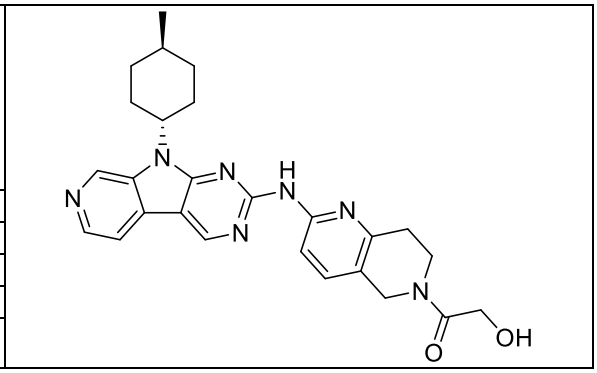
Product data sheet

MedKoo Cat#: 406521 Name: FLX925 (AMG-925) CAS#: 1401033-86-0 Chemical Formula: $C_{26}H_{29}N_7O_2$ Exact Mass: 471.23827 Molecular Weight: 471.55	
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:
FLX925, also known as AMG-925, is a potent and selective type 1 inhibitor of FLT3 that retains its cellular potency against clinically relevant secondary resistance mutations in FLT3 occurring with quizartinib or sorafenib treatment (FLX925 IC50: MOLM13ITD, 15 nM; MOLM13ITD/D835, 28 nM; MV4-11ITD, 16 nM; MV4-11ITD/D835, 19 nM; MV4-11ITD/N841, 16 nM; MV4-11ITD/F691, 73 nM).

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	0.01	0.02

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.12 mL	10.60 mL	21.21 mL
5 mM	0.42 mL	2.12 mL	4.24 mL
10 mM	0.21 mL	1.06 mL	2.12 mL
50 mM	0.04 mL	0.21 mL	0.42 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. Li C, Liu L, Liang L, Xia Z, Li Z, Wang X, McGee LR, Newhall K, Sinclair A, Kamb A, Wickramasinghe D, Dai K. AMG 925 is a dual FLT3/CDK4 inhibitor with the potential to overcome FLT3 inhibitor resistance in acute myeloid leukemia. Mol Cancer Ther. 2015 Feb;14(2):375-83. doi: 10.1158/1535-7163.MCT-14-0388. Epub 2014 Dec 8. PMID: 25487917.

2. Keegan K, Li C, Li Z, Ma J, Ragains M, Coberly S, Hollenback D, Eksterowicz J, Liang L, Weidner M, Huard J, Wang X, Alba G, Orf J, Lo MC, Zhao S, Ngo R, Chen A, Liu L, Carlson T, Quéva C, McGee LR, Medina J, Kamb A, Wickramasinghe D, Dai K. Preclinical evaluation of AMG 925, a FLT3/CDK4 dual kinase inhibitor for treating acute myeloid leukemia. Mol Cancer Ther. 2014 Apr;13(4):880-9. doi: 10.1158/1535-7163.MCT-13-0858. Epub 2014 Feb 13. PMID: 24526162.

In vivo study

1. Keegan K, Li C, Li Z, Ma J, Ragains M, Coberly S, Hollenback D, Eksterowicz J, Liang L, Weidner M, Huard J, Wang X, Alba G, Orf J, Lo MC, Zhao S, Ngo R, Chen A, Liu L, Carlson T, Quéva C, McGee LR, Medina J, Kamb A, Wickramasinghe D, Dai K. Preclinical evaluation of AMG 925, a FLT3/CDK4 dual kinase inhibitor for treating acute myeloid leukemia. Mol Cancer Ther. 2014 Apr;13(4):880-9. doi: 10.1158/1535-7163.MCT-13-0858. Epub 2014 Feb 13. PMID: 24526162.

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7. Bioactivity

Biological target:

FLX925 (AMG 925) is a potent, selective, and orally available FLT3/CDK4 dual inhibitor with IC50s of 2±1 nM and 3±1 nM, respectively.

In vitro activity

FLX925 (AMG 925) also inhibits CDK6, CDK2, and CDK1 in kinase assays with IC50s of 8±2 nM, 375±150 nM, 1.90±0.51 μM, respectively. A fair overall kinase selectivity of AMG 925 is as determined by KinomScan against a panel of 442 various kinases. Cellular selectivity (on-target vs. off-target activity) of AMG 925 is about 50-fold as evaluated by comparison of its growth-inhibiting activity in RB-positive (RB+) and RB-negative (RB-) non- acute myeloid leukemia (AML) cancer cell lines. AMG 925 potently inhibits growth of AML cell lines MOLM13 (FLT3-ITD; IC50=19 μM) and Mv4-11 (FLT3-ITD; IC50=18 μM).

Reference: Mol Cancer Ther. 2014 Apr;13(4):880-9. http://mct.aacrjournals.org/cgi/pmidlookup?view=long&pmid=24526162

In vivo activity

MOLM13 tumor-bearing mice are dosed twice daily by oral administration 6 hours apart with 12.5, 25, or 37.5 mg/kg AMG 925. Tumors are then harvested 3, 9, 12, and 24 hours after the first dose, and analyzed for levels of P-STAT5 and P-RB. Maximum inhibition of P-STAT5 and P-RB is achieved at 6 and 12 hours respectively at the 37.5 mg/kg dose of AMG 925. Interestingly, a rebound of P-STAT5 at 24 hours is observed, possibly as a result of compensational feedback. The pharmacodynamic responses of P-STAT5 and P-RB inhibition correlated with plasma concentrations of AMG 925. AMG 925 inhibits AML xenograft tumor growth by 96% to 99% without significant body weight loss. The antitumor activity of AMG 925 correlates with the inhibition of STAT5 and retinoblastoma protein (RB) phosphorylation, the pharmacodynamic markers for inhibition of FLT3 and CDK4, respectively. In addition, AMG 925 is also found to inhibit FLT3 mutants (e.g., D835Y) that are resistant to the current FLT3 inhibitors (e.g., AC220 and Sorafenib).

Reference: Mol Cancer Ther. 2014 Apr;13(4):880-9. http://mct.aacrjournals.org/cgi/pmidlookup?view=long&pmid=24526162