

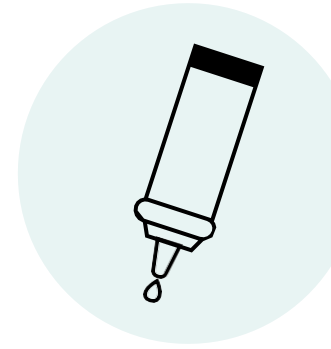
Redefining Topical Therapy: A Mucoadhesive NanoParticle Platform for Sustained Drug Delivery in Ophthalmology and Beyond

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Introduction



- Glaucoma is a leading cause of irreversible blindness worldwide. Early intervention is critical, yet topical therapies often fail due to low adherence, with studies reporting that as few as 20% of patients use the prescribed regimen. [1]
- Poor compliance coupled with limited ocular bioavailability of conventional eye drops drives significant unmet need in glaucoma management.

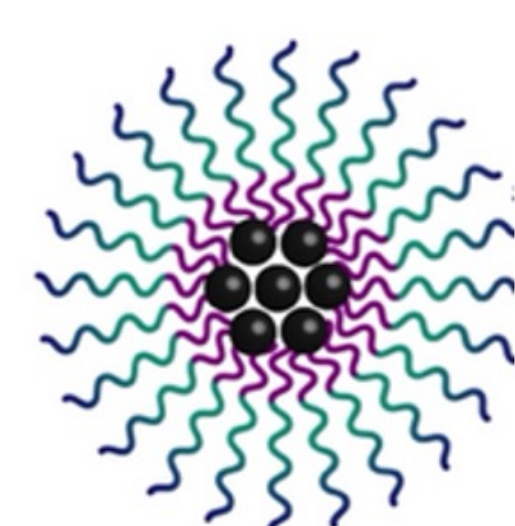


- Our proprietary Mucoadhesive Nanoparticles (MNP) platform enables enhanced formulation of poorly soluble drugs — allowing higher drug loading, improved retention and sustained release on the mucosal surfaces, shown here through the ocular surface.

MNP BENEFITS

- Polymeric micelles adhere to mucosal surfaces and enable fewer administrations with sustained release and reducing off-target effects
- Localized delivery to site of action
- Reduced Dosing Frequency
- Greater Bioavailability at target

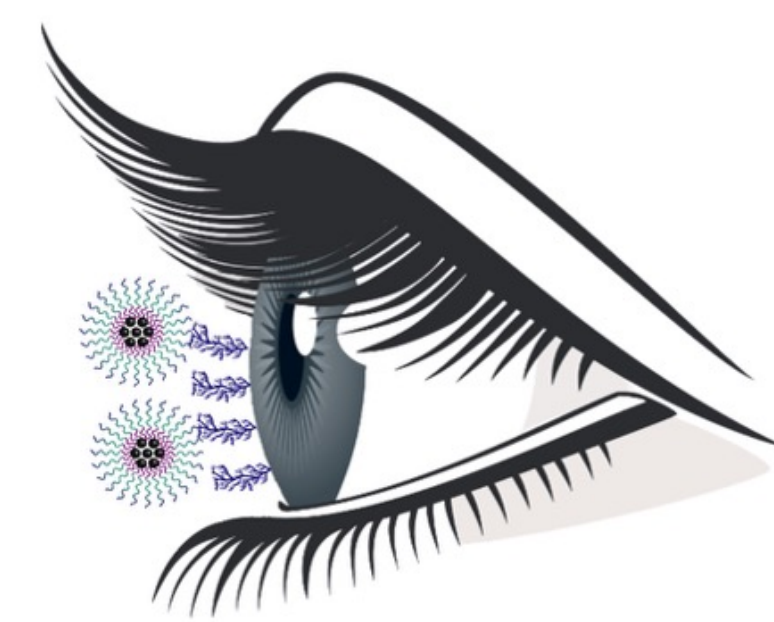
MNPs



Enable sustained release through encapsulation (fewer doses needed)



Mucosal Binding



Polymeric micelles adhere to mucosal surfaces

Objective

With glaucoma as our lead indication, the goal of this work was to characterize OPT-101 latanoprost-loaded MNPs. This included optimizing the encapsulation of latanoprost, evaluating the *in vivo* drug levels within aqueous tissues and determining the formulation's effect on IOP in normotensive dogs.

