

## Product Data Sheet

Product Name: BMS-202

Cat. No.: GC16762

### Chemical Properties

Cas. No. 1675203-84-5

Chemical Name N-(2-(((2-methoxy-6-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyridin-3-yl)methyl)amino)ethyl)acetamide

SMILES CC1=C(COC2=NC(OC)=C(CNCCNC(C)=O)C=C2)C=CC=C1C3=CC=CC=C3

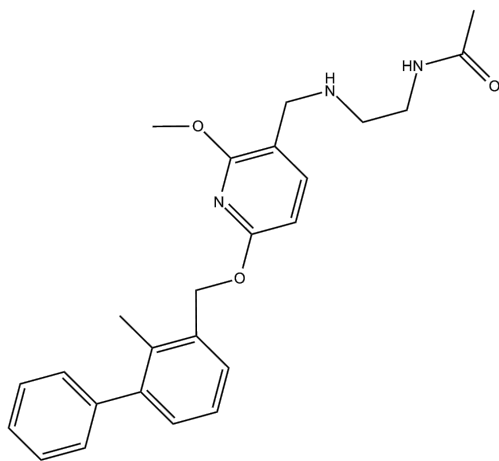
Formula  $C_{25}H_{29}N_3O_3$  M.Wt 419.52

Solubility DMSO : 100 mg/mL (238.37 mM),  
Need ultrasound. Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



### Protocol

#### Cell experiment [1]:

Cell lines U251, LN229, and HEB cells

**Caution: Product has not been fully validated for medical applications. For research use only.**

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**Preparation Method** For the cell proliferation assay,  $1-1.5 \times 10^3$  cells/well were seeded in 96-well plates and cultured for 24h and 48h. The control group included DMEM without BMS-202; the blank group was without any cells or culture media; the vehicle included BMS-202 solution without cells.

**Reaction Conditions** 10μM, 48h incubation

**Applications** BMS-202 apparently inhibits the proliferation of GBM cells both *in vitro*.

### Animal experiment [2]:

**Animal models** SKH-1 mice (Charles River Laboratories, strain code 477)

**Preparation Method** Male transgenic SKH-1 mice heterozygous for the TPA-Response Element–driven luciferase transgene (AP-1 luciferase mice, n=3) were treated topically on their backs with 200 μl of 8 mM BMS-202 or vehicle control (acetone). For all mice receiving BMS-202, the compound was applied twice before (24 hours and 1 hour) as well as immediately after UV exposure.

**Dosage form** 8mM, 200ul, topically introduction on skin

**Applications** UV-induced cleavage of procaspase-3, a hallmark of acute skin photodamage, was attenuated by topical BMS-202. BMS-202 antagonizes UV-induced PD-L1 expression both at the mRNA and protein levels in SKH-1 epidermis.

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### References:

- [1]Yang, Xueou et al. "Metabolic remodeling by the PD-L1 inhibitor BMS-202 significantly inhibits cell malignancy in human glioblastoma." *Cell death & disease* vol. 15,3 186. 4 Mar. 2024, doi:10.1038/s41419-024-06553-5
- [2]Dickinson, Sally E et al. "Inhibition of UV-Induced Stress Signaling and Inflammatory Responses in SKH-1 Mouse Skin by Topical Small-Molecule PD-L1 Blockade." *JID innovations : skin science from molecules to population health* vol. 4,2 100255. 5 Jan. 2024, doi:10.1016/j.xjidi.2023.100255

### Background

BMS-202 is a nonpeptidic PD-1/PD-L1 complex inhibitor binding to PD-L1 and blocks human PD-1/PD-L1 interaction ( $IC_{50}=53.6nM$ ) to prevent cancer cells from escaping antitumor immune responses<sup>[1,2]</sup>. The binding of the PD-L1 molecule in the BMS-202/PD-L1 complexes is similar to the binding of the anti-PD-L1 nanobody KN035 and VH domain of avelumab at N-terminal loop in PD-1, occluding the PD-1 interaction surface of PD-L1s<sup>[3]</sup>.

