Pralsetinib

Cat. No.: HY-112301

CAS No.: 2097132-94-8

Molecular Formula: $C_{27}H_{32}FN_9O_2$

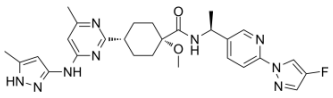
Molecular Weight: 533.6

Target: RET

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (187.41 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8741 mL	9.3703 mL	18.7406 mL
5 mM	0.3748 mL	1.8741 mL	3.7481 mL
10 mM	0.1874 mL	0.9370 mL	1.8741 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.69 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.69 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (4.69 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Pralsetinib (BLU-667) is a highly potent, selective RET inhibitor. Pralsetinib (BLU-667) inhibits WT RET, RET mutants V804L, V804M, M918T and CCDC6-RET fusion with IC_{50}s of 0.4, 0.3, 0.4, 0.4, and 0.4 nM, respectively[1].

IC_{50} & Target

IC50: 0.4 nM (Wild type RET), 0.3 nM (RET V804L), 0.4 nM (RET V804M), 0.4 nM (RET M918T), 0.4 nM (CCDC6-RET)[1]

In Vitro

Pralsetinib (BLU-667) demonstrates more than 10-fold increased potency over approved MKIs against oncogenic RET

	variants and resistance mutants[1]. Pralsetinib (BLU-667) demonstrates potent activity (IC_{50}=0.4 nM) against common oncogenic RET alterations, including RET M918T, an activating mutation found in MTC, as well as the CCDC6-RET fusion observed in PTC and NSCLC[1]. Pralsetinib (BLU-667) suppresses RET pathway signaling in a panel of RET-driven cell lines: LC2/ad (CCDC6-RET, NSCLC), MZ-CRC-1 (RET M918T, MTC), and TT (RET C634W, MTC)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Pralsetinib (BLU-667) potently inhibits growth of NSCLC and thyroid cancer xenografts driven by various RET mutations and fusions without inhibiting vascular endothelial growth factor receptor 2 (VEGFR-2)[1]. Pralsetinib (BLU-667) shows dose dependent activity against both KIF5B-RET Ba/F3 and KIF5B-RET V804L Ba/F3 allograft tumors with doses as low as 10 mg/kg twice-daily[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	KIF5B-RET Ba/F3 cells are exposed to compound concentrations ranging from 25 μM to 95.4 pM for 48 hours, and proliferation is assessed with Cell Titer Glo. TT, MZ-CRC-1, TPC-1 or LC2/ad cells are exposed to compound for 4 days and proliferation is measured by BrdU incorporation[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] BALB/c nude mice are inoculated subcutaneously into the right flank with KIF5B-RET Ba/F3 cells, KIF5B-RET V804L Ba/F3 cells, or TT cells. For all experiments, mice are dosed twice-daily with vehicle, 3 mg/kg, 10 mg/kg, or 30 mg/kg Pralsetinib (Blu667) or once-daily with 60 mg/kg Pralsetinib (Blu667; administered orally) or 60 mg/kg XL184[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancers (Basel). 2021, 13(8), 1909.
- Int J Mol Sci. 2021, 22(4), 1887.
- Transl Oncol. 2021 Jan;14(1):100887.

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REFERENCES

[1]. Subbiah V, et al. Precision Targeted Therapy With BLU-667 for RET-Driven Cancers. American Association for Cancer Research. 10.1158/2159-8290.CD-18-0338.

Caution: Product has not been fully validated for medical applications. For research use only.

India Contact:
Life Technologies (India) Pvt. Ltd.
306, Aggarwal City Mall, Opposite M2K Pitampura, Delhi – 110034 (INDIA). Ph: +91-11-42208000, 42208111, 42208222, Mobile: +91-9810521400, Fax: +91-11-42208444
Email: customerservice@lifetechindia.com Website: www.lifetechindia.com