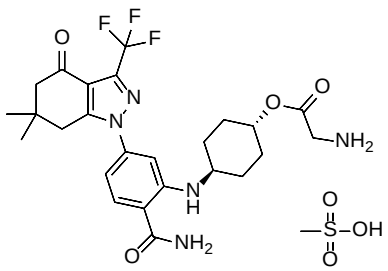
Product data sheet

MedKoo Cat#: 206835 Name: PF-04929113 mesylate CAS#: 1173111-67-5 (mesylate) Chemical Formula: $C_{26}H_{34}F_3N_5O_7S$ Molecular Weight: 617.64	
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:

PF-04929113, also known as SNX-5422; is a synthetic prodrug targeting the human heat-shock protein 90 (Hsp90) with potential antineoplastic activity. Although the mechanism of action remains to be fully elucidated, Hsp90 inhibitor SNX-5542 is rapidly converted to SNX-2112, which accumulates in tumors relative to normal tissues. SNX-2112 inhibits Hsp90, which may result in the proteasomal degradation of oncogenic client proteins, including HER2/ERBB2, and the inhibition of tumor cell proliferation.

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	46.85	75.85

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.62 mL	8.10 mL	16.19 mL
5 mM	0.32 mL	1.62 mL	3.24 mL
10 mM	0.16 mL	0.81 mL	1.62 mL
50 mM	0.03 mL	0.16 mL	0.32 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. Lamoureux F, Thomas C, Yin MJ, Kuruma H, Fazli L, Gleave ME, Zoubeidi A. A novel HSP90 inhibitor delays castrate-resistant prostate cancer without altering serum PSA levels and inhibits osteoclastogenesis. Clin Cancer Res. 2011 Apr 15;17(8):2301-13. doi: 10.1158/1078-0432.CCR-10-3077. Epub 2011 Feb 24. Erratum in: Clin Cancer Res. 2011 Jul 15;17(14):4916. PMID: 21349995; PMCID: PMC4437585.

In vivo study

1. Lamoureux F, Thomas C, Yin MJ, Kuruma H, Fazli L, Gleave ME, Zoubeidi A. A novel HSP90 inhibitor delays castrate-resistant prostate cancer without altering serum PSA levels and inhibits osteoclastogenesis. Clin Cancer Res. 2011 Apr 15;17(8):2301-13. doi: 10.1158/1078-0432.CCR-10-3077. Epub 2011 Feb 24. Erratum in: Clin Cancer Res. 2011 Jul 15;17(14):4916. PMID: 21349995; PMCID: PMC4437585.

7. Bioactivity

Biological target:

PF 04217903 mesylate is a highly selective, high affinity MET inhibitor (Ki = 6-7 nM against wild type c-Met).

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In vitro activity

PF-04928473 inhibited cell growth in a panel of prostate cancer cells, induced cell cycle arrest at sub-G1 and led to apoptosis and increased caspase-3 activity. These biologic events were accompanied by decreased activation of Akt and Erk as well as decreased expression of Her2, and decreased AR expression and activation in vitro. PF-04928473 abrogated RANKL-induced osteoclast differentiation by affecting NF-kB activation and Src phosphorylation.

Reference: Clin Cancer Res. 2011 Jul 15;17(14):4916. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4437585/

In vivo activity

The effects of PF-04929113 on castrate-resistant LNCaP tumor growth were evaluated. Mice treated with PF-04929113 (n=8) exhibited a significant decrease in tumor volume compared with control mice starting at the day 17 (240mm3 and 1293.9mm3, respectively) and after 45 days (459.2mm3 and 2818.2mm3, respectively; Fig. 3A). When each animal was considered individually, the incidence of mice progressing with a tumor volume $\geqslant$ 500mm3 was significantly diminished by day 22 in PF-04929113-treated animals (0/8) compared with controls (8/8, Fig 3B). Rate of tumor progression at days 10 and 45 was also significantly decreased (1947.8mm3 for control mice vs 244.1mm3 for treated mice, $p<0.001$) in the treatment group, compared with control mice (Fig 3C). Consequently, progression-free ($p<0.001$) and cancer specific ($p<0.001$) survival were significantly prolonged in the PF-04929113-treated group (Fig 3D). These data demonstrate that targeting Hsp90 by PF-04929113 significantly inhibits castrate resistant tumor growth and prolongs survival in the LNCaP tumor model.

Reference: Clin Cancer Res. 2011 Jul 15;17(14):4916. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4437585/