid and hematological tumor cells that are dependent on JAK2 activity for growth and survival. Of note, ganetespib treatment results in sustained depletion of JAK2, including the constitutively active JAK2(V617F) mutant, with subsequent loss of STAT activity and reduced STAT-target gene expression. The NCI-H1975 non-small cell lung cancer (NSCLC) cell line expresses the Hsp90 client EGFRL858R/T790M, a constitutively activated and erlotinib-resistant form of EGFR, and ganetespib treatment resulted in a dose-dependent decrease in EGFR expression in these cells (Fig. 2A). Moreover, ganetespib also induced potent degradation of JAK2 and loss of phosphorylated STAT3 in a dose-dependent manner. Inactivation of AKT and GSK3β, proteins important in regulating apoptosis, was observed with a similar dose response to that of JAK2/STAT3 signaling. Recently it was shown that JAK2 can modulate the activity of additional apoptotic regulators such as BAD and BCL-XL to promote cell survival. Consistent with this, a concomitant reduction was detected in the levels of phosphorylated BAD (Fig. 2A), thus reducing the pro-apoptotic activity of this protein. These data suggest a potential mechanism to account for the cytotoxic response observed with ganetespib treatment (Fig. 1A).

Response: PLoS One. 2011 Apr 14;6(4):e18552. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/21533169/

In vivo activity

In mice bearing NCI-H1975 (EGFR L858R/T790M) xenografts, ganetespib was rapidly eliminated from plasma and normal tissues but was maintained in tumor with t(1/2) 58.3 hours, supporting once-weekly dosing experiments, in which ganetespib produced greater tumor growth inhibition than 17-AAG. However, after a single dose, reexpression of mutant EGFR occurred by 72 hours, correlating with reversal of antiproliferative and proapoptotic effects. Consecutive day dosing resulted in xenograft regressions, accompanied by more sustained pharmacodynamic effects. Ganetespib also showed activity against mouse lung adenocarcinomas driven by oncogenic ERBB2 YVMA.

Reference: Clin Cancer Res. 2012 Sep 15;18(18):4973-85. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/22806877/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.