# AT13148

**Cat. No.:** HY-16071

**CAS No.:** 1056901-62-2

**Molecular Formula:** $C_{17}H_{16}ClN_3O$

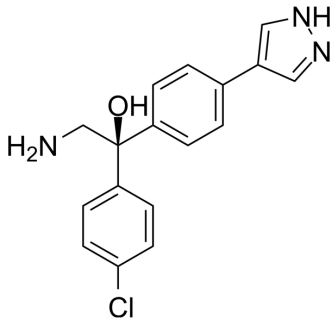
**Molecular Weight:** 313.78

**Target:** Akt; PKA; ROCK; Ribosomal S6 Kinase (RSK)

**Pathway:** PI3K/Akt/mTOR; Stem Cell/Wnt; TGF-beta/Smad; Cell Cycle/DNA Damage; Cytoskeleton; MAPK/ERK Pathway

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 2 years |
| | -20°C | 1 year |




## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 50 mg/mL (159.35 mM; Need ultrasonic)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 3.1869 mL | 15.9347 mL | 31.8695 mL |
| | 5 mM | 0.6374 mL | 3.1869 mL | 6.3739 mL |
| | 10 mM | 0.3187 mL | 1.5935 mL | 3.1869 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 (7.97 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.97 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.97 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

AT13148 is an orally active and ATP-competitive, multi-AGC kinase inhibitor with $IC_{50}$s of 38 nM/402 nM/50 nM, 8 nM, 3 nM, and 6 nM/4 nM for Akt1/2/3, p70S6K, PKA, and ROCKI/II, respectively.

**$IC_{50}$ & Target**

| | | | |
|---|---|---|---|
| Akt1<br>38 nM ($IC_{50}$) | p70S6K<br>8 nM ($IC_{50}$) | Akt3<br>50 nM ($IC_{50}$) | Akt2<br>402 nM ($IC_{50}$) |
| PKA | ROCKII | ROCKI | SGK3 |

| | | | | |
|---|---|---|---|---|
| | 3 nM ($IC_{50}$) | 4 nM ($IC_{50}$) | 6 nM ($IC_{50}$) | 63 nM ($IC_{50}$) |
| | RSK1<br>85 nM ($IC_{50}$) | CHK2<br>860 nM ($IC_{50}$) | Aurora B<br>1840 nM ($IC_{50}$) | |

**In Vitro**

AT13148 inhibits a panel of kinases at 10 μM, and the $IC_{50}$ values for p70S6K, PKA, ROCKI, and ROCKII are all less than 10 nM and those for AKT1, 2, and 3 are 38, 402, and 50 nM, respectively. For the related AGC kinases RSK1 and SGK3, the $IC_{50}$ values are 85 and 63 nM, respectively. In contrast, $IC_{50}$ values for the non-AGC kinases CHK2 and Aurora B are both greater than 800 nM. AT13148 potently inhibits proliferation with $GI_{50}$ values of 1.5 to 3.8 μM across a selected panel of cancer cell lines[1]. AT13148 treatment in gastric cancer cells dramatically suppresses activation of multiple AGC kinases, including Akt (at p-Thr-308), p70S6 kinase (p70S6K), glycogen synthase kinase 3β (GSK-3β) and p90 ribosomal S6 kinase (RSK)[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**In Vivo**

Oral drug administration of 5 mg/kg of AT13148 results in complete bioavailability. Clear inhibition of phosphorylation of the AKT substrates GSK3β, tuberin, and the p70S6K target S6RP are also observed in PTEN-deficient MES-SA human uterine tumor xenografts after treatment with 40 and 50 mg/kg p.o. of AT13148[1]. Oral gavage of AT13148 at well-tolerated doses significantly inhibits HGC27 xenograft tumor growth in nude mice. AGC activity is also dramatically decreased in AT13148-administrated HGC27 tumors[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

**Kinase Assay** [1]

AT13148 is assayed against 40 kinases and the percentage inhibition at 10 μM of AT13148 is determined. Individual $IC_{50}$ values are measured for selected kinases using ATP concentrations equivalent to the $K_m$ for each enzyme.

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**Cell Assay** [2]

Cells are seeded onto 96-well micro-plates at a density of $1\times10^4$ cells per well. After treatment, MTT solution (0.5 mg/mL) is added for 2-3 h. The MTT-purple formazan productions are dissolved in 0.1 N hydrochloric acid, and optical density (OD) is obtained through the micro-plate reader at 570 nm wavelength.

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**Animal Administration** [1]

For pharmacokinetic analysis, male athymic BALB/c mice are obtained from Harlan. AT13148 is formulated in 10% DMSO, 1% Tween-20, and 89% saline and administered at 5 mg/kg i.v. or p.o. Duplicate samples of heparinized whole blood are collected by cardiac puncture at 1, 2, 4, 6, 8, 16, 24, and 72 hours after dosing. Plasma and tissues (liver, kidney, spleen, and muscle are also taken) are prepared and frozen at −20°C until analysis. AT13148 is extracted from plasma and tissues using acetonitrile containing an internal standard and quantified using a liquid chromatography tandem mass spectrometry (LC-MS/MS) method and appropriate standard curves. Pharmacokinetic parameters are determined using WinNonLin software version 5.2.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Curr Res Transl Med. 2022 Jul;70(3):103343.
- Methods Mol Biol. 2018;1711:351-398.

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## REFERENCES

[1]. Yap TA, et al. AT13148 is a novel, oral multi-AGC kinase inhibitor with potent pharmacodynamic and antitumor activity. Clin Cancer Res. 2012 Jul 15;18(14):3912-23.

[2]. Xi Y, et al. AT13148, a first-in-class multi-AGC kinase inhibitor, potently inhibits gastric cancer cells both in vitro and in vivo. Biochem Biophys Res Commun. 2016 Sep 9;478(1):330-6



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