*In vitro* experiments show that BMS-202 inhibits cell malignancy in human glioblastoma (10 $\mu$ M; 48h)<sup>[4]</sup>. BMS-202 also suppresses the synthesis and secretion of gonadotropins and enhances apoptosis via p38 MAPK signaling pathway in a mouse pituitary L $\beta$ t2 cell model (20 $\mu$ M; 24h)<sup>[5]</sup>. BMS-202 may act as an inhibitor of programmed cell death ligand (0.1 $\mu$ M, 1 $\mu$ M, 10 $\mu$ M, 100  $\mu$ M, and 500 $\mu$ M; 48h) in HaCaT immortalized human keratinocytes<sup>[6]</sup>.

*In vivo* experiments show that BMS-202 performs an anti-tumor effect in the humanized MHC-double knockout NOG mouse (20mg/kg; 9 times; i.v)<sup>[7]</sup>. BMS-202 also significantly attenuated UV-induced activator protein-1 transcriptional activity in SKH-1 bioluminescent reporter mouse skin (8mM, 200ul; topically introduction on skin)<sup>[8]</sup>.

### References:

- [1] Liu, Jin et al. "Discovery and Crystallography Study of Novel Biphenyl Ether and Oxadiazole Thioether (Non-Arylmethylamine)-Based Small-Molecule PD-1/PD-L1 Inhibitors as Immunotherapeutic Agents." *\*Journal of medicinal chemistry\** vol. 66,18 (2023): 13172-13188. doi:10.1021/acs.jmedchem.3c01141

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- [2] Bailly, Christian, and Gérard Vergoten. "Flurbiprofen as a biphenyl scaffold for the design of small molecules binding to PD-L1 protein dimer." *\*Biochemical pharmacology\** vol. 178 (2020): 114042. doi:10.1016/j.bcp.2020.114042
- [3] Zak, Krzysztof M et al. "Structural Biology of the Immune Checkpoint Receptor PD-1 and Its Ligands PD-L1/PD-L2." *\*Structure (London, England : 1993)\**vol. 25,8 (2017): 1163-1174. doi:10.1016/j.str.2017.06.011
- [4] Yang, Xueou et al. "Metabolic remodeling by the PD-L1 inhibitor BMS-202 significantly inhibits cell malignancy in human glioblastoma." *\*Cell death & disease\** vol. 15,3 186. 4 Mar. 2024, doi:10.1038/s41419-024-06553-5
- [5] Jiang, Ying et al. "The PD-1/PD-L1 binding inhibitor BMS-202 suppresses the synthesis and secretion of gonadotropins and enhances apoptosis via p38 MAPK signaling pathway." *\*Drug development research\** vol. 83,1 (2022): 176-183. doi:10.1002/ddr.21857
- [6] Shafi, Hasham et al. "Comprehensive Advanced Physicochemical Characterization and In Vitro Human Cell Culture Assessment of BMS-202: A Novel Inhibitor of Programmed Cell Death Ligand." *\*Pharmaceutics\** vol. 16,11 1409. 1 Nov. 2024, doi:10.3390/pharmaceutics16111409
- [7] Ashizawa, Tadashi et al. "Antitumor activity of the PD-1/PD-L1 binding inhibitor BMS-202 in the humanized MHC-double knockout NOG mouse." *\*Biomedical research (Tokyo, Japan)\** vol. 40,6 (2019): 243-250. doi:10.2220/biomedres.40.243
- [8] Dickinson, Sally E et al. "Inhibition of UV-Induced Stress Signaling and Inflammatory Responses in SKH-1 Mouse Skin by Topical Small-Molecule PD-L1 Blockade." *\*JID innovations : skin science from molecules to population health\** vol. 4,2 100255. 5 Jan. 2024, doi:10.1016/j.xjidi.2023.100255

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