# 产品名称：R428 (BGB324)
# 产品别名：Bemcentinib

## 生物活性：

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| **Description** | Bemcentinib (R428) is a potent and selective inhibitor of Axl with an $IC_{50}$ of 14 nM. |
| **$IC_{50}$ & Target** | IC50: 14 nM (Axl kinase) |
| **In Vitro** | Bemcentinib (R428) (2μM) significantly interferes with mechanisms of migration and invasion of Axlpos melanoma cells at levels comparable to Axl knockdown[1]. Bemcentinib (R428) synergizes with CDDP to enhance suppression of liver micrometastasis[2]. Bemcentinib (R428) (50 nM-1μM) causes a concentration-dependent inhibition of preadipocyte differentiation into mature adipocytes, as evidenced by reduced lipid uptake[3]. |
| ***In Vivo*** | Bemcentinib (R428) (125 mg/kg, p.o.) significantly blocks MDA-MB-231-luc-D3H2LN metastases development in two independent mouse models of breast cancer dissemination, suppresses both tumor angiogenesis and vascular endothelial growth factor (VEGF)-induced corneal neovascularization in vivo[2]. Bemcentinib (R428) (75 mg/kg/day, 25 mg/kg twice daily, p.o.) makes mice keep on a high-fat diet resulted in significantly reduced weight gain and subcutaneous and gonadal fat mass[3]. |
| **Solvent&Solubility** | ***In Vitro:*** **DMSO : 10.25 mg/mL (20.23 mM;** Need ultrasonic and warming) |

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
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| | 1 mM | 1.9738 mL | 9.8689 mL | 19.7379 mL |
| | 5 mM | 0.3948 mL | 1.9738 mL | 3.9476 mL |
| | 10 mM | 0.1974 mL | 0.9869 mL | 1.9738 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: ≥ 0.71 mg/mL (1.40 mM); Clear solution

此方案可获得 ≥ 0.71 mg/mL (1.40 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 7.1 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: ≥ 0.71 mg/mL (1.40 mM); Clear solution

此方案可获得 ≥ 0.71 mg/mL (1.40 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 7.1 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: ≥ 0.71 mg/mL (1.40 mM); Clear solution<br>此方案可获得 ≥ 0.71 mg/mL (1.40 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 7.1 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 |
| **References** | [1]. Sensi M, et al. Human cutaneous melanomas lacking MITF and melanocyte differentiation antigens express a functional Axl receptor kinase. J Invest Dermatol. 2011 Dec;131(12):2448-57.<br>[2]. Holland SJ, et al. R428, a selective small molecule inhibitor of Axl kinase, blocks tumor spread and prolongs survival in models of metastatic breast cancer. Cancer Res. 2010 Feb 15;70(4):1544-54.<br>[3]. Lijnen HR, et al. Growth arrest-specific protein 6 receptor antagonism impairs adipocyte differentiation and adipose tissue development in mice. J Pharmacol Exp Ther. 2011 May;337(2):457-64. |

**实验参考：**

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| **Cell Assay** | Cells maintained for 24 hours in serum-free medium are harvested and transferred to the upper chamber ($1.5\times10^5$ cells per well) of uncoated (migration) or matrigel-coated (invasion) 24-well chambers. RPMI medium containing 10% fetal bovine serum is added to the lower chamber. Bemcentinib (R428) (2 μM) or vehicle (DMSO, 0.25%) is added for 2 hours to cells before loading them in the upper chambers. Both the upper and lower chambers contain the drug or vehicle. Quantification of migrating/invading cells is obtained by measuring their fluorescent signals with a 480/520 nm filter set on an Infinite M1000 microplate reader 20 or 42 hours later, respectively. [1] |
| **Animal Administration** | Seven- to 8-wk-old female NCr nu/nu mice are injected intracardially with bioluminescent MDA-MB-231-luc-D3H2LN cell suspension. Oral dosing with Bemcentinib (R428) (125 mg/kg, p.o.) or vehicle twice daily begins 2 h before cell implantation and continue to day 21 (n=20). Metastatic burden is quantified by in vivo bioluminescence imaging on day 22 and analyzed using the Wilcoxon rank sum test. [2] |
| **References** | [1]. Sensi M, et al. Human cutaneous melanomas lacking MITF and melanocyte differentiation antigens express a functional Axl receptor kinase. J Invest Dermatol. 2011 Dec;131(12):2448-57.<br>[2]. Holland SJ, et al. R428, a selective small molecule inhibitor of Axl kinase, blocks tumor spread and prolongs survival in models of metastatic breast cancer. Cancer Res. 2010 Feb 15;70(4):1544-54.<br>[3]. Lijnen HR, et al. Growth arrest-specific protein 6 receptor antagonism impairs adipocyte differentiation and adipose tissue development in mice. J Pharmacol Exp Ther. 2011 May;337(2):457-64. |