Purpose: To evaluate the pharmacology, ocular distribution, and safety of MIM-D3. MIM-D3 is a small molecule NGF peptidomimetic, which has potential to increase conjunctival and tear glycoconjugate secretion in vitro and in vivo. Methods: (a) Scopolamine-treated rats were dosed daily with vehicle, 0.4%, 1% or 2.5% MIM-D3 for 17 days. Tear breakup time (tBUT), corneal staining and tear glycoconjugate levels were evaluated during for 28-days. (b) Rabbits received topical doses of vehicle, 0.5%, 1% or 2% MIM-D3 four times/day for 7-days. On day 8, the aqueous humor, conjunctiva, cornea, iris, and eyelid were collected for MIM-D3 analysis. (c) Male and female rabbits and dogs were dosed topically with vehicle, 1%, 3% or 5% MIM-D3 eight times/day for 28-days. Biomicroscopy (McDonald-Shadduck) and dilated ophthalmoscopy were evaluated predose and at the end of each week. Gross ocular observations for irritation (Draize scoring scale) were monitored twice daily. Ocular tissues were evaluated by histopathology. Results: (a) Dry eye conditions were established 5 days after subcutaneous implantation of a scopolamine pump in rats. Daily topical instillation of 1% MIM-D3 (days 5-21) produced a significant decrease in corneal staining, increase in tBUT and tear glycoconjugates on day 28. (b) MIM-D3 was detected in relatively high concentrations in the rabbit eyelid and conjunctiva, low concentrations in the cornea and minimal detection in the aqueous humor and iris. (c) No signs of ocular toxicity were observed in rabbits and dogs in any MIM-D3 dose groups. There was a dose-dependent increase in discharge noted in dogs, but not rabbits, dosed ≥3% MIM-D3 after the 8th daily dose. There was mild congestion and chemosis, without any correlating histopathology. Conclusions: MIM-D3 improved clinical signs of dry eye in an experimental rat model. Therapeutic concentrations of MIM-D3 were achieved in the rabbit conjunctiva. MIM-D3 exhibited an excellent ocular safety profile in rabbits and dogs, which supports clinical development as a topical agent for the potential treatment of dry eye.