Product Data Sheet

Product Name: Pralsetinib (Blu667)
Cat. No.: GC31780

Chemical Properties

Cas. No.	2097132-94-8		
SMILES	O=C([C@@]1(OC)CC[C@@H](C2=NC(NC3=NNC(C)=C3)=CC(C)=N2)CC1)N[C@H](C4=CC=C(N5N=CC(F)=C5)N=C4)C		
Formula	$C_{27}H_{32}FN_9O_2$	M.Wt	533.6
Solubility	DMSO : ≥ 100 mg/mL (187.41 mM);Water : < 0.1 mg/mL (insoluble)	Storage	Store at 4°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	Pralsetinib (Blu667)		

Protocol

Cell experiment [1]:

Cell lines	T47D and MCF7 ERα+ breast cancer cells (human breast cancer cell lines)
Preparation Method	T47D and MCF7 cells stably expressing ESR1 fusion proteins or ESR1 LBD point mutants (Y537S, D538G) were maintained in hormone-deprived CSS media. Cells were treated with Pralsetinib at clinically relevant concentrations (100-500nM) for 48 hours to 2 weeks.

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Reaction Conditions	100-500nM; 48h to 2 weeks.
Applications	Pralsetinib significantly inhibited cell growth of ESR1 fusion-driven breast cancer cells, with IC_{50} values of ~100-120nM. Pralsetinib treatment potently inhibited RET phosphorylation (p-RET Y905) and downstream signaling pathways including ERK (p-ERK T202/Y204) and STAT3 (p-STAT3 Y705). Pralsetinib also induced apoptosis.

Animal experiment [2]:

Animal models	Female athymic nude mice (nu/nu)
Preparation Method	Mice were intracardially or intracranially inoculated with luciferase-expressing MDA-MB-231-BrM breast cancer cells. Mice received daily oral administration of Pralsetinib (10-30mg/kg; for 2 weeks) starting one day after tumor cell inoculation. For the treatment model, Pralsetinib administration began 10-14 days post-inoculation after brain metastases were established. Mice were monitored by bioluminescent imaging twice weekly.
Dosage form	10-30mg/kg; oral gavage; daily for 2 weeks.

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Applications	Pralsetinib treatment significantly reduced brain metastasis burden by 67% in the preventative model when administered early (30mg/kg). In the intracranial model, Pralsetinib (10mg/kg) significantly suppressed established brain tumor growth and enhanced tumor cell apoptosis.

References:
[1] Gu Y, Xue M, Wang Q, et al, Novel Strategy of Proxalutamide for the Treatment of Prostate Cancer through Coordinated Blockade of Lipogenesis and Androgen Receptor Axis. Int J Mol Sci. 2021 Dec 8;22(24):13222.
[2] Zhou T, Xu W, Zhang W, et al. Preclinical profile and phase I clinical trial of a novel androgen receptor antagonist GT0918 in castration-resistant prostate cancer. Eur J Cancer. 2020 Jul;134:29-40.

Background

Pralsetinib (Blu667) is a selective inhibitor of the rearranged during transfection (RET) kinase, indicated for the treatment of certain RET-altered positive tumors[1-2]. By selectively inhibiting RET fusions and mutations, Pralsetinib blocks downstream signaling pathways such as MAPK and PI3K-AKT, thereby suppressing tumor cell proliferation and

inducing apoptosis[3-4].

In vitro, treatment of RET-altered thyroid cancer and non-small cell lung cancer cells (TPC1, LC-2/ad, TT, and MZCRC1) with Pralsetinib (2-5μM) significantly inhibited cell proliferation and induced cell death[5]. In T47D and MCF7 breast cancer cells expressing transcriptionally active ESR1 fusion proteins or ERα ligand-binding domain point mutations (Y537S, D538G), Pralsetinib (100-500nM) markedly suppressed cell growth[6].

In vivo, daily oral administration of Pralsetinib (10-30mg/kg) in female athymic nude mice intracranially inoculated with MDA-MB-231-BrM triple-negative breast cancer cells. Pralsetinib significantly inhibited intracranial tumor growth[7]. In a C57BL/6 mouse model bearing orthotopic lung adenocarcinoma tumors derived from Trim24-Ret cell lines, daily oral treatment with Pralsetinib (20mg/kg) for 8 weeks induced significant tumor shrinkage, although acquired resistance emerged after 3 weeks of treatment[8].

References:
[1] Markham A. Pralsetinib: First Approval. Drugs. 2020 Nov;80(17):1865-1870.
[2] Nguyen L, Monestime S. Pralsetinib: Treatment of metastatic RET fusion-positive non-small cell lung cancer. Am J Health Syst Pharm. 2022 Mar 21;79(7):527-533
[3] Syed YY. Pralsetinib: A Review in Advanced RET Fusion-Positive NSCLC. Drugs. 2022 May;82(7):811-816.
[4] Griesinger F, Curigliano G, Thomas M, et al. Safety and efficacy of pralsetinib in RET fusion-positive non-small-cell lung cancer including as first-line therapy: update from the ARROW trial. Ann Oncol. 2022 Nov;33(11):1168-1178.
[5] Hu X, Liu X, Khatri U, et al. The heterogeneous transition state of resistance to RET kinase inhibitors converges on ERK1/2-driven Aurora A/B kinases. Drug Resist Updat. 2023 May;68:100958.
[6] Gou X, Kim BJ, Anurag M, et al. Kinome Reprogramming Is a Targetable Vulnerability in ESR1 Fusion-Driven Breast Cancer. Cancer Res. 2023 Oct 2;83(19):3237-3251.
[7] Regua AT, Bindal S, Najjar M, et al. RET Receptor Tyrosine Kinase Promotes Breast Cancer Metastasis to the Brain and RET Inhibitors Pralsetinib and Selpercatinib Suppress Breast Cancer Brain Metastases. bioRxiv [Preprint]. 2025 Oct 8:2025.10.07.680986.
[8] Hinz TK, Le AT, Doan T, et al. Modeling acquired TKI resistance and effective combination therapeutic strategies in murine RET+ lung adenocarcinoma. bioRxiv [Preprint]. 2025 Jun 7:2025.06.04.657911.

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