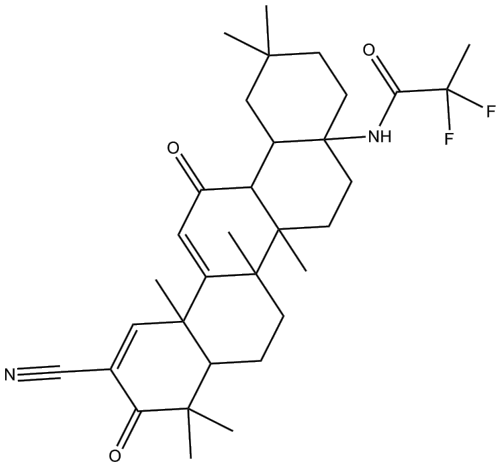
Product Data Sheet

Product Name: Omaveloxolone (RTA-408)
Cat. No.: GC13693

Chemical Properties

Cas. No.	1474034-05-3		
Formula	$C_{33}H_{44}F_2N_2O_3$	M.Wt	554.71
Solubility	≥ 55.5mg/mL in DMSO, ≥ 25.05mg/mL in EtOH	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

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Cell experiment [1]:

Cell lines	Human colorectal adenocarcinoma cell lines HT-29 and HCT-116
Preparation Method	A549/DDP cell line was cultured in RPMI-1640 medium supplemented with 10% fetal bovine serum from the same supplier, along with 5mg/mL of penicillin/streptomycin. To preserve their resistance to Cisplatin (DDP), A549/DDP cells were routinely exposed to 1μg/mL of DDP. Cells in the logarithmic growth phase were collected and treated with trypsin to generate a uniform single-cell suspension. The cells were then seeded into six-well plates at a density of 500 cells per 10μL of culture medium. Following seeding, the cells were treated with a range of Omaveloxolone concentrations-0, 0.15, 0.3, 0.6, 1.2, 2.4, and 4.8μM for 24h to evaluate the compound's effects on cell viability and proliferation. Cellular ferrous iron content was determined using a commercial iron detection kit. Protein was ectracted for Western blotting analysis.
Reaction Conditions	0.15-4.8μM; 24h
Applications	Omaveloxolone induced ferroptosis in cisplatin-resistant A549/DDP lung adenocarcinoma cells, downregulated WWP1, stabilized NCOA4, promoted ferritinophagy, and triggered iron overload and cell death.

Animal experiment [2]:

Animal models	Nrf2-deficient male C57BL/6J mice

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Preparation Method	24h before surgery, Nrf2-deficient male C57BL/6J mice were intraperitoneally administered with Omaveloxolone (100μg/kg body weight) or 0.1% DMSO in PBS as the vehicle. A unilateral ischemia with simultaneous contralateral nephrectomy mouse model was made by surgery. The blood samples were obtained from the inferior vena cava at a designated timing point after reperfusion. The blood urea nitrogen and serum creatinine levels were measured by commercially available assay kits to assess renal function. The left kidney tissues harvested at 24h postischemia were fixed for Kidney Histology and Immunohistochemistry analyses. Malondialdehyde (MDA), carbonylated protein, total antioxidant capacity (T-AOC), total glutathione (T-GSH), and glutathione to glutathione disulfide (GSH/GSSG) ratio in the supernatant of renal cortical homogenate were estimated by using each assay kit, according to the manufacturer's instructions.
Dosage form	100μg/kg; i.p.; 24h before surgery
Applications	Omaveloxolone (100μg/kg; i.p.; 24h before surgery) significantly reduced serum creatinine and blood urea nitrogen levels, decreased renal tubular necrosis, and enhanced Nrf2 nuclear translocation and GSH-related antioxidant gene expression in Nrf2-deficient male C57BL/6J mice subjected to unilateral renal ischemia-reperfusion injury.

References:

[1] Wang X, Liu T, Fei Y, et al. RTA-408 overcomes cisplatin-resistant lung cancer by inhibiting WWP1-mediated NCOA4 ubiquitination to induce ferritinophagy and ferroptosis. *Free Radic Biol Med*. 2025;238:595-610.
[2] Han P, Qin Z, Tang J, et al. RTA-408 Protects Kidney from Ischemia-Reperfusion Injury in Mice via Activating Nrf2 and Downstream GSH Biosynthesis Gene. *Oxid Med Cell Longev*. 2017;2017:7612182.

Background

Product Data Sheet

Background

Omaveloxolone (RTA-408) is an antioxidant inflammation modulator (AIM), which activates Nrf2 and suppresses nitric oxide (NO)[1]. Omaveloxolone is usually used in research related to inflammation, oxidative stress and Friedreich Ataxia [2][3].

In vitro, Omaveloxolone (0.15-4.8μM; 24h) induced ferroptosis in cisplatin-resistant A549/DDP lung adenocarcinoma cells, downregulated WWP1, stabilized NCOA4, promoted ferritinophagy, and triggered iron overload, lipid peroxidation, and cell death[4]. Omaveloxolone (0-500nM; 72h) reduced cell viability in EB-associated SCC cell lines and normal human epidermal keratinocytes in a dose-dependent manner[5].

In vivo, Omaveloxolone (17.5mg/kg/day; i.p.; 3 days) significantly increased 35-day survival and restored normal hematopoietic stem and progenitor cell frequency and function in C57BL/6 mice exposed to 7.5 Gy total body irradiation[6]. Omaveloxolone (100μg/kg; i.p.; 24h before surgery) significantly reduced serum creatinine and blood urea nitrogen levels, decreased renal tubular necrosis and ROS production, and enhanced Nrf2 nuclear translocation and GSH-related antioxidant gene expression in Nrf2-deficient male C57BL/6J mice subjected to unilateral renal ischemia-reperfusion injury[7].

References:
[1] Probst BL, Trevino I, McCauley L, et al. RTA 408, A Novel Synthetic Triterpenoid with Broad Anticancer and Anti-Inflammatory Activity. *PLoS One*. 2015;10(4):e0122942.
[2] Hao J, Zhou J, Hu S, et al. RTA 408 ameliorates diabetic cardiomyopathy by activating Nrf2 to regulate mitochondrial fission and fusion and inhibiting NF-κB-mediated inflammation. *Am J Physiol Cell Physiol*. 2024;326(2):C331-C347.
[3] Lee A. Omaveloxolone: First Approval. *Drugs*. 2023;83(8):725-729.
[4] Wang X, Liu T, Fei Y, et al. RTA-408 overcomes cisplatin-resistant lung cancer by inhibiting WWP1-mediated NCOA4 ubiquitination to induce ferritinophagy and ferroptosis. *Free Radic Biol Med*. 2025;238:595-610.
[5] Cohen-Nowak AJ, Cohen AJ, Correia ED, Portocarrero CP, South AP, Nikbakht N. Omaveloxolone attenuates squamous cell carcinoma growth and disease severity in an Epidermolysis Bullosa mouse model. *Exp Dermatol*. 2022;31(7):1083-1088.
[6] Goldman DC, Alexeev V, Lash E, Guha C, Rodeck U, Fleming WH. The triterpenoid RTA 408 is a

robust mitigator of hematopoietic acute radiation syndrome in mice. *Radiat Res*. 2015;183(3):338-344.
[7] Han P, Qin Z, Tang J, et al. RTA-408 Protects Kidney from Ischemia-Reperfusion Injury in Mice via Activating Nrf2 and Downstream GSH Biosynthesis Gene. *Oxid Med Cell Longev*. 2017;2017:7612182.