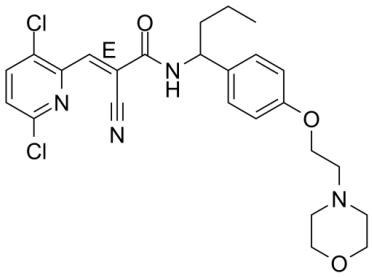
Data Sheet

Product Name:	EOAI3402143
Cat. No.:	CS-0040552
CAS No.:	1699750-95-2
Molecular Formula:	C25H28Cl2N4O3
Molecular Weight:	503.42
Target:	Deubiquitinase
Pathway:	Cell Cycle/DNA Damage
Solubility:	H2O : < 0.1 mg/mL (insoluble); DMSO : 50 mg/mL (99.32 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

EOAI3402143 is a **deubiquitinase** (**DUB**) inhibitor, which inhibits dose-dependently inhibits **Usp9x/Usp24** and **Usp5**. IC50 & Target:
Usp5[1]
Usp9x[1][2][3]
Usp24[2]
In Vitro: EOAI3402143 retains potent Usp9x and Usp5 inhibitory activity[1]. EOAI3402143 dose-dependently inhibits Usp9x and Usp24 activity, increases tumor cell apoptosis[2]. Treatment of UM-2, UM-6, UM-16, and UM-76 with Usp9x inhibitor EOAI3402143 (G9) dose-dependently suppresses cell survival, while 600 nM of EOAI3402143 completely suppresses UM-2 3D colony growth when compared to untreated vehicle controls[3]. **In Vivo:** To examine this potential, the effect of EOAI3402143 (G9) treatment is investigated on human MIAPACA2 tumor xenografts. Human MIAPACA2 cells are injected subcutaneously into NSG mice. Primary tumor development is monitored by caliper measurements, and once measurable, mice are separated into two groups and are treated with either vehicle control (PEG300/DMSO) or G9 at 15 mg/kg. Tumor growth, animal weight, behavior, and mobility are monitored during treatment. In parallel, murine 8041 tumors are also established and subjected to similar G9 treatment and tumor monitoring regimen as the human MIAPACA2 xenografts. Consistent with the in vitro findings, Usp9x inhibition results in the suppression of tumor growth in human tumor xenografts, but any significant effect on the growth of 8041 tumors xenografts is not observed, although the Usp9x activity is inhibited effectively by EOAI3402143 treatment in both human MIAPACA2 and mouse 8041 xenograft tumors[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [3]**UM-2, UM-6, UM-16, and UM-76 cells** are seeded in a 96-well plate at 5000 per well in the presence of the indicated concentration of **EOAI3402143 (1, 2, 3, 4, and 5 μM)** for 3 days in a CO_2 incubator at 37°C. Twenty microliters of 5 g/L MTT solution are added to each well for 2 hours at 37°C. The cells are then lysed in 10% SDS buffer, and absorbance at 570 nm relative to a reference wavelength of 630 nm is determined with a microplate reader. To examine proliferation using the MTT assay, cells are plated in triplicates, and the samples are processed for MTT assay at day 0, 1, 2, 3, and 4[3].
Animal Administration: EOAI3402143 is prepared in DMSO:PEG300 (1:1) (Mice)[3].[3]Mice[3]
NSG [NOD/SCID/IL2r-g (null)] mice are injected mid-dorsally with 2×10^6 8041 or 5×10^6 MIAPACA2 cells in 0.1 mL of Matrigel/DMEM suspension. Tumors are allowed to establish to about 100 mm^3, after which mice are tumor size matched and allocated to five per treatment group (vehicle or EOAI3402143) for 8041 tumor-bearing mice and four per treatment group for MIAPACA2 tumor-bearing mice. **EOAI3402143** is administered in DMSO:PEG300 (1:1) by **i.p injection** every other day at **15 mg/kg**. Tumor size is monitored by caliper measurements twice a week, and tumor volume is calculated[3].

References:

[1]. Potu H, et al. Usp5 links suppression of p53 and FAS levels in melanoma to the BRAF pathway. Oncotarget. 2014 Jul 30;5(14):5559-69.

[2]. Peterson LF, et al. Targeting deubiquitinase activity with a novel small-molecule inhibitor as therapy for B-cell malignancies. Blood. 2015 Jun 4;125(23):3588-97.

[3]. Pal A, et al. Usp9x Promotes Survival in Human Pancreatic Cancer and Its Inhibition Suppresses Pancreatic Ductal Adenocarcinoma In Vivo Tumor Growth. Neoplasia. 2018 Feb;20(2):152-164.

CAIndexNames:

2-Propenamide, 2-cyano-3-(3,6-dichloro-2-pyridinyl)-N-[1-[4-[2-(4-morpholinyl)ethoxy]phenyl]butyl]-, (2E)-

SMILES:

ClC1=C(/C=C(C(NC(CCC)C2=CC=C(OCCN3CCOCC3)C=C2)=O)\C#N)N=C(Cl)C=C1.[E]

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