# 产品名称：AT13387
# 产品别名：Onalespib

**生物活性：**

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| **Description** | Onalespib (AT13387) is a potent inhibitor of Hsp90, with a $K_d$ of 0.71 nM. |
| **$IC_{50}$ & Target** | HSP90 |
| | 0.71 nM (Kd) |
| **In Vitro** | Onalespib (Compound 35) is a potent inhibitor of Hsp90, with $K_d$ of 0.71 nM. Onalespib shows potent antiproliferative activity in HCT116 cells, with an $IC_{50}$ of 31 nM. Onalespib also strongly inhibits the proliferation of a panel of human tumor cell lines, showing $IC_{50}$ of < 100 nM[1]. Onalespib exhibits cytotoxic activity against many of the PPTP cell lines, with median $IC_{50}$ of 41 nM [2]. |
| **In Vivo** | Onalespib (60 mg/kg, ip 3 days on and 3 days off for four cycles) shows antitumor activity in nude BALB/c mice bearing early stage HCT116 human colon carcinoma xenografts[1]. Onalespib (40 or 60 mg/kg, i.p.) induces significant differences in EFS distribution compared to controls in 17% evaluable solid tumor xenografts, but in none of the ALL xenografts[2]. |

**Solvent&Solubility**

***In Vitro:***

**DMSO : 50 mg/mL (122.09 mM;** ultrasonic and warming and heat to 60°C)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.4419 mL | 12.2094 mL | 24.4188 mL |
| | 5 mM | 0.4884 mL | 2.4419 mL | 4.8838 mL |
| | 10 mM | 0.2442 mL | 1.2209 mL | 2.4419 mL |

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

***In Vivo:***

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.10 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.10 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。

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| | 3.请依序添加每种溶剂： 10% DMSO →90% corn oil<br>Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution<br>此方案可获得 ≥ 2.5 mg/mL (6.10 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。<br><br>4.请依序添加每种溶剂： 50% PEG300 →50% saline<br>Solubility: 16.67 mg/mL (40.71 mM); Suspended solution; Need ultrasonic |
| **References** | [1]. Woodhead AJ, et al. Discovery of (2,4-dihydroxy-5-isopropylphenyl)-[5-(4-methylpiperazin-1-ylmethyl)-1,3-dihydroisoindol-2-yl]methanone (AT13387), a novel inhibitor of the molecular chaperone Hsp90 by fragment based drug design. J Med Chem. 2010 Aug 26;53(16):5956-69.<br>[2]. Kang MH, et al. Initial testing (Stage 1) of AT13387, an HSP90 inhibitor, by the pediatric preclinical testing program. Pediatr Blood Cancer. 2012 Jul 15;59(1):185-8. |

**实验参考：**

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| **Cell Assay** | In vitro testing is performed using DIMSCAN. Cells are incubated in the presence of Onalespib for 96 hours at concentrations from 1 nM to 10 μM[2]. |
| **Animal Administration** | HCT116 cells are injected SC into the right hind flank of male nude BALB/c mice. Tumours are apparent 7 to 10 days later. Mice are arranged into matched groups of 12 according to tumour volume giving a group mean of approximately 100 mm[3] at initiation of dosing. Tumour volumes are measured every 2 days. Statistical significance between groups is assessed using nonparametric one-way ANOVA. Mice are given the lactate salt of Onalespib using a repeated cycle of dosing of once per day for three days, no dose for three days, once per day for three days etc., for four dosing cycles at 60 mg/kg/dose (as free base equivalents) dissolved in 17.5% hydroxypropyl-β-cyclodextrin via the IP route. Control mice receive dose vehicle only via the same route. Tolerability is assessed by recording body weight, clinical observations and survival[1]. |
| **References** | [1]. Woodhead AJ, et al. Discovery of (2,4-dihydroxy-5-isopropylphenyl)-[5-(4-methylpiperazin-1-ylmethyl)-1,3-dihydroisoindol-2-yl]methanone (AT13387), a novel inhibitor of the molecular chaperone Hsp90 by fragment based drug design. J Med Chem. 2010 Aug 26;53(16):5956-69.<br>[2]. Kang MH, et al. Initial testing (Stage 1) of AT13387, an HSP90 inhibitor, by the pediatric preclinical testing program. Pediatr Blood Cancer. 2012 Jul 15;59(1):185-8. |