

产品名称: **RRX-001**

产品别名: **RRx-001**

**生物活性:**

|                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                         |
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| <b>Description</b> | RRx-001, a hypoxia-selective epigenetic agent and studied as a radio- and chem-sensitizer, triggers apoptosis and overcomes drug resistance in myeloma. RRx-001 exhibits potent anti-tumor activity with minimal toxicity[1]. RRx-001 is a dual small molecule checkpoint inhibitor by downregulating CD47 and SIRP- $\alpha$ [2]. RRx-001 is a potent inhibitor of G6PD and shows potent antimalarial activity[3].                                                                                                                                                         |                                                                                                                                                                         |
| <b>In Vitro</b>    | RRx-001 (0-5 $\mu$ M, 24 hours) inhibits MM cells growth and overcomes resistance to novel and conventional therapies[1].<br>RRx-001 blocks migration of MM cells and associated angiogenesis[1].<br>RRx-001 induces significant G1 phase growth arrest, with concomitant decrease in S phase. RRx-001 triggers significant apoptosis in MM cells[1].<br>RRx-001 inhibits DNA methylation by downregulating DNA methyltransferases[1].<br>RRx-001 and the supernatant of RRx-001-treated macrophages downregulates CD47 on tumor cells and SIRP $\alpha$ on macrophages[2]. |                                                                                                                                                                         |
|                    | <b>Cell Viability Assay[1]</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                         |
|                    | Cell Line:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Human MM-cell lines (MM.1S, RPMI-8226, H929, ARP1, KMS-11, OPM2, LR5, ANBL6.WT), along with drug resistant cell lines such as (MM.1R, Dox40, LR5, ANBL6.BR, RPMI-8226). |
|                    | Concentration:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 0-5 $\mu$ M.                                                                                                                                                            |
|                    | Incubation Time:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 24 hours.                                                                                                                                                               |
|                    | Result:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Induced a dose-dependent significant ( $p < 0.05$ ) decrease in viability of all cell lines.                                                                            |
|                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                         |
| <b>In Vivo</b>     | RRx-001 (5 mg/kg or 10 mg/kg, I.V., thrice-weekly for 24 days) inhibits tumor growth and prolongs survival in a xenograft mouse model[1].<br>RRx-001 (10 mg/kg, IP, twice a week and once a day) exhibits potent anti-cancer activity on the A549 lung cancer model dependent on the presence of tumor-associated macrophages (TAMs) in tumor tissue[2].                                                                                                                                                                                                                    |                                                                                                                                                                         |
|                    | <b>Animal Model:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | CB-17 SCID-mice were subcutaneously inoculated with $5.0 \times 10^6$ MM.1S cells in 100 $\mu$ L of serum-free RPMI 1640 medium[1].                                     |
|                    | <b>Dosage:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 5 mg/kg or 10 mg/kg.                                                                                                                                                    |
|                    | <b>Administration:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | I.V., thrice-weekly for 24 days.                                                                                                                                        |
|                    | <b>Result:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Blocked MM tumor growth and enhances survival.<br>Treatment was well tolerated, suggested by no apparent weight loss.                                                   |
|                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                         |
|                    | <b>Animal Model:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Female BALB/c nude mice ( $19.2 \pm 1.7$ g) based on A549 lung cancer model[2].                                                                                         |
|                    | <b>Dosage:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 10 mg/kg.                                                                                                                                                               |
|                    | <b>Administration:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | IP, twice a week and once a day.                                                                                                                                        |
|                    | <b>Result:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Resulted in the most significant tumor growth retardation.<br>Reduction of resident macrophages in tumor-bearing mice attenuates the antitumor activity of RRx-001.     |
|                    | <b>In Vitro:</b><br><b>DMSO : <math>\geq 100</math> mg/mL (373.11 mM)</b><br><br>* " $\geq$ " means soluble, but saturation unknown.                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                         |

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|                    | Preparing Stock Solutions                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <div> <div>Solvent</div> <div>Mass</div> <div>Concentration</div> </div> | 1 mg      | 5 mg       | 10 mg      |
|                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 1 mM                                                                     | 3.7311 mL | 18.6553 mL | 37.3107 mL |
|                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 5 mM                                                                     | 0.7462 mL | 3.7311 mL  | 7.4621 mL  |
|                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 10 mM                                                                    | 0.3731 mL | 1.8655 mL  | 3.7311 mL  |
| Solvent&Solubility | <p>*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。</p> <p>储备液的保存方式和期限：-80℃，6 months；-20℃，1 month。-80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。</p> <p><b>In Vivo:</b></p> <p>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 <b>In Vitro</b> 方式配制澄清的储备液，再依次添加助溶剂：</p> <p>——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</p> <p>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 (9.33 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (9.33 mM，饱和度未知) 的澄清溶液。</p> <p>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<br/>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。</p> <p>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 (9.33 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (9.33 mM，饱和度未知) 的澄清溶液。</p> <p>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。</p> <p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil<br/>Solubility: ≥ 2.5 mg/mL (9.33 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (9.33 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。</p> <p>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。</p> |                                                                          |           |            |            |
|                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                          |           |            |            |
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| References         | <p>[1]. Das DS, et al. A novel hypoxia-selective epigenetic agent RRx-001 triggers apoptosis and overcomes drug resistance in multiple myeloma cells. <i>Leukemia</i>. 2016 Nov;30(11):2187-2197.</p> <p>[2]. Yalcin O, et al. From METS to malaria: RRx-001, a multi-faceted anticancer agent with activity in cerebral malaria. <i>Malar J</i>. 2015 May 28;14:218.</p> <p>[3]. Cabrales P, et al. RRx-001 Acts as a Dual Small Molecule Checkpoint Inhibitor by Downregulating CD47 on Cancer Cells and SIRP-α on Monocytes/Macrophages. <i>Transl Oncol</i>. 2019 Apr;12(4):626-632.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                          |           |            |            |