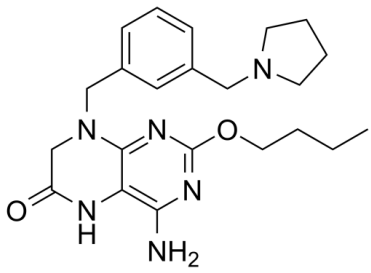
Data Sheet

Product Name:	Vesatolimod
Cat. No.:	CS-1352
CAS No.:	1228585-88-3
Molecular Formula:	C22H30N6O2
Molecular Weight:	410.51
Target:	Apoptosis; HBV; HCV; HIV; Toll-like Receptor (TLR)
Pathway:	Anti-infection; Apoptosis; Immunology/Inflammation
Solubility:	DMSO : ≥ 16.67 mg/mL (40.61 mM); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

Vesatolimod (GS-9620) is a potent, selective and orally active agonist of **Toll-Like Receptor (TLR7)** with an **EC_{50}** of 291 nM. IC50 & 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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Vesatolimod (GS-9620) is dissolved in DMSO and stored, and then diluted with appropriate medium before use[1].[1]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:** [2]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.

CAIndexNames:

6(5H)-Pteridinone, 4-amino-2-butoxy-7,8-dihydro-8-[[3-(1-pyrrolidinylmethyl)phenyl]methyl]-

SMILES:

O=C1NC2=C(N)N=C(OCCCC)N=C2N(CC3=CC=CC(CN4CCCC4)=C3)C1

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA