Product Data Sheet

Product Name: AZD 5153
Cat. No.: GC13014

Chemical Properties

Cas. No.	1869912-39-9		
Chemical Name	(3R)-4-[2-[4-[1-(3-methoxy-1,2,4-triazolo[4,3-b]pyridazin-6-yl)-4-piperidinyl]phenoxy]ethyl]-1,3-dimethyl-2-piperazinone		
SMILES	COC1=NN=C2N1N=C(N3CCC(C4=CC=C(OCCN5[C@H](C)C(N(C)CC5)=O)C=C4)CC3)C=C2		
Formula	$C_{25}H_{33}N_7O_3$	M.Wt	479.6
Solubility	≤20mg/ml in ethanol;20mg/ml in DMSO;20mg/ml in dimethyl formamide	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	AZD 5153		

Protocol

Cell experiment [1]:

Cell lines	42D (t-NEPC), H660 (de novo NEPC), LNCaP, V16D, MR49F, PC3 prostate cancer cell lines and patient-derived organoid (PDO) models

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Preparation Method	Cells were maintained in appropriate culture media supplemented with fetal bovine serum at 37°C, 5% CO_2. Cells were treated with AZD 5153 at 0.25-2μM for specified time periods.
Reaction Conditions	0.25-2μM; 24-72h
Applications	AZD 5153 significantly inhibited cell proliferation and colony formation in a dose-dependent manner across all tested prostate cancer cell lines. The inhibitor induced apoptosis, as evidenced by increased cleavage of PARP1 and caspase3. AZD 5153 monotherapy significantly inhibited tumor growth in both de novo neuroendocrine prostate cancer (NEPC) and treatment-induced NEPC patient-derived xenograft (PDX) models, achieving near-complete tumor growth blockade. AZD 5153 also demonstrated superior efficacy compared to JQ1 (50mg/kg) in suppressing tumor growth. Mechanistically, AZD 5153 treatment reduced local chromatin accessibility and H3K27ac marks at lineage plasticity program genes, and decreased expression of key neuroendocrine drivers including ASCL1 and SOX2 in tumor tissues. treatment strongly suppressed the expression of key lineage plasticity (LP) program drivers including BRN2, ASCL1, SOX2, and NEPC markers SYP, ENO2, and CHGA. Mechanistically, AZD 5153 reduced RNAPII phosphorylation at serine 2 (pSer2-RNAPII) and decreased local chromatin accessibility at LP program genes.

Animal experiment [2]:

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Animal models	BALB/c nude mice bearing H660, LuCaP145.2, and LuCaP35ENZR prostate cancer xenografts
Preparation Method	Mice were intraperitoneally administered AZD 5153 (10mg/kg) five times per week for 21 days. Treatment commenced when tumor volumes reached approximately 100mm^3. Mice were sacrificed when tumors reached ethical endpoints or at study completion for tumor analysis.
Dosage form	10mg/kg; i.p.; Five times per week for 3 weeks.
Applications	AZD 5153 monotherapy significantly inhibited tumor growth in both de novo neuroendocrine prostate cancer (NEPC) and treatment-induced NEPC patient-derived xenograft (PDX) models, achieving near-complete tumor growth blockade. AZD 5153 also demonstrated superior efficacy compared to JQ1 (50mg/kg) in suppressing tumor growth. Mechanistically, AZD 5153 treatment reduced local chromatin accessibility and H3K27ac marks at lineage plasticity program genes, and decreased expression of key neuroendocrine drivers including ASCL1 and SOX2 in tumor tissues.

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References:
[1] Zhu H, Shen M, Zhu Y, et al. AZD5153 enhances the chemo-sensitivity of gemcitabine on pancreatic cancer cells in vitro and in vivo. Cancer Cell Int. 2025 Aug 26;25(1):315.
[2] Zhang X, Yang Y, Zou H, et al. Effective therapeutic targeting of tumor lineage plasticity in neuroendocrine prostate cancer by BRD4 inhibitors. Acta Pharm Sin B. 2025 Mar;15(3):1415-1429.

Background

AZD 5153 is a bivalent BET/BRD4 bromodomain inhibitor with an IC_{50} of 5nM for BRD4, which simultaneously binds to both bromodomains of BRD4, significantly modulates MYC, E2F, and mTOR transcriptional programs, and inhibits the expression of NSD3 target genes[1-2]. AZD 5153 can be used in research related to hematological malignancies such as acute myeloid leukemia, multiple myeloma, and diffuse large B-cell lymphoma, as well as solid tumors including pancreatic cancer[3-4].

