产品名称：GS-9620
产品别名：维沙莫德 ；Vesatolimod

生物活性：

Description	Vesatolimod (GS-9620) is a potent, selective and orally active agonist of Toll-Like Receptor (TLR7) with an EC50 of 291 nM.
IC_{50} & Target	EC50: 291 nM (TLR7), 9 μM (TLR8)[3]
In Vitro	Vesatolimod (GS-9620) rapidly internalizes into cells and preferentially localizes to and signals from endo-lysosomal compartments. To test this hypothesis, the kinetics of cellular uptake of the compound in Daudi cells using tritiated Vesatolimod (^{3}H-GS-9620) is measured. The kinetics of ^{3}H-GS-9620 accumulation is rapid, reaching concentration-dependent steady-state equilibrium in approximately thirty minutes. Measured intracellular concentration of ^{3}H-Vesatolimod is 5-fold higher than the extracellular concentration of ^{3}H-GS-9620 used to treat cells. Increases in intracellular ^{3}H-Vesatolimod concentrations are roughly proportional with increasing concentrations of ^{3}H-GS-9620[1].
In Vivo	Single oral doses of Vesatolimod (GS-9620) at 0.3 and 1 mg/kg in uninfected chimpanzees demonstrates a dose- and exposure-related induction of serum IFN-α, select cytokines/chemokines, and IFN-stimulated genes (ISG) in the peripheral blood and liver. Following oral administration at 0.3 (n=3), and 1 mg/kg (n=3 and n=4), Vesatolimod (GS-9620) C_{max} is 3.6±3.5, 36.8±34.5, and 55.4±81.0 nM, respectively. Peak serum IFN responses occur at 8 h post-dose. The mean peak levels of induced serum IFN-α are 66 and 479 pg/mL at doses of 0.3 and 1 mg/kg, respectively. Vesatolimod (GS-9620) treatment induces ISG transcripts including ISG15, OAS-1, MX1, IP-10 (CXCL10), and I-TAC (CXCL11) in peripheral blood mononuclear cells (PBMC) at 0.3 mg/kg and in both PBMC and the liver at 1 mg/kg[2].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 16.67 mg/mL (40.61 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4360 mL	12.1800 mL	24.3599 mL
5 mM	0.4872 mL	2.4360 mL	4.8720 mL
10 mM	0.2436 mL	1.2180 mL	2.4360 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: ≥ 1.67 mg/mL (4.07 mM); Clear solution

此方案可获得 ≥ 1.67 mg/mL (4.07 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 16.699999 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: 1.67 mg/mL (4.07 mM); Suspended solution; Need ultrasonic 此方案可获得 1.67 mg/mL (4.07 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 16.699999 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 1.67 mg/mL (4.07 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (4.07 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。 以 1 mL 工作液为例，取 100 μL 16.699999 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Rebbapragada I, et al. Molecular Determinants of GS-9620-Dependent TLR7 Activation. PLoS One. 2016 Jan 19;11(1):e0146835. [2]. Lanford RE, et al. GS-9620, an Oral Agonist of Toll-Like Receptor-7, Induces Prolonged Suppression of Hepatitis B Virus in Chronically Infected Chimpanzees. Gastroenterology. 2013 Feb 13. pii: S0016-5085(13)00169-8. [3]. D Tumas, et al. Preclinical Characterization of GS-9620, A Potent and Selective Oral TLR7 Agonist.

实验参考：

Cell Assay	Daudi cells are incubated for indicated times with varying concentrations [^{3}H]Vesatolimod (GS-9620) (0.7μCi/mL). Cell associated radioactivity is extracted with ice cold 80% ethanol and measured using liquid scintillation counting. The total amount of Vesatolimod in cells is calculated from a calibration curve for Vesatolimod (GS-9620) mass versus radioactivity. Cell volume is measured[1].
Animal Administration	Chimpanzee[2] Chimpanzees are used. The trial design includes 4 weeks of pre-study evaluation (Day-28, -13 and just prior to first dose) and two cycles of oral Vesatolimod (GS-9620) treatment every other day three times per week for 4 weeks with one cycle at 1 mg/kg, and, after a one week rest, a second cycle at 2 mg/kg. Animals are also intensely monitored for 14 weeks after treatment to assess tolerability and durability of response.
References	[1]. Rebbapragada I, et al. Molecular Determinants of GS-9620-Dependent TLR7 Activation. PLoS One. 2016 Jan 19;11(1):e0146835. [2]. Lanford RE, et al. GS-9620, an Oral Agonist of Toll-Like Receptor-7, Induces Prolonged Suppression of Hepatitis B Virus in Chronically Infected Chimpanzees. Gastroenterology. 2013 Feb 13. pii: S0016-5085(13)00169-8. [3]. D Tumas, et al. Preclinical Characterization of GS-9620, A Potent and Selective Oral TLR7 Agonist.