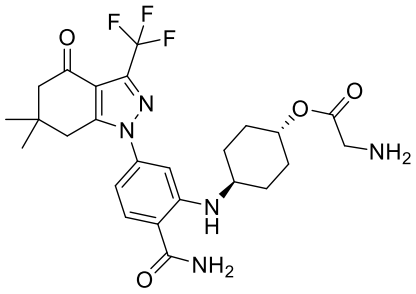
Product data sheet

MedKoo Cat#: 206217 Name: PF-04929113 free base CAS#: 908115-27-5 (free base) Chemical Formula: $C_{25}H_{30}F_3N_5O_4$ Exact Mass: 521.22499 Molecular Weight: 521.53	
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	1.0	1.9

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.92 mL	9.59 mL	19.17 mL
5 mM	0.38 mL	1.92 mL	3.83 mL
10 mM	0.19 mL	0.96 mL	1.92 mL
50 mM	0.04 mL	0.19 mL	0.38 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. Huang KH, Veal JM, Fadden RP, Rice JW, Eaves J, Strachan JP, Barabasz AF, Foley BE, Barta TE, Ma W, Silinski MA, Hu M, Partridge JM, Scott A, DuBois LG, Freed T, Steed PM, Ommen AJ, Smith ED, Hughes PF, Woodward AR, Hanson GJ, McCall WS, Markworth CJ, Hinkley L, Jenks M, Geng L, Lewis M, Otto J, Pronk B, Verleysen K, Hall SE. Discovery of novel 2-aminobenzamide inhibitors of heat shock protein 90 as potent, selective and orally active antitumor agents. J Med Chem. 2009 Jul 23;52(14):4288-305. doi: 10.1021/jm900230j. PMID: 19552433.

In vivo study

1. Huang KH, Veal JM, Fadden RP, Rice JW, Eaves J, Strachan JP, Barabasz AF, Foley BE, Barta TE, Ma W, Silinski MA, Hu M, Partridge JM, Scott A, DuBois LG, Freed T, Steed PM, Ommen AJ, Smith ED, Hughes PF, Woodward AR, Hanson GJ, McCall WS, Markworth CJ, Hinkley L, Jenks M, Geng L, Lewis M, Otto J, Pronk B, Verleysen K, Hall SE. Discovery of novel 2-aminobenzamide inhibitors of heat shock protein 90 as potent, selective and orally active antitumor agents. J Med Chem. 2009 Jul 23;52(14):4288-305. doi: 10.1021/jm900230j. PMID: 19552433.

2. 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:

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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-04929113 (SNX-5422) is a potent and selective HSP90 inhibitor with Kd of 41 nM and induces Her-2 degradation with IC50 of 37 nM.

In vitro activity

All compounds summarized showed potent antiproliferative activity against a broad range of cancer cell types (Table 5). Compound (10) exhibited potent effects on Her2 stability and caused expected up-regulation of Hsp70 (Table 6). Additionally, treatment with the inhibitor down regulated both the MAPK and AKT signaling pathways as measured by the loss of p-S6 and p-ERK in treated cells. These pathways are implicated in uncontrolled cellular division and antiapoptotic signaling and have been targeted for drug development.

Reference: J Med Chem. 2009 Jul 23;52(14):4288-305. https://doi.org/10.1021/jm900230j

In vivo activity

Shown in Figure 8 is the in vivo antitumor activity of PF-04929113 (10) in an HT-29 human colon tumor xenograft model. The compound was orally administered to mice bearing subcutaneous tumors 3 times a week for 3 weeks (qod × 3/2 × 3) at 5, 10, 25, and 50 mg/kg. The 50 mg/kg dose was the most efficacious, demonstrating a 67% growth delay over vehicle control. Median time to end point (TTE) for the 50 mg/kg group was 43.2 days compared to 25.9 days for vehicle control. Two of 10 animals survived to the end of the study (61 days). The 25 mg/kg dose showed tumor growth delay but at a much lower percentage (14%). Median TTE was not statistically significant over vehicle control. On the basis of body weight measurements and clinical observations, compound 10 was well tolerated at all dose levels tested. No treatment related deaths were observed.

Reference: J Med Chem. 2009 Jul 23;52(14):4288-305. https://doi.org/10.1021/jm900230j