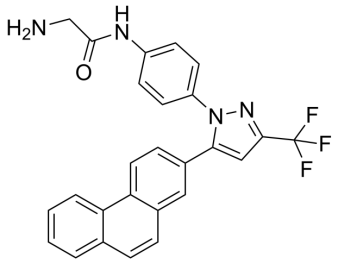
OSU-03012

Cat. No.:	HY-10547
CAS No.:	742112-33-0
Molecular Formula:	$C_{26}H_{19}F_3N_4O$
Molecular Weight:	460.45
Target:	PDK-1; Autophagy
Pathway:	PI3K/Akt/mTOR; Autophagy
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (217.18 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1718 mL	10.8589 mL	21.7179 mL
	5 mM	0.4344 mL	2.1718 mL	4.3436 mL
	10 mM	0.2172 mL	1.0859 mL	2.1718 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.43 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.43 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	OSU-03012 (AR-12; PDK1 inhibitor AR-12) is a blood-brain permeable PDK-1 inhibitor with an IC_{50} of 5 μM[1][3].
IC_{50} & Target	IC50: 5 μM (PDK-1)[1]
In Vitro	OSU-03012 inhibits PC-3 cells viability with IC_{50} values of 5 μM. The effects of OSU-03012 on PC-3 cell proliferation in 10% FBS-supplemented medium are also examined. OSU-03012 induces apoptotic death in PC-3 cells in 1% FBS-containing

	medium in a dose-dependent manner, as demonstrated by DNA fragmentation and PARP cleavage. OSU-03012 is effective in suppressing PC-3 cell proliferation at sub-μM, consistent with that noted in 1% serum[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	All of the SCID/Rag2 mice develop two MDA-MB-435/LCC6/Her-2 tumors and are assigned to either the vehicle control or OSU-03012 (200 mg/kg) treatment group, which is given orally for 3 days. OSU-03012 remarkably decreases EGFR protein expression in the tumors by ~48% compared with expression levels found in the tumors taken from mice that receive the vehicle control. OSU-03012 also prevents Y-box binding protein-1 (YB-1) from binding to the EGFR promoter at the 1b and 2a sites[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	PC-3 ($p53^{-/-}$) human androgen-nonresponsive prostate cancer cells are cultured in RPMI 1640 supplemented with 10% fetal bovine serum (FBS) at 37°C in a humidified incubator containing 5% CO_2. The effect of Celecoxib and its derivatives (e.g., OSU-03012) (2.5 μM, 5 μM, 7.5 μM and 10 μM) on PC-3 cell viability is assessed by using the MTT assay in six replicates. Cells are grown in 10% FBS- supplemented RPMI 1640 in 96-well, flat-bottomed plates for 24 h, and are exposed to various concentrations of Celecoxib derivatives (e.g., OSU-03012) dissolved in DMSO (final concentration ≤0.1%) in 1% serum-containing RPMI 1640 for different time intervals. Controls receive DMSO vehicle at a concentration equal to that in drug-treated cells. The medium is removed, replaced by 200 μL of 0.5 mg/mL of MTT in 10% FBS-containing RPMI 1640, and cells are incubated in the CO_2 incubator at 37°C for 2 h. Supernatants are removed from the wells, and the reduced MTT dye is solubilized in 200 μL/well DMSO. Absorbance at 570 nm is determined on a plate reader[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] SCID/Rag2m mice (6-8 weeks old, female) are subcutaneously injected with 1×10^7 MDA-MB-435/LCC6 cells stably transfected with HER-2/neu. Each mouse is inoculated with the cells on the right and left sides of the lower back. A total of eight mice are injected, each harboring two tumors. After 6 weeks, the mice are randomly assigned into groups (vehicle, 0.5% methyl cellulose/0.1% Tween 80, or OSU-03012 at 200 mg/kg/day). Mice are dosed daily for 3 days with either the vehicle or OSU-03012 by oral gavage. On the fourth day, the study is terminated, mice are sacrificed, and the tumors are collected for chromatin immunoprecipitation (ChIP) and protein isolations. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Autophagy. 2022 Jul 1;1-14.
- J Virol. 2021 Feb 24;95(10):e02436-20.
- Antimicrob Agents Chemother. 2020 Jul 22;64(8):e00236-20.

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REFERENCES

[1]. Zhu J, et al. From the cyclooxygenase-2 inhibitor celecoxib to a novel class of 3-phosphoinositide-dependent protein kinase-1 inhibitors. Cancer Res. 2004 Jun 15;64(12):4309-18.

[2]. To K, et al. The phosphoinositide-dependent kinase-1 inhibitor 2-amino-N-[4-[5-(2-phenanthrenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]-acetamide (OSU-03012)

prevents Y-box binding protein-1 from inducing epidermal growth factor receptor. Mol Pharmacol. 2007 Sep;72(3):641-52.

[3]. Tina X Lee, et al.Growth Inhibitory and Anti-Tumour Activities of OSU-03012, a Novel PDK-1 Inhibitor, on Vestibular Schwannoma and Malignant Schwannoma Cells. Eur J Cancer

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