Methods

In Vitro Drug Loading

- Polymer synthesis:** As per previous protocols [2], co-polymers were synthesized by RAFT polymerization consisting of PBA, MAA and PLA. Micelles loaded with latanoprost were formed by precipitation into PBS buffer from acetone.
- Drug Loading & Release:** Encapsulation (polymer concentration of 5 mg/mL) was optimized for drug loading at either high or low levels (0.2% or 0.05%) and drug release was into sink PBS conditions. HPLC was used to assess drug levels.

In Vivo Studies

- Safety Study:** Loaded and unloaded MNPs were dropped on New Zealand White Rabbits and examined under a slit lamp and by Optical Coherence Tomography (OCT) to assess the safety and tolerability of the particles.
- Mouse Glaucoma Model Study:** Intraocular pressure (IOP) was measured in a mouse genetic closed angle glaucoma model [3], with IOP measured by a tonometer.
- Normotensive Dog Study:** MNPs containing 0.05% latanoprost concentrations were dropped in normotensive beagle dogs, with IOP measured by a tonometer.
- PK Study:** New Zealand White Rabbits were used for a pharmacokinetic study comparing latanoprost-loaded MNPs to branded latanoprost and unloaded MNPs. The aqueous humor was harvested and the amount of latanoprost was determined via LC-MS.

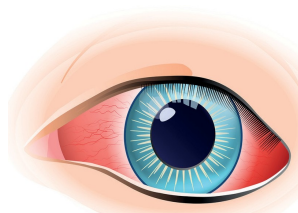
Use Beyond Glaucoma & Ophthalmology

Our MNP technology features:

- Modular Design** Compatible with a wide range of small-molecule APIs
- Multiple Asset Pipeline Potential** Scalable manufacturing with modular CMC approach
- De-risked Regulatory Pathway** 505(b)(2) pathway enables speed to market and patent extensions
- Low Cost of Goods Sold (COGS)** Simple supply chain supports cost-effective production

The MNP platform has shown positive results in indications beyond glaucoma:

- Pre-clinical studies in dry eye disease (cyclosporine A) and uveitis models (completed in collaboration with **Afecta Pharmaceuticals**) have shown similar increased retention and drug penetration.
- The MNP delivery system is not limited to ophthalmology — its mucoadhesive, sustained-release, solubility-enhancing properties make it broadly applicable to mucosal therapies (e.g., nasal, respiratory and urogenital applications are currently under investigation) where improved local bioavailability is critical. The technology is also currently developed for animal health applications.

