产品名称：**CZ415**
产品别名：**CZ415**

## 生物活性：

| | | | |
|---|---|---|---|
| **Description** | CZ415 is a potent and highly selective mTOR inhibitor with a pIC50 of 8.07. CZ415 inhibits mTORC1 and mTORC2 protein complex. | | |
| **$IC_{50}$ & Target** | mTOR | mTORC1 | mTORC2 |
| | 8.07 ($pIC_{50}$) | | |
| **In Vitro** | Inhibition of phosphorylation for both downstream targets results in 14.5 nM IC50 for pS6RP and 14.8 nM for pAKT. The immunosuppressive effect of CZ415 is measured by detecting secreted IFNγ after 18 hours in stimulated human whole blood and the resulting IC50 is 226 nM. As a predictor for cardiotoxicity, the activity of CZ415 against the human cardiac ion channel hERG is assessed in a whole-cell patch-clamp assay in HEK293 cells resulting in an IC50 of 48 μM[1]. | | |
| **In Vivo** | CZ415 is a highly selective mTOR inhibitor showing in vivo efficacy in a collagen induced arthritis (CIA) model. For full characterization of CZ415 and to enable improved dose predictions, the pharmacokinetic (PK) profile is assessed in rat. PK and oral bioavailability are determined after of 1 mg/kg intravenous (iv) bolus and 3 mg/kg oral (po) administration. The observed plasma clearance, corresponding to 45% liver blood flow, suggests that sufficient levels of free compound are circulating in the animal over time. The oral uptake is rapid with a Tmaxmax of 0.5 h and bioavailability F = 44% indicates very good absorption from the gut[1]. | | |
| **Solvent&Solubility** | ***In Vitro:***<br>**DMSO： ≥ 31 mg/mL (67.46 mM)**<br>* "≥" means soluble, but saturation unknown. | | |

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.1760 mL | 10.8800 mL | 21.7599 mL |
| | 5 mM | 0.4352 mL | 2.1760 mL | 4.3520 mL |
| | 10 mM | 0.2176 mL | 1.0880 mL | 2.1760 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。

| | |
|---|---|
| **References** | [1]. Cansfield AD, et al. CZ415, a Highly Selective mTOR Inhibitor Showing in Vivo Efficacy in a Collagen Induced Arthritis Model. ACS Med Chem Lett. 2016 Jun 10;7(8):768-73. |

## 实验参考：

| | |
|---|---|
| **Animal Administration** | Mice[1]<br>To determine the effects of CZ415 on its pharmacological target, dose-dependent changes in phosphorylation levels of S6 Ribosomal Protein and Akt - both downstream targets of mTOR are assessed. CZ415 is administered orally at 1, 3 and 10 mg/kg to mice 1 h before anti-CD3 stimulus. 15 min after stimulation, spleens are dissected and analyzed for pS6RP and pAKT levels. A dose related significant inhibition of phosphorylation of both S6RP and Akt are observed after compound administration. In particular, 1 and 3 mg/kg CZ415 could fully inhibit S6RP phosphorylation induced |

| | |
|---|---|
| | by anti-CD3 stimulation and 10 mg/kg additionally decreased the constitutive phosphorylation levels as measured in the control group. |
| **References** | [1]. Cansfield AD, et al. CZ415, a Highly Selective mTOR Inhibitor Showing in Vivo Efficacy in a Collagen Induced Arthritis Model. ACS Med Chem Lett. 2016 Jun 10;7(8):768-73. |