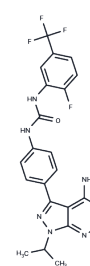


## AD80

## Chemical Properties

CAS No. :	1384071-99-1
Formula:	C <sub>22</sub> H <sub>19</sub> F <sub>4</sub> N <sub>7</sub> O
Molecular Weight:	473.43
Storage:	Powder: -20°C for 3 years   In solvent: -80°C for 1 year Actual storage temperature shall be subject to the COA.



## Biological Description

Description	AD80, a multikinase inhibitor, targets RET, RAF, SRC, and S6K with significantly reduced activity on mTOR.
Targets(IC50)	Raf,c-RET,S6 Kinase,Src
In vitro	AD80 and AD81 effectively inhibit key signaling molecules (RET, RAF, SRC, S6K) with significantly diminished mTOR activity compared to AD57 and AD58. Specifically, AD80 stands out for its proficient inhibition of the Ras-Erk pathway, showcasing a well-balanced polypharmacological profile that targets Ret, Raf, Src, Tor, and S6K, yielding high efficacy with minimal toxicity. Furthermore, AD80 demonstrates potent anti-proliferative effects on MZ-CRC-1 and TT thyroid cancer cells in vitro, likely mediated by triggering apoptosis. Additionally, AD80 uniquely suppresses S6K1 in conjunction with inhibiting the TAM family tyrosine kinase AXL, preventing S6K1 phosphorylation and its association with mTOR. This leads to a sustained inhibition of S6K1-driven signaling and protein synthesis, underscoring its therapeutic potential.
In vivo	AD80 significantly improves survival rates, rescuing 50% of mice transplanted with PTEN-deficient leukemia cells. When administered orally, both AD80 and AD81 remarkably allow 70-90% of Drosophila ptc>dRetMEN2B model animals to reach adulthood, surpassing the effectiveness of AD57. Furthermore, AD80 demonstrates superior tumor growth inhibition and minimizes body-weight fluctuations compared to vandetanib in a mouse xenograft model.
Cell Research	MZ-CRC-1 (MEN2B) and TT (MEN2A) cells are treated with AD80 (0.2 nM to 20 μM) for 7 days and cell viability is quantitated by MTT assay.
Animal Research	Mice showing established growing tumors are separated into vehicle or drug treatment groups. A similar range of tumor sizes is selected for each experiment (vehicle vs AD57; vehicle vs AD80 vs Vandetanib). Vehicle, AD57 (20 mg/kg), AD80 (30 mg/kg), or Vandetanib (50 mg/kg) are administered by oral gavage (PO; per os or by mouth) once daily, five times a week. Tumor and body weight measurements are performed 3 times a week.

## Solubility Information

## A DRUG SCREENING EXPERT

Solubility	DMSO: 60 mg/mL (126.73 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 1 mg/mL (2.11 mM),Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

### Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1122 mL	10.5612 mL	21.1224 mL
5 mM	0.4224 mL	2.1122 mL	4.2245 mL
10 mM	0.2112 mL	1.0561 mL	2.1122 mL
50 mM	0.0422 mL	0.2112 mL	0.4224 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

### Reference

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- Liu H, et al. Pharmacologic Targeting of S6K1 in PTEN-Deficient Neoplasia. *Cell Rep*. 2017 Feb 28;18(9):2088-2095.
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