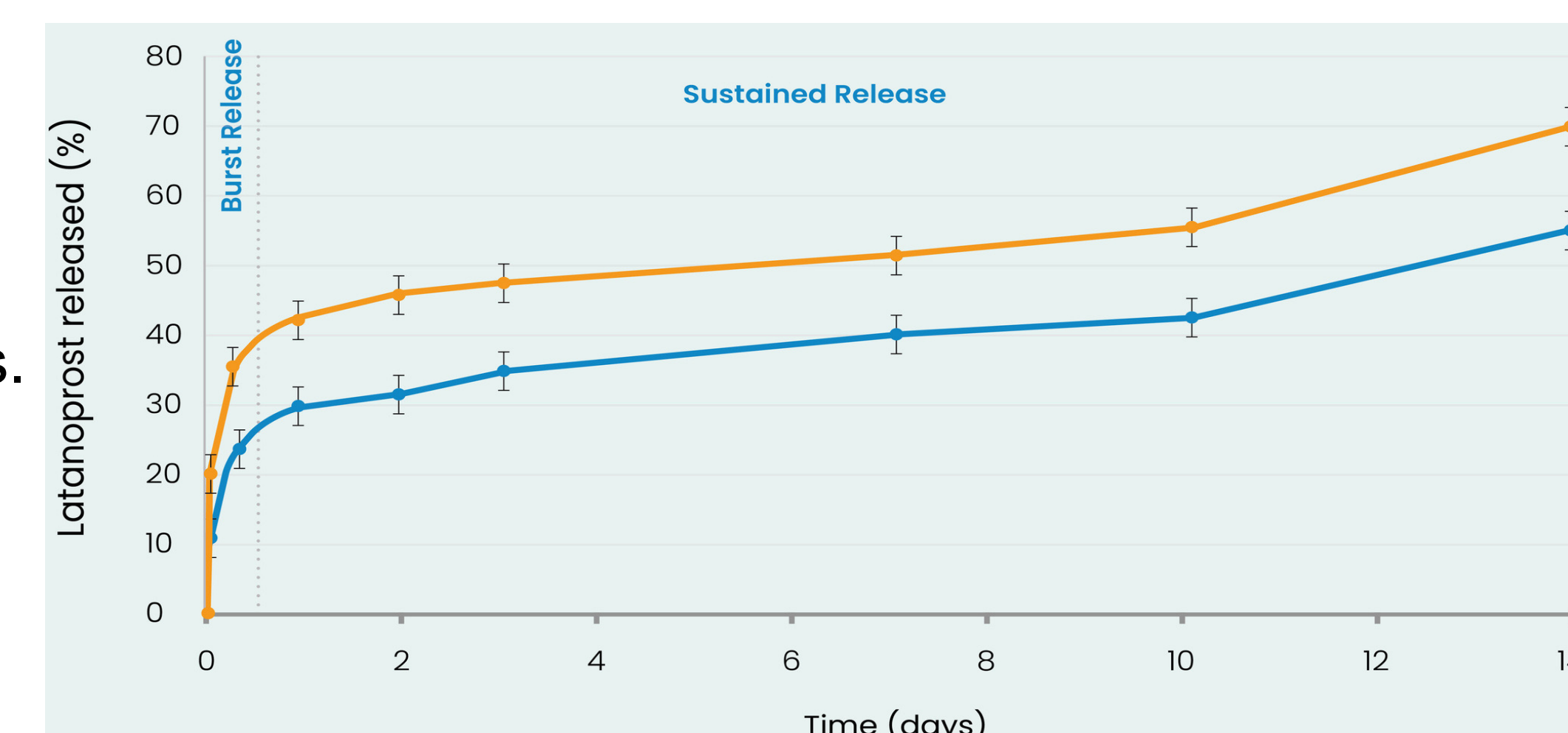


Results

In Vitro Drug Loading & Release

- Drug loading could be achieved up to 40x commercial latanoprost concentrations (up to 0.2%) with no additional co-solvents required.
- Drug release was sustained for 2 weeks.

Figure 1: Drug release was sustained up to two weeks using high (orange) or low (blue) loading. It exhibits an initial burst release, followed by a sustained release.



In Vivo Studies

- The MNPs showed excellent safety and tolerability profiles, both within the anterior and posterior of the eye.

Figure 2: Rabbit eyes with PBS (left) and MNPs (right), showing no ocular irritation or edema. This was confirmed throughout the 28 days of dropping.

