CYM5442 is a potent, highly-selective and orally active sphingosine 1-phosphate (S1P1) receptor agonist with an EC50 of 1.35 nM. CYM5442 is inactive against S1P2, S1P3, S1P4, and S1P5. CYM5442 activates S1P1-dependent p42/p44-MAPK phosphorylation. CYM5442 exerts retinal neuroprotection. CYM5442 can easily penetrate the central nervous system (CNS) [1] [2].

**Western Blot Analysis**

- **Cell Line:** HEK293 cells stably expressing S1P1 fused to GFP on the carboxy-terminus
- **Concentration:** 0.5 µM
- **Incubation Time:** 0 minutes, 2 minutes, 5 minutes, 10 minutes, 30 minutes, 60 minutes
- **Result:** Stimulated S1P1 phosphorylation in a time-dependent manner.

**In Vivo**

- **Animal Model:** Adult male albino Wistar rats (8-10 weeks old; 180-230 g) infected ocular endothelin-1 (ET-1) [2]
- **Dosage:** 1 mg/kg

CYM5442 (0.5 µM; 0-60 minutes; HEK293 cells) treatment stimulates S1P1 phosphorylation in a time-dependent manner in P32-orthophosphate labeled cells [1]. CYM5442 activates S1P1-dependent p42/p44-MAPK phosphorylation in CHO-K1 cells transfected with S1P1 with an EC50 of 46 nM. The R120 for alanine (R120A) mutant is still able to maintain p42/p44-MAPK activity when incubated with CYM5442 (EC50 of 67 nM). Activation of p42/p44-MAPK by CYM5442 in E121A S1P1 cells is concentration dependent, with a mean EC50 value of 134 nM [1].
<table>
<thead>
<tr>
<th>Administration:</th>
<th>Intraperitoneal injection; daily; for 5 days</th>
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<td>Result:</td>
<td>Visual evoked potentials (VEP) showed preserved visual function. Showed significantly higher retinal ganglion cells (RGCs) numbers.</td>
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REFERENCES
