# 产品名称：WYE-125132 (WYE-132)
# 产品别名：WYE-132

## 生物活性：

| | |
|---|---|
| **Description** | WYE-132 (WYE-125132) is a highly potent, ATP-competitive, and specific mTOR kinase inhibitor ($IC_{50}$: 0.19±0.07 nM; >5,000-fold selective versus PI3Ks). WYE-132 (WYE-125132) inhibits mTORC1 and mTORC2. |

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

| mTORC1 | mTORC2 | mTOR | PI3Kα | PI3Kδ | hSMG1 |
|---|---|---|---|---|---|
| | | 0.19 nM ($IC_{50}$) | 1.179 μM ($IC_{50}$) | 2.38 μM ($IC_{50}$) | 1.25 μM ($IC_{50}$) |

**In Vitro**

WYE-132 (WYE-125132) potently inhibits recombinant mTOR via an ATP-competitive mechanism. WYE-132 is a potent antiproliferative agent against a panel of cancer cell lines with IC50 values generally in the nanomolar range. In the typical 3-day dose-response studies, WYE-132 exhibits a more profound antiproliferative activity than CCI-779 in MDA361 and other cells, as shown by the sharper inhibition at doses up to 10 μM. Fluorescence-activated cell sorting (FACS) analysis of inhibitor-treated (1 μM, 24 hours) MDA468, PC3MM2, U87MG, A549, and HCT116 cells indicates that WYE-132 elicits a more profound increase in G1-phase and a reduction in S-phase cells than CCI-779. The WYE-132-induced cell death is evident at 10 and 30 nM (6.2% and 13%, respectively) and is dose dependent, reaching 47% at 1 μM and 59% at 3 μM[1].

***In Vivo***

A single i.v. administration of 50 mg/kg WYE-132 (WYE-125132) into tumor-bearing mice leads to suppression of P-S6K(T389) and P-AKT(S473) for at least 8 hours in PC3MM2, MDA361, HCT116, and HT29 tumors, whereas the steady-state level of P-AKT(T308) is not significantly reduced, indicating that the antitumor efficacy of WYE-132 under such dosing regimens reflects the suppression of mTOR rather than PI3K. Oral administration of WYE-132 causes dose-dependent tumor growth delay in the PI3K/mTOR- and HER2-hyperactive MDA361 tumors with significant antitumor activity at 5 mg/kg, which correlates with a suppression P-S6 and P-AKT(S473) but not P-AKT(T308). An optimal dose of 50 mg/kg WYE-132 induces a substantial regression of large MDA361 tumors. WYE-132 also causes a potent and substantial tumor growth delay in the PTEN-null U87MG glioma[1].

**Solvent&Solubility**

***In Vitro:***

**DMSO : 25 mg/mL** (**48.11 mM;** Need ultrasonic)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 1.9246 mL | 9.6228 mL | 19.2456 mL |
| | 5 mM | 0.3849 mL | 1.9246 mL | 3.8491 mL |
| | 10 mM | 0.1925 mL | 0.9623 mL | 1.9246 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<br>Solubility: ≥ 2.5 mg/mL (4.81 mM); Clear solutio<br>此方案可获得 ≥ 2.5 mg/mL (4.81 mM，饱和度未知) 的澄清溶液。<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 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。<br><br>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)<br>Solubility: ≥ 2.5 mg/mL (4.81 mM); Clear solution<br>此方案可获得 ≥ 2.5 mg/mL (4.81 mM，饱和度未知) 的澄清溶液。<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 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 |
| **References** | [1]. Yu K, et al. Beyond rapalog therapy: preclinical pharmacology and antitumor activity of WYE-125132, an ATP-competitive and specific inhibitor of mTORC1 and mTORC2.Cancer Res. 2010 Jan 15;70(2):621-631. |

**实验参考：**

| | |
|---|---|
| **Cell Assay** | Cell lines of MDA-MB-361, MDA-MB-231, MDA-MB-468, BT549, LNCap, A549, H1975, H157, H460, U87MG, A498, 786-O, HCT116, MG63, Rat1, HEK293, HeLa and PC3MM2 are used. MDA361 cells are treated for 3 d with CCI-779 and WYE-132 (0.1 nM, 1 nM, 10 nM,100 nM, 1000 nM 10μM and 100μM). Cell growth assays and $IC_{50}$ determination are performed. For immunoblotting, cultured cells are treated as indicated. Total cell lysates are prepared using NuPAGE lithium dodecyl sulfate sample buffer and immunoblotted with various antibodies[1]. |
| **Animal Administration** | Mice[1]<br>For mTOR biomarker studies, various tumors (400 $mm^3$) grown s.c. in female nude mice are dosed by a single i.v. or oral injection with vehicle or WYE-125132 formulated in 5% ethanol, 2% Tween 80, and 5% polyethylene glycol-400. Tumor lysates are prepared and immunoblotted. For efficacy studies, nude mice bearing U87MG, MDA361, H1975, A549, A498, or 786-O tumors are staged and randomized into treatment groups (n=10). Mice are dosed orally with vehicle or WYE-125132 following qd x5 cycle regimen (5 d on, 2 d off) for up to four cycles. Temsirolimus/CCI-779 is formulated as WYE-132 and dosed i.v. once weekly. Bevacizumab is formulated in PBS and dosed i.p. via its clinical regimen (200 μg/mouse; once weekly). Tumor growth is monitored and analyzed. |
| **References** | [1]. Yu K, et al. Beyond rapalog therapy: preclinical pharmacology and antitumor activity of WYE-125132, an ATP-competitive and specific inhibitor of mTORC1 and mTORC2.Cancer Res. 2010 Jan 15;70(2):621-631. |