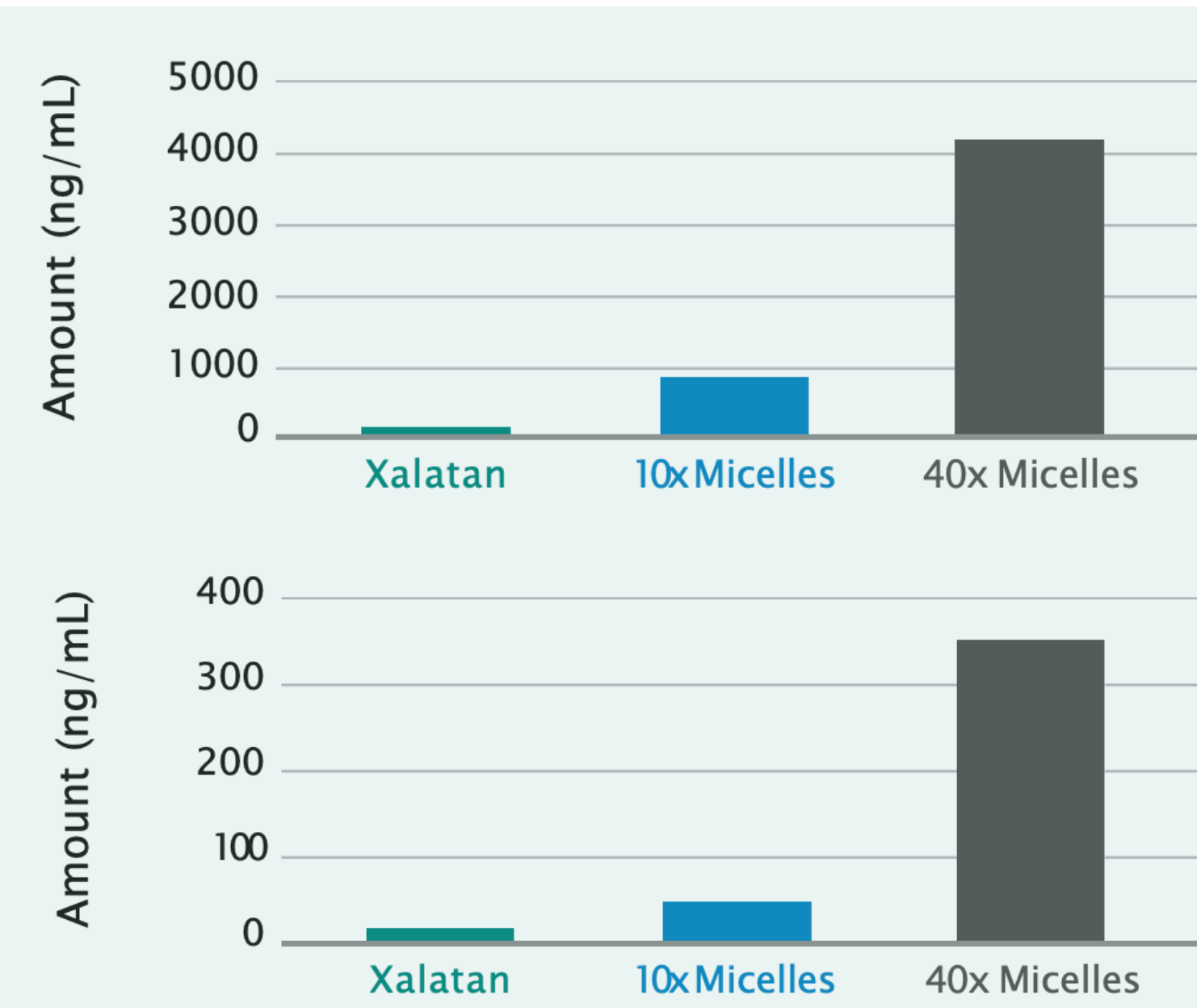
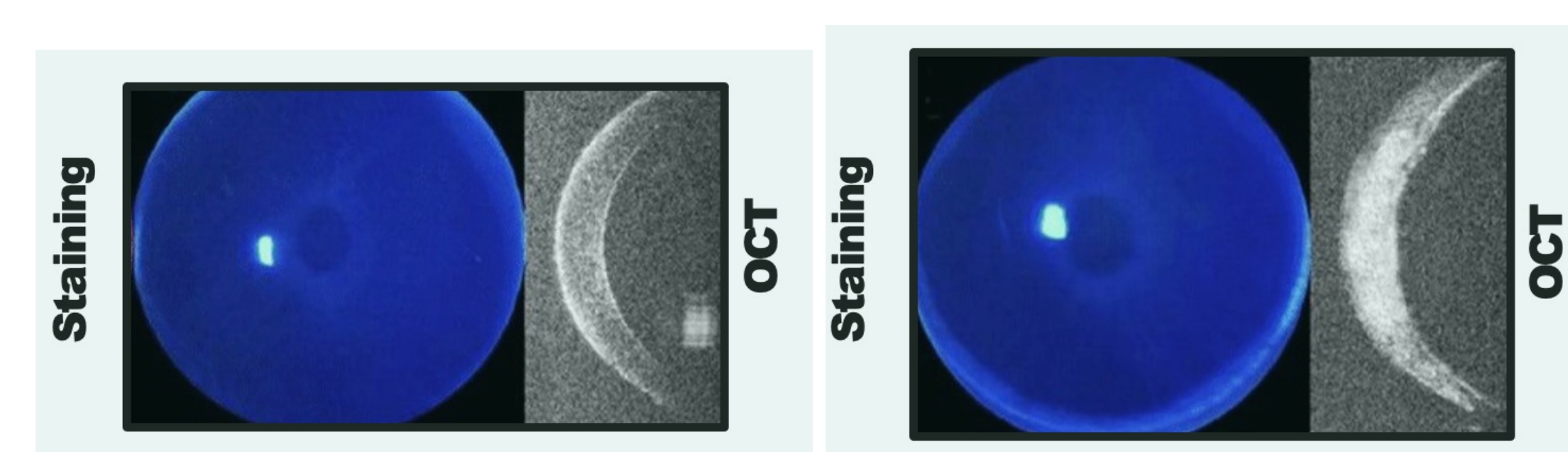