In vitro, AZD 5153 (0.25-2μM) was combined with Gemcitabine (0.5-4μM) to treat human pancreatic cancer cell lines (BXPC-3 and PANC-1) for 12-72 hours. AZD 5153 significantly enhanced the inhibitory effect of Gemcitabine on cell proliferation, synergistically inhibited colony formation, and induced significant apoptosis, characterized by the

formation of apoptotic bodies, chromatin condensation, and increased levels of cleaved PARP and cleaved Caspase-3 proteins[5]. AZD 5153 (10-20μM) was combined with the CDK9 inhibitor CDKI-73 (25-100μM) to treat multiple prostate cancer cell lines (LNCaP, V16D, MR49F, PC3) and patient-derived organoid models from castration-resistant prostate cancer (CRPC) for 24 hours. AZD 5153 significantly enhanced the anti-proliferative effects of CDKI-73, leading to a more pronounced reduction in the protein and mRNA levels of pSer2-RNAPII, MCL-1, and MYC[6].

In vivo, AZD 5153 (10mg/kg/day) was administered intraperitoneally to mice bearing H660, LuCaP145.2, or LuCaP35ENZR tumors (five times per week for 21 days, starting when tumor volumes reached approximately 100 mm^3). AZD 5153 monotherapy almost completely blocked tumor growth and significantly inhibited the expression of key lineage plasticity program drivers (such as ASCL1 and SOX2) in the tumors[7]. AZD 5153 (3mg/kg) was administered intraperitoneally in combination with the PARP inhibitor olaparib (50mg/kg) to mice bearing ovarian cancer patient-derived xenograft (PDX) or ID8 cells (five times per week from day 14 to day 21 after implantation). AZD 5153 synergized with olaparib to significantly inhibited tumor growth, and by downregulating PTEN expression. AZD 5153 disrupted DNA replication stability, enhanced DNA damage and chromosomal breaks, thereby reversing olaparib resistance[8].

References:
[1] Rhyasen GW, Hattersley MM, Yao Y, et al. AZD5153: A Novel Bivalent BET Bromodomain Inhibitor Highly Active against Hematologic Malignancies. Mol Cancer Ther. 2016 Nov;15(11):2563-2574.
[2] Lin CH, Kuo JC, Li D, et al. AZD5153, a Bivalent BRD4 Inhibitor, Suppresses Hepatocarcinogenesis by Altering BRD4 Chromosomal Landscape and Modulating the Transcriptome of HCC Cells. Front Cell Dev Biol. 2022 Mar 24;10:853652.
[3] Zhang P, Li R, Xiao H, et al. BRD4 Inhibitor AZD5153 Suppresses the Proliferation of Colorectal Cancer Cells and Sensitizes the Anticancer Effect of PARP Inhibitor. Int J Biol Sci. 2019 Jul 21;15(9):1942-1954.
[4] Liu C, Huang Y, Qin T, et al. AZD5153 reverses palbociclib resistance in ovarian cancer by inhibiting cell cycle-related proteins and the MAPK/PI3K-AKT pathway. Cancer Lett. 2022 Mar 1;528:31-44.
[5] Zhu H, Shen M, Zhu Y, et al. AZD5153 enhances the chemo-sensitivity of gemcitabine on pancreatic cancer cells in vitro and in vivo. Cancer Cell Int. 2025 Aug 26;25(1):315.

[6] Rahman R, Rahaman MH, Hanson AR, et al. CDK9 inhibition inhibits multiple oncogenic transcriptional and epigenetic pathways in prostate cancer. Br J Cancer. 2024 Oct;131(6):1092-1105.
[7] Zhang X, Yang Y, Zou H, et al. Effective therapeutic targeting of tumor lineage plasticity in neuroendocrine prostate cancer by BRD4 inhibitors. Acta Pharm Sin B. 2025 Mar;15(3):1415-1429.
[8] Huang Y, Liu C, You L, et al. Synergistic effect of PARP inhibitor and BRD4 inhibitor in multiple models of ovarian cancer. J Cell Mol Med. 2023 Mar;27(5):634-649.

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