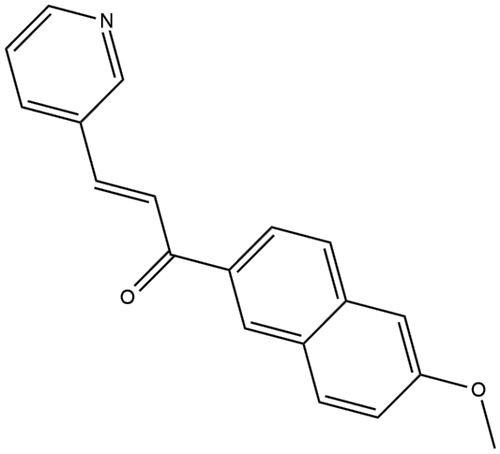
Product Data Sheet

Product Name: DMU2139
Cat. No.: GC19416

Chemical Properties

Cas. No.	1821143-80-9		
SMILES	O=C(C1=CC=C2C=C(OC)C=CC2=C1)/C=C/C3=CC=CN=C3		
Formula	$C_{19}H_{15}NO_2$	M.Wt	289.33
Solubility	Soluble in DMSO	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 HEK293 cells

Product Data Sheet

Preparation Method	The recombinant HEK293 cells expressing CYP enzymes (1×10^5 cells/well) were seeded in a black 96-well transparent-bottom plate with a volume of 50μl. DMU2139 was added to the wells at different concentrations (1, 2, 4, 8, 10, 20, 40, 60, 80, and 100nM) and incubated at 37°C with 8% CO_2 for 30 minutes. After incubation, 5μM of the fluorescent substrate 7-ethoxythioflavinol was added to each well, 25μl per well, and the mixture was shaken before the determination of 7-ethoxythioflavinol-O-demethylase (EROD) activity. Fluorescence detection was performed using the appropriate emission wavelength (530/30nm) and excitation wavelength (590/40nm).
Reaction Conditions	1, 2, 4, 8, 10, 20, 40, 60, 80, and 100nM; 30min
Applications	DMU2139 treatment inhibited the CYP1B1 activity in HEK293 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models	Balb/c nude mice
Preparation Method	Balb/c nude mice were raised under standard conditions and had free access to food and water. A2780 cells in the logarithmic growth phase were prepared at a concentration of 1×10^8 cells/ml, and 100μl of the cell suspension was subcutaneously injected into the axilla of each nude mouse. From the second day after injection, the tumor size was measured. When the average tumor volume reached approximately $100mm^3$, olaparib was administered intraperitoneally at a dose of 50mg/kg every 4 days, or in combination with DMU2139 (30mg/kg; i.p.) for 24 days. Measurements were taken using a vernier caliper every four days, and the formula for calculating tumor volume was: Volume (mm^3) = (length×width^2)/2.

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Dosage form	30mg/kg; every 4 days for 24 days; i.p.
Applications	DMU2139 treatment in combination with olaparib significantly inhibited the growth of A2780 cell-xenograft tumors in mice.

References:
[1] Horley N J, Beresford K J M, Chawla T, et al. Discovery and characterization of novel CYP1B1 inhibitors based on heterocyclic chalcones: Overcoming cisplatin resistance in CYP1B1-overexpressing lines[J]. European journal of medicinal chemistry, 2017, 129: 159-174.
[2] Xue Y, Yin T, Yuan S, et al. CYP1B1 promotes PARPi-resistance via histone H1. 4 interaction and increased chromatin accessibility in ovarian cancer[J]. Drug Resistance Updates, 2024, 77: 101151.

Background

DMU2139 is a potent CYP1B1 inhibitor, with an IC_{50} value of 9nM[1]. DMU2139 coordinates with heme and interacts with the hydrophobic residues Phe134 and Phe231 through p-p stacking since the hydrophobic naphthyl group[2]. DMU2139 has been used in combination with cisplatin to overcome the resistance mediated by CYP1B1 and make cancer cells re-sensitized to cisplatin[3].

In vivo, the combination treatment of DMU2139 (30mg/kg) and olaparib (50mg/kg), administered by intraperitoneal injection every 4 days for 24 days, significantly inhibited tumor growth in a xenograft mouse model of A2780 cells[4].

References:
[1] Horley N J, Beresford K J M, Chawla T, et al. Discovery and characterization of novel CYP1B1 inhibitors based on heterocyclic chalcones: Overcoming cisplatin resistance in CYP1B1-overexpressing lines[J]. European journal of medicinal chemistry, 2017, 129: 159-174.
[2] Raju B, Choudhary S, Narendra G, et al. Molecular modeling approaches to address drug-metabolizing enzymes (DMEs) mediated chemoresistance: a review[J]. Drug Metabolism Reviews, 2021, 53(1): 45-75.
[3] Alsubait A, Aldossary W, Rashid M, et al. CYP1B1 gene: Implications in glaucoma and cancer[J].

Journal of cancer, 2020, 11(16): 4652.
[4] Xue Y, Yin T, Yuan S, et al. CYP1B1 promotes PARPi-resistance via histone H1. 4 interaction and increased chromatin accessibility in ovarian cancer[J]. Drug Resistance Updates, 2024, 77: 101151.