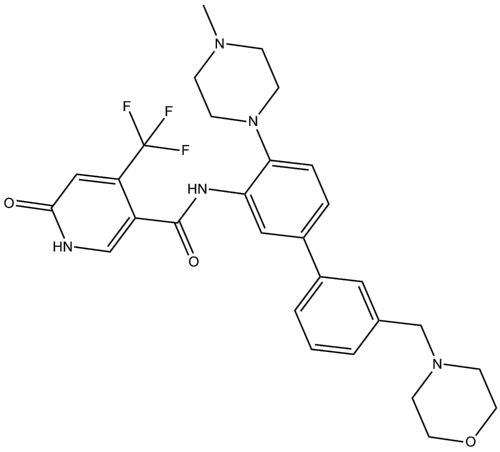
Product Data Sheet

Product Name: OICR-9429
Cat. No.: GC16397

Chemical Properties

Cas. No.	1801787-56-3		
Chemical Name	N-(4-(4-methylpiperazin-1-yl)-3'-(morpholinomethyl)-[1,1'-biphenyl]-3-yl)-6-oxo-4-(trifluoromethyl)-1,6-dihydropyridine-3-carboxamide		
SMILES	O=C(C(C(C(F)(F)F)=C1)=CNC1=O)NC2=CC(C3=CC=CC(CN4CCOCC4)=C3)=CC=C2N5CCN(C)CC5		
Formula	$C_{29}H_{32}F_3N_5O_3$	M.Wt	555.59
Solubility	DMSO: 0.5 mg/ml (with gentle warming),Methanol: 0.5 mg/ml (with gentle warming)	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

Product Data Sheet

Cell experiment [1]:

Cell lines	T24, UM-UC-3, and TCCSUP cells
Preparation Method	Cells were grown in a 37 °C, 5% CO_2 cell incubator with humidified atmosphere. Then the cells were treated with 0, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 200, 300, and 400μM OICR-9429 for 48h. Cell viability was detected using the MTT assay.
Reaction Conditions	0-400μM; 48h
Applications	OICR-9429 inhibited the cell proliferation of bladder cancer cell lines in a dose-dependent manner.

Animal experiment [1]:

Animal models	BALB/c nude mice
Preparation Method	For the xenograft mouse model, a total of 3×10^6 UM-UC-3 cells were injected subcutaneously into the right side of the dorsum, and there were 6 nude mice in every treatment group. Five days after injection, tumour-bearing mice were randomly assigned into four groups that received control solvent, OICR-9429 (60mg/kg), cisplatin (4mg/kg), or a combination of small dose OICR-9429 (30mg/kg) and cisplatin (2.5mg/kg). OICR-9429 was diluted in a combination solution of 5% DMSO + 40% PEG300 + 2% Tween 80 + 53% sterilized water, and cisplatin was diluted in sterilized PBS solution. OICR-9429 and chemotherapy were given every 2 days by intraperitoneal injection. After 16 days of treatment, the mice were euthanized, and tumours were surgically dissected. The tumour and organ specimens were fixed in 4% paraformaldehyde, embedded in paraffin, and then stained with H&E staining.

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Product Data Sheet

Dosage form	30 and 60mg/kg/day; every 2 days for 16 days; i.p.
Applications	OICR-9429 treatment significantly inhibited the tumor growth of bladder cancer cell xenograft mice, enhanced chemosensitivity and reduced the toxicity of cisplatin.

References:
[1] Zhang J, Zhou Q, Xie K, et al. Targeting WD repeat domain 5 enhances chemosensitivity and inhibits proliferation and programmed death-ligand 1 expression in bladder cancer. *J Exp Clin Cancer Res*. 2021;40(1):203. Published 2021 Jun 21.

Background

OICR-9429 is an effective and highly potent inhibitor of the WD repeat domain 5 (WDR5) with a K_d value of 93 ± 28nM [1]. WDR5 is a common scaffold protein that typically forms a nucleosome-modifying protein complex with histones. OICR-9429 binds competitively to the central peptide binding pocket of WDR5, blocking the interaction between WDR5 and the mixed-lineage leukemia (MLL) protein [2-3]. OICR-9429 can be used in the research of various cancers such as non-MLL rearrangement leukemia, colon cancer, pancreatic cancer, prostate cancer, and bladder cancer [4].

In vitro, OICR-9429 (0-400μM; 48h) inhibited the cell proliferation and metastasis of bladder cancer cell lines (T24, UM-UC-3, and TCCSUP) in a dose-dependent manner, promoted the level of cell apoptosis, and reduced the H3K4me3 level in the cells [5]. OICR-9429 (75 and 100μM; 48h) treatment significantly reduced the viability and colony formation ability of PCa cells in a dose-dependent manner, and induced G0/G1 phase arrest [6].

In vivo, OICR-9429 (30 and 60mg/kg/day; every 2 days for 16 days; i.p.) treatment significantly inhibited the tumor growth of bladder cancer cell (BCa) xenograft mice, enhanced chemosensitivity, and reduced the toxicity of cisplatin in BCa [5]. OICR-9429 (1mg/kg/day; i.p.) treatment reduced the peritoneal cell density and the thickness of the interstitial dense zone in mice with peritoneal fibrosis induced by methylglyoxal (MGO), decreased the number of H3K4me3 positive cells, and alleviated the peritoneal fibrosis and inflammation in mice [7].

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References:

[1] Grebien F, Vedadi M, Getlik M, et al. Pharmacological targeting of the Wdr5-MLL interaction in C/EBPα N-terminal leukemia. *Nat Chem Biol*. 2015;11(8):571-578.
[2] Migliori, V., Mapelli, M., and Guccione, E. On WD40 proteins: Propelling our knowledge of transcriptional control Epigenetics 7(8), 815-822 (2012).
[3] Guccione, E., Bassi, C., Casadio, F., et al. Methylation of histone H3R2 by PRMT6 and H3K4 by an MLL complex are mutually exclusive. Nature 449, 933-937 (2007).
[4] Gurung R, Om D, Pun R, et al. Recent Progress in Modulation of WD40-Repeat Domain 5 Protein (WDR5): Inhibitors and Degraders. Cancers 2023, 15, 3910[EB/OL].(2023)
[5] Zhang J, Zhou Q, Xie K, et al. Targeting WD repeat domain 5 enhances chemosensitivity and inhibits proliferation and programmed death-ligand 1 expression in bladder cancer. *J Exp Clin Cancer Res*. 2021;40(1):203. Published 2021 Jun 21.
[6] Zhou Q, Chen X, He H, et al. WD repeat domain 5 promotes chemoresistance and Programmed Death-Ligand 1 expression in prostate cancer[J]. Theranostics, 2021, 11(10): 4809.
[7] Hara D, Sasaki K, Doi S, et al. Targeting MLL1/WDR5-Mediated Epigenetic Regulation Mitigates Peritoneal Fibrosis by Reducing p16INK4a[J]. The FASEB Journal, 2025, 39(8): e70543.

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