THERAPEUTICS IN THE 2025 PIPELINE



Get familiar with exciting new treatments coming to market this year.

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If you are anything like us, hearing someone in eye care announce that there's "another option" makes you feel simultaneously giddy and overwhelmed. However, we feel, in the end, the more diverse options we have to offer our patients, the better we will be able to customize their care and gain better outcomes so, keep 'em coming!

That being said, with a steady stream of new treatment options being approved, it's important to stay on top of what's new. A number of exciting pharmaceutical options are expected in the anterior segment realm this year, which we would like to highlight. A few nonpharmaceutical treatments stood out to us as well, which we'll cover separately (see *Not Therapeutics, But New Devices to Know*.) Let's work our way through the list of new options, sorted by the diseases they treat.

DRY EYE DISEASE

Pharmaceuticals that treat dry eye disease (DED) continue to evolve as we gain options for more specific, direct treatment of the different etiologies of ocular surface disease. This year, we can expect to see two new products on the market that will be useful in our dry eye tool bag.

Reproxalap

The significant role of inflammation in ocular surface disease is undeniable. However, as clinicians, we often run into the challenge of controlling this sign adequately without the risk of inducing side effects such as glaucoma and cataract development with steroid therapy. Reproxolap (Aldeyra Therapeutics/AbbVie) may help fill that void by providing significant antiinflammatory therapy rather acutely. Reproxolap is a first-of-its-kind aldehyde-inhibiting molecule designed to neutralize reactive aldehyde species (RASP), which have been shown to be prevalent inflammatory components of ocular surface disease. Reproxalap binds to RASP, preventing their interaction with cell membranes and proteins, in turn, reducing oxidative damage and subsequent inflammatory cascade of cytokine release and immune cell activation. By targeting RASP, Reproxalap disrupts upstream levels of inflammation in DED, potentially offering an alternative to conventional therapies such as corticosteroids or immunomodulators. This topical medication may also have applications for allergic conjunctivitis and other inflammatory-related ocular conditions.[1]

FDA approval for Reproxalap was expected in 2024, but the agency denied the new drug application (NDA) due to insufficient evidence

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NOT THERAPEUTICS, BUT NEW DEVICES TO KNOW

MEIBOMIAN GLAND DYSFUNCTION

The expansion of in-office meibomian gland treatments offers much-needed nonpharmaceutical approaches for the treatment of DED.

Thermomechanical Device

A new device targeting evaporative dry eye disease due to meibomian gland dysfunction uses thermomechanical energy to noninvasively restore gland function and tear stability as well as improve Ocular Surface Disease Index (OSDI) scores, promising significant relief in just 2 minutes. The Tixel i (Novoxel) uses a 400˚C heated, pulsating titanium tip to safely deliver treatment to the upper and lower eyelids, unclogging meibomian glands, liquifying meibum, and improving gland function.[1]

One clinical study confirmed improved gland function and symptom relief.[2] With a reported statistically significant reduction in OSDI scores from 47.47 ± 18.62 at visit one to 21.43 ± 13.07 at visit five, and improved noninvasive tear breakup time at both study sites, 5.0 ± 2.6 to 7.1 ± 1.3 and 6.5 ± 3.1 to 13.2 ± 3.2. At baseline, 80% of participants reported severe dry eye symptoms, while only 36.2% reported severe dry eye symptoms at the conclusion of the study.

The Tixel i received FDA approval in November.

GLAUCOMA

The LiGHT trial[3] was monumental for treatment of glaucoma in the United States, as is proved the safety and efficacy of selective laser trabeculoplasty (SLT) as a first line treatment for glaucoma. A groundbreaking new SLT technology has come to market that will change the landscape of early interventional glaucoma forever.

SLT

In July, Belkin Vision's Direct Selective Laser Trabeculoplasty (DSLT) technology was acquired, along with Belkin Vision, by Alcon.[4] The Voyager DSLT device, formerly the Belkin Eagle, delivers laser energy directly to the trabecular meshwork through the limbus, eliminating the need for gonioscopy or an open angle. Indicated for primary open-angle glaucoma and ocular hypertension, the Nd:YAG laser ensures precise delivery of 120 pulses of 1.8 mJ in approximately 2.4 seconds in a circular and consecutive pattern, selectively stimulating pigmented trabecular meshwork cells. This leads to stretching of uveoscleral tissue and dilation of Schlemm canal, causing an increase in outflow of aqueous humor. The Voyager uses eye-tracking technology to automatically stop when it detects eye movement.

Clinical studies show that DSLT has similar efficacy to traditional SLT, and the majority of patients are able to use less IOP-lowering medications even at 12 months postoperatively.[5-7] Additionally, it may lead to fewer IOP spikes and less inflammation compared with conventional SLT by delivering energy directly to the trabecular meshwork and bypassing the anterior chamber, offering a safer and more efficient option for managing glaucoma.

This device was approved by the FDA in December 2023 and is actively launching in early 2025.

IOP-Adjusting Pump

In June, the FDA granted DeNovo Classification of the FSYX Ocular Pressure Adjusting Pump (OPAP; Balance Ophthalmics) for adults with normal-tension and open-angle glaucoma.[8] The FSYX, pronounced "physics" goggles are sized to fit tightly over the eyes while negative pressure is applied through the attached pump so IOP is instantly lowered without the use of medication or an invasive procedure.

NOT THERAPEUTICS, BUT NEW DEVICES TO KNOW (CONT'D.)

Drug-Eluting Contact Lens

Patients with mild to moderate glaucoma and ocular hypertension may someday benefit from MediPrint medicated contact lenses (MediPrint Ophthalmics