Corporation, Bedford, MA. The bioanalytical work was performed to assess the presence of the device from depots in a topical ophthalmic drug delivery device (TODDD™). The lower limit of quantitation was 0.5 ng/mL.

Methods
The right eyes of 8 ocular normotensive adult beagle dogs were fitted with ocular ring devices, each containing 2 latanoprost-drug depots (cylindrical cores, 600 µg latanoprost). The depots were fitted with ocular ring devices, each containing 2 latanoprost-drug depots (cylindrical cores, 600 µg latanoprost). The device with blank depots containing no latanoprost was placed on the right eye of 1 additional animal. All left eyes remained untreated. Clinical slit-lamp exams were performed pre-placement on Day 1 and post-placement on Days 1, 2, and 7. Diallylamine was measured pre- and post-placement on Day 1, and on Days 4, 8, and 16. Plasma samples were collected on Day 1 prior to, and approximately 4 hours after device insertion, and on Day 8. Tear samples were collected on Day 16 by Schirmer strip in the lower cul-de-sac. Tear and plasma samples were analyzed by LC/MS/MS for latanoprost and latanoprost acid. The lower limit of quantitation was 0.5 ng/mL.

Results
IOP reduction in the treated eye was approximately 3 mmHg on Day 4 (n=6) and Day 8 (n=4), and 7 mmHg on Day 16 (n=3) in the dogs that had retained the latanoprost-loaded devices, representing a 31-42% reduction in normotensive IOP from baseline. This response is consistent in magnitude to what has been achieved with latanoprost eye drops in this species. There was no effect on IOP in the animal wearing the placebo device. The IOP returned to baseline levels in all eyes after removal of the devices. A range of 25 - 215 ng/mL latanoprost was recovered from the tears of animals wearing the drug devices. No latanoprost was detected in any plasma samples, or in the tear samples from untreated eyes.

Conclusions
This study demonstrates the therapeutic feasibility of these sustained-release depots. Although long-term retention of a ring device configuration of these particular dimensions in this species was not achieved, in vitro analysis of the wound devices and of the extended latanoprost release profile from new devices relative to tear levels measured at Day 16 indicates that sustained IOP-lowering would be achieved over a 2-3 month wear period. These results support the use of these depots in the TODDD design for human use.

Advantages of TODDD™ Platform:

- Eliminates prevalent poor eye drop insertion and dosing issues
- Adaptable to the drugs and combinations of drugs currently delivered by eye drops
- Fewer compliance issues. Continuous, 90+ day 24/7 release of drug independent of patient dosing regimen
- Preservative free
- Excellent retention and easy confirmation
- Simple replacement in less than a minute
- Fewer, perhaps elimination of, systemic side-effects resulting from eye drop excess drug delivery
- Can incorporate less soluble drugs not suitable for aqueous solution

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