Figure 3: Aqueous humor levels in rabbit eyes at 1 hour (top) and 6 hours (bottom) after dosing. The greater drug loading results in improved drug amounts.

- IOP remained reduced for multiple days in glaucoma models and normotensive animals. Drug levels in ocular tissues rose with dose and were higher than expected from concentration alone, consistent with improved surface retention and bioavailability.

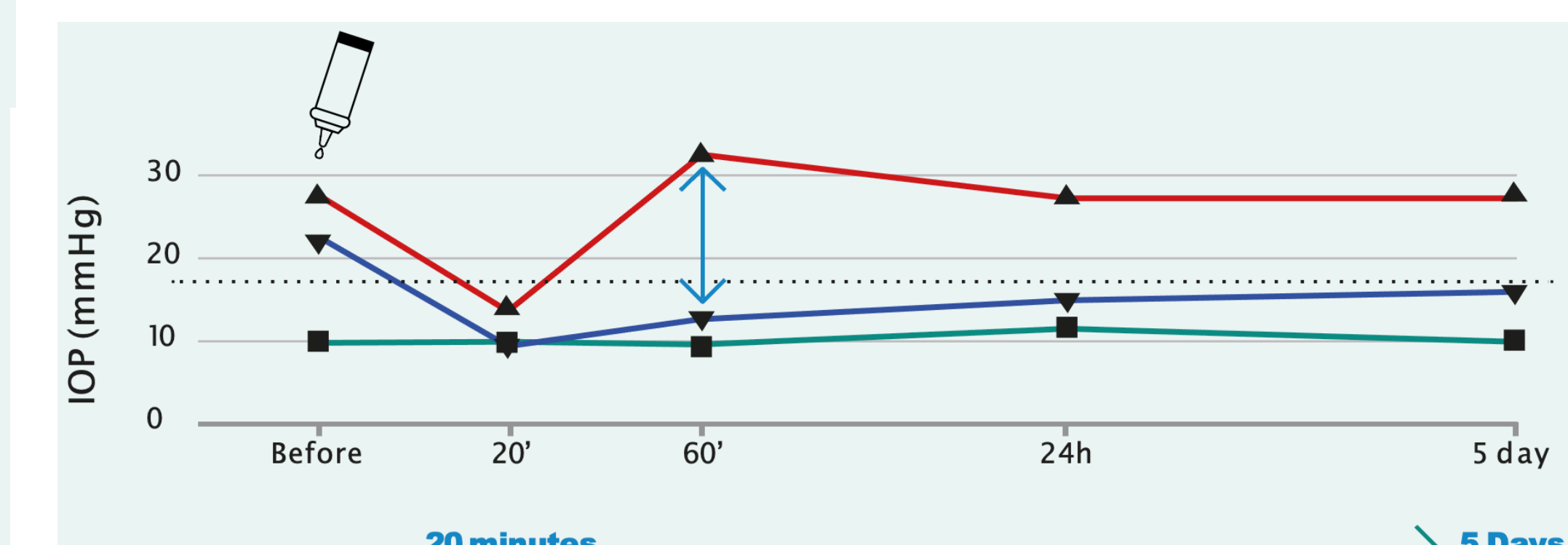


Figure 4: Genetic mouse model for glaucoma with a healthy mouse (green) shown against the model dosed with Xalatan (red) and OPT-101 (blue). IOP rebound is rapid with Xalatan but slow with MNPs.

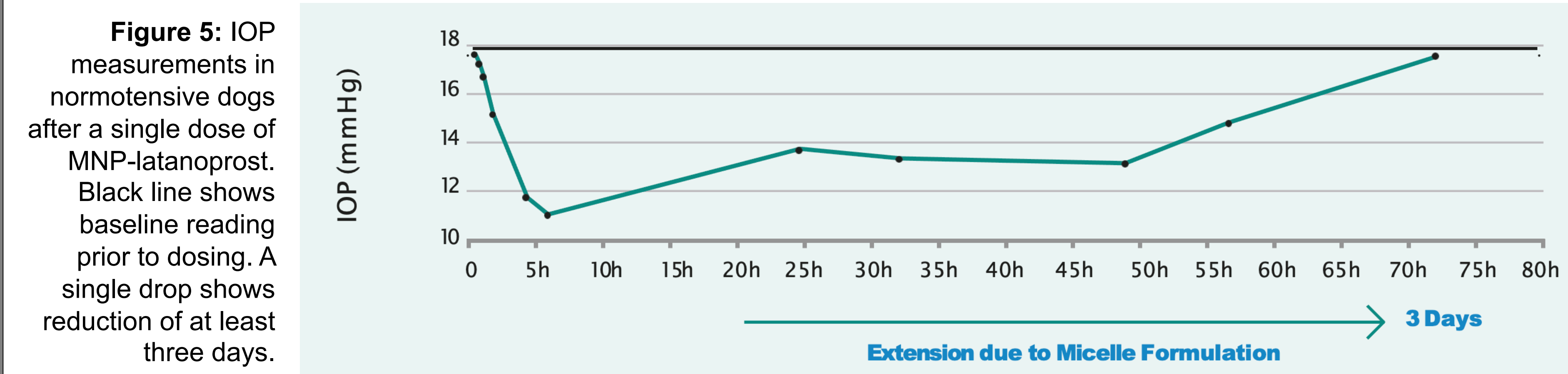


Figure 5: IOP measurements in normotensive dogs after a single dose of MNP-latanoprost. Black line shows baseline reading prior to dosing. A single drop shows reduction of at least three days.

Conclusions

- Our once-weekly latanoprost-MNP (OPT-101) program demonstrates that mucoadhesive nanoparticles can fundamentally improve glaucoma therapy by sustaining intraocular pressure reduction and addressing the critical issue of poor patient adherence. This proof of concept establishes both clinical and commercial differentiation for a first-line, premium topical glaucoma treatment.
- MNP formulations of cyclosporine A and non-steroidal agents show equivalent or superior outcomes in dry eye disease and uveitis animal models, confirming the platform's ability to enhance solubility and treatment outcomes across ophthalmic indications.
- The MNP polymer architecture is agnostic to the API, allowing the same formulation principles to extend beyond ophthalmology, to nasal, pulmonary, bladder, and other mucosal surfaces. Our technology offers a versatile delivery solution for multiple therapeutic indications where local, sustained release and improved solubility remain key unmet needs.

References and Acknowledgements

- [1] Shafranov G. Glaucoma Today. 2006;07-08.
- [2] Prosperi-Porta, G.. Biomacromolecules. 2016; 17:1449-1457.
- [3] Taiyab A et al. J Neurosci Res. 2022;100(2):638–652.

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