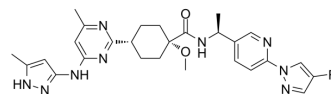


Pralsetinib

Cat. No.:	HY-112301		
CAS No.:	2097132-94-8		
Molecular Formula:	C ₂₇ H ₃₂ FN ₉ O 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 Concentration	Mass		
		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

- 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
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (4.69 mM); Clear solution
- 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 IC₅₀s of 0.4, 0.3, 0.4, 0.4, and 0.4 nM, respectively^[1].

IC₅₀ & 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 (IC₅₀=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.

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