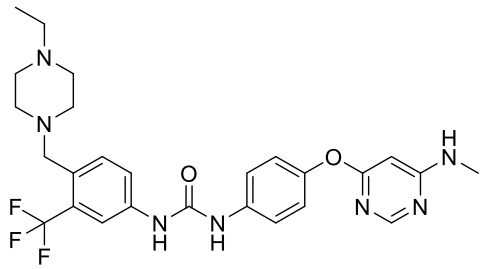
Product data sheet

MedKoo Cat#: 406211 Name: AST487 CAS#: 630124-46-8 Chemical Formula: $C_{26}H_{30}F_3N_7O_2$ Exact Mass: 529.24131 Molecular Weight: 529.56	
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:

AST487, also known as NVP-AST487, is a RET kinase inhibitor/FLT3 inhibitor. The RET kinase has emerged as a promising target for the therapy of medullary thyroid cancers (MTC) and of a subset of papillary thyroid cancers. NVP- AST487 has an IC(50) of 0.88 mumol/L on RET kinase, inhibits RET autophosphorylation and activation of downstream effectors, and potently inhibited the growth of human thyroid cancer cell lines with activating mutations of RET but not of lines without RET mutations. NVP- AST487 induced a dose-dependent growth inhibition of xenografts of NIH3T3 cells expressing oncogenic RET, and of the MTC cell line TT in nude mice. NVP- AST487 inhibited calcitonin gene expression in vitro in TT cells, in part, through decreased gene transcription.

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	100	188.84
Ethanol	33	62.32

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.89 mL	9.44 mL	18.88 mL
5 mM	0.38 mL	1.89 mL	3.78 mL
10 mM	0.19 mL	0.94 mL	1.89 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. Weisberg E, Roesel J, Bold G, Furet P, Jiang J, Cools J, Wright RD, Nelson E, Barrett R, Ray A, Moreno D, Hall-Meyers E, Stone R, Galinsky I, Fox E, Gilliland G, Daley JF, Lazo-Kallanian S, Kung AL, Griffin JD. Antileukemic effects of the novel, mutant FLT3 inhibitor NVP-AST487: effects on PKC412-sensitive and -resistant FLT3-expressing cells. Blood. 2008 Dec 15;112(13):5161-70. doi: 10.1182/blood-2008-02-138065. Epub 2008 Sep 26. PMID: 18820131; PMCID: PMC2597611.

2. Akeno-Stuart N, Croyle M, Knauf JA, Malaguarnera R, Vitagliano D, Santoro M, Stephan C, Grosios K, Wartmann M, Cozens R, Caravatti G, Fabbro D, Lane HA, Fagin JA. The RET kinase inhibitor NVP-AST487 blocks growth and calcitonin gene expression through distinct mechanisms in medullary thyroid cancer cells. Cancer Res. 2007 Jul 15;67(14):6956-64. doi: 10.1158/0008-5472.CAN-06-4605. PMID: 17638907.

In vivo study

Product data sheet

1. Weisberg E, Roesel J, Bold G, Furet P, Jiang J, Cools J, Wright RD, Nelson E, Barrett R, Ray A, Moreno D, Hall-Meyers E, Stone R, Galinsky I, Fox E, Gilliland G, Daley JF, Lazo-Kallanian S, Kung AL, Griffin JD. Antileukemic effects of the novel, mutant FLT3 inhibitor NVP-AST487: effects on PKC412-sensitive and -resistant FLT3-expressing cells. Blood. 2008 Dec 15;112(13):5161-70. doi: 10.1182/blood-2008-02-138065. Epub 2008 Sep 26. PMID: 18820131; PMCID: PMC2597611.

2. Akeno-Stuart N, Croyle M, Knauf JA, Malaguarnera R, Vitagliano D, Santoro M, Stephan C, Grosios K, Wartmann M, Cozens R, Caravatti G, Fabbro D, Lane HA, Fagin JA. The RET kinase inhibitor NVP-AST487 blocks growth and calcitonin gene expression through distinct mechanisms in medullary thyroid cancer cells. Cancer Res. 2007 Jul 15;67(14):6956-64. doi: 10.1158/0008-5472.CAN-06-4605. PMID: 17638907.

7. Bioactivity

Biological target:

AST 487 is a RET kinase inhibitor with IC50 of 880 nM, inhibits RET autophosphorylation and activation of downstream effectors, also inhibits Flt-3 with IC50 of 520 nM.

In vitro activity

Treatment of FLT3-ITD-Ba/F3 cells and D835Y-Ba/F3 cells with NVP-AST487 potently inhibited cellular proliferation (IC50 < .005 μM; Figure 1B,C). Supplementation of culture media with WEHI, used as a source of IL-3, led to rescue of the cells, suggesting that NVP-AST487 selectively inhibits FLT3-ITD and has no effect on IL-3 signaling. The antiproliferative activity of NVP-AST487 was not blunted by addition of human serum (Figure S3). Cells expressing the novel point mutant FLT3-N841I also showed sensitivity to NVP-AST487 (Figure S1). Parental Ba/F3 cells were not affected by up to 0.1 μM NVP-AST487 (Figure 1B). Similarly, the results of a CFU-GM colony formation assay showed no toxicity of human bone marrow progenitor cells at concentrations up to 0.1 μM NVP-AST487 (Figure 1D). A dose-dependent increase of apoptotic cells was observed in FLT-ITD-Ba/F3 cells cultured in the presence of NVP-AST487 (at concentrations up to 0.1 μM; Figure 4A). Viability of cells cultured in the presence of the inhibitor in media supplemented with IL-3 was preserved following 3 days of treatment (Figure 4A). Induction of apoptosis was similarly observed in D835Y-Ba/F3 cells treated for 3 days in the presence of NVP-AST487 at concentrations of 0.01 μM and 0.1 μM (Figure 4B). There was no apparent induction of apoptosis of parental Ba/F3 cells cultured with IL-3 in the presence of NVP-AST487 for the same length of time (Figure 4C).

Reference: Blood. 2008 Dec 15;112(13):5161-70. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/18820131/

In vivo activity

The ability of the inhibitor, NVP-AST487, to inhibit proliferation of mutant FLT3-expressing cells in vivo was investigated using athymic nude mice that had been inoculated with FLT3-ITD-Ba/F3 cells via tail-vein injection. Mice were orally administered vehicle (10% NMP-90% PEG300), 30 mg/kg NVP-AST487 (“low-dose” NVP-AST487), or 50 mg/kg NVP-AST487 (“high-dose” NVP-AST487) for a total of 21 days by gavage. Drug was not administered on weekends. All vehicle-treated mice died after 24 days following initial injection of the FLT3-ITD-Ba/F3 cells, whereas the majority of NVP-AST487–treated mice (at both doses) survived up to day 29 (Figure 6A). Median survival for vehicle control mice was 20 days; median for low- and high-dose mice was 30 days. The survival was different among the 3 groups (P < .001). Vehicle control mice died sooner than the low-dose-treated mice (P < .001) and sooner than the high-dose-treated mice (P = .005). There was no significant difference in survival between the low- and high-dose mice (P = .70).

Reference: Blood. 2008 Dec 15;112(13):5161-70. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/18820131/

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.