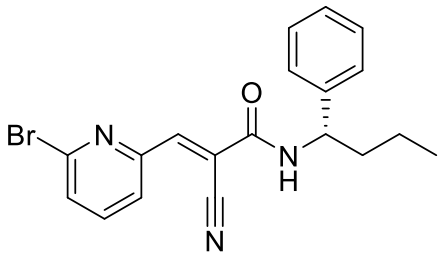
Product data sheet

MedKoo Cat#: 406176 Name: Degrasyn CAS#: 856243-80-6 Chemical Formula: $C_{19}H_{18}BrN_3O$ Exact Mass: 383.06332 Molecular Weight: 384.27	
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:

Degrasyn, also known as WP1130, is a small molecule that specifically and rapidly down-regulates both wild-type and mutant Bcr/Abl protein without affecting bcr/abl gene expression in chronic myelogenous leukemia (CML) cells. WP1130 was more effective in reducing leukemic versus normal hematopoietic colony formation and strongly inhibited colony formation of cells derived from patients with T315I mutant Bcr/Abl-expressing CML in blast crisis. WP1130 suppressed the growth of K562 heterotransplanted tumors as well as both wild-type Bcr/Abl and T315I mutant Bcr/Abl-expressing BaF/3 cells transplanted into nude mice. WP1130 may be useful in treating CML.

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	64.0	166.55
Ethanol	30.0	78.07

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.60 mL	13.01 mL	26.02 mL
5 mM	0.52 mL	2.60 mL	5.20 mL
10 mM	0.26 mL	1.30 mL	2.60 mL
50 mM	0.05 mL	0.26 mL	0.52 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. Kapuria V, Peterson LF, Fang D, Bornmann WG, Talpaz M, Donato NJ. Deubiquitinase inhibition by small-molecule WP1130 triggers aggresome formation and tumor cell apoptosis. Cancer Res. 2010 Nov 15;70(22):9265-76. doi: 10.1158/0008-5472.CAN-10-1530. Epub 2010 Nov 2. PMID: 21045142.
2. Kim S, Woo SM, Min KJ, Seo SU, Lee TJ, Kubatka P, Kim DE, Kwon TK. WP1130 Enhances TRAIL-Induced Apoptosis through USP9X-Dependent miR-708-Mediated Downregulation of c-FLIP. Cancers (Basel). 2019 Mar 11;11(3):344. doi: 10.3390/cancers11030344. PMID: 30862047; PMCID: PMC6469024.

In vivo study

1. Li J, Li H, Zhu W, Zhou B, Ying J, Wu J, Zhang H, Sun H, Gao S. Deubiquitinase inhibitor degrasyn suppresses metastasis by targeting USP5-WT1-E-cadherin signalling pathway in pancreatic ductal adenocarcinoma. J Cell Mol Med. 2020 Jan;24(2):1370-1382. doi: 10.1111/jcmm.14813. Epub 2019 Dec 17. PMID: 31845546; PMCID: PMC6991651.

2. Bartholomeusz G, Talpaz M, Bornmann W, Kong LY, Donato NJ. Degrasyn activates proteasomal-dependent degradation of c-Myc. Cancer Res. 2007 Apr 15;67(8):3912-8. doi: 10.1158/0008-5472.CAN-06-4464. PMID: 17440106.

7. Bioactivity

Biological target:

Degrasyn (WP1130) is a cell-permeable deubiquitinase (DUB) inhibitor, directly inhibiting DUB activity of USP9x, USP5, USP14, and UCH37 that also downregulates the antiapoptotic proteins Bcr-Abl (IC50: 1.8 μM) and JAK2.

In vitro activity

An in vitro analysis using cell lysates was performed to investigate direct DUB inhibition by WP1130. Briefly, untreated Z138 cell lysates were incubated with 5 μmol/L WP1130 or vehicle alone for 1 hour at 37°C, followed by labeling with HA-UbVS. Incubation of cell lysate with WP1130 showed a reduction of HA labeling of the same DUBs as those noted in intact cells (Fig. 4C), suggesting that WP1130 caused direct DUB inhibition. As shown in Fig. 5A, treatment with 5 μ mol/L WP1130 reduced the activities of USP9x, USP5, and UCH-L1 by ⩾80% (detail in Supplementary Fig. S4). No inhibition was observed against UCH-L3 activity, suggesting that WP1130 may be partly selective. The loss of USP5 activity was confirmed using HA-UbVS labeling, which showed ~80% reduction in HA labeling on incubation with WP1130 (Fig. 5B). Interestingly, observed a time-dependent increase in cathepsin B activity from the lysates of WP1130-treated cells (Supplementary Fig. S5) was also observed.

Reference: Cancer Res. 2010 Nov 15;70(22):9265-76. https://pubmed.ncbi.nlm.nih.gov/21045142/

In vivo activity

To determine whether degrasyn can reduce the tumorigenicity in a xenograft model, PANC‐1 cells were injected subcutaneously into right flank of mice to construct xenograft mouse model. All xenografted mice were divided in two groups according to degrasyn treatment or not. Tumours in degrasyn‐treated mice were significantly smaller than those in control mice (Figure7A). Similarly, tumour growth was significantly reduced in degrasyn‐treated mice compared with control mice (Figure7B). Furthermore, degrasyn reduced the average tumour volume by 43% compared with negative control (Figure7C). Also, degrasyn treatment resulted in 36% decrease in average tumour weight (Figure7D). Consistent with the results in cell lines, degrasyn reduced the protein levels of WT1 but increased E‐cadherin (Figure7E).

Reference: J Cell Mol Med. 2020 Jan; 24(2): 1370–1382. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6991651/

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.