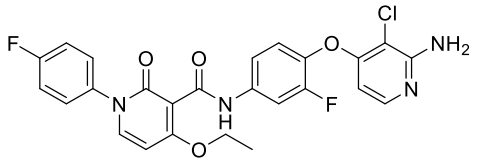
Product data sheet

MedKoo Cat#: 200527 Name: BMS-777607 CAS#: 1025720-94-8 Chemical Formula: $C_{25}H_{19}ClF_2N_4O_4$ Exact Mass: 512.10629 Molecular Weight: 512.89	
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:

BMS-777607, also known as BMS-817378 and ASLAN-002, a Met tyrosine kinase inhibitor, is an inhibitor of MET tyrosine kinase with potential antineoplastic activity. MET tyrosine kinase inhibitor BMS-777607 binds to c-Met protein, or hepatocyte growth factor receptor (HGFR), preventing binding of hepatocyte growth factor (HGF) and disrupting the MET signaling pathway; this agent may induce cell death in tumor cells expressing c-Met. c-Met, a receptor tyrosine kinase overexpressed or mutated in many tumor cell types, plays an important role in tumor cell proliferation, survival, invasion, and metastasis, and in tumor angiogenesis.

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	48.0	93.59
DMF	20.0	38.99
DMF:PBS (pH 7.2) (1:7)	0.1	0.19

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.95 mL	9.75 mL	19.50 mL
5 mM	0.39 mL	1.95 mL	3.90 mL
10 mM	0.19 mL	0.97 mL	1.95 mL
50 mM	0.04 mL	0.19 mL	0.39 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. Lauter M, Weber A, Torka R. Targeting of the AXL receptor tyrosine kinase by small molecule inhibitor leads to AXL cell surface accumulation by impairing the ubiquitin-dependent receptor degradation. Cell Commun Signal. 2019 Jun 6;17(1):59. doi: 10.1186/s12964-019-0377-8. PMID: 31171001; PMCID: PMC6555758.
2. Wu CC, Weng CS, Hsu YT, Chang CL. Antitumor effects of BMS-777607 on ovarian cancer cells with constitutively activated c-MET. Taiwan J Obstet Gynecol. 2019 Jan;58(1):145-152. doi: 10.1016/j.tjog.2018.11.027. PMID: 30638469.

In vivo study

1. Wang R, Xu X, Li Y, Li J, Yao C, Wu R, Jiang Q, Shi D. A C-Met chemical inhibitor promotes fracture healing through interacting with osteogenic differentiation via the mTORC1 pathway. Exp Cell Res. 2019 Aug 1;381(1):50-56. doi: 10.1016/j.yexcr.2019.03.037. Epub 2019 Apr 26. PMID: 31034806.

2. Khaibullina A, Adjei EA, Afangbedji N, Ivanov A, Kumari N, Almeida LEF, Quezado ZMN, Nekhai S, Jerebtsova M. RON kinase inhibition reduces renal endothelial injury in sickle cell disease mice. Haematologica. 2018 May;103(5):787-798. doi: 10.3324/haematol.2017.180992. Epub 2018 Mar 8. PMID: 29519868; PMCID: PMC5927980.

7. Bioactivity

Biological target:

BMS 777607 is a Met-related inhibitor for c-Met, Axl, Ron and Tyro3 with IC50s of 3.9 nM, 1.1 nM, 1.8 nM and 4.3 nM, respectively.

In vitro activity

This study performed flow cytometry analysis of Hs578T cells after stimulation of AXL by exogenous GAS6 for 30 min and 2 hours, in combination with BMS77607 treatment. Two different extra-cellularly binding anti-AXL antibodies were used, namely Ab 154 and Ab 259/2. This study analyzed the cell surface expression without cell membrane permeabilisation and total AXL abundance of Hs578T cell after cell membrane permeabilisation. Exogenous GAS6 stimulation resulted in a significant cell surface and total AXL depletion within 2 h to 50% or 60%. 0.5 μM BMS (BMS 777607) completely abolished the depletion of AXL from the cell surface (Fig. 5a-b). This study shows that internalization of AXL is suppressed by BMS and assumed that this is caused by inhibition of AXL ubiquitination (Fig. 5c-f).

Reference: Cell Commun Signal. 2019; 17: 59. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6555758/

In vivo activity

Here, BMS-777607 with an intermittent low-dose administration led to an augmentation of bone callus in mice after a standardized femur osteotomy. On the basis of the radiological analysis data, BMS-777607 could induce the rapid formation of a callus during the early stage of fracture healing, and this effect provides initial stabilization to help the bone heal more quickly. Even though the callus size was different between the two groups at week 3, there was no distinct structural modification because of the existence of integrity external collars in both groups. Moreover, Safranin O staining indicated BMS-777607 promoted early rapid proliferation of an exterior callus, which suggested that BMS-777607 played a crucial role in intramembranous ossification during external callus formation, thus reflecting that osteoblast proliferation and differentiation was the major target.

Reference: Exp Cell Res. 2019 Aug 1;381(1):50-56. https://pubmed.ncbi.nlm.nih.gov/31034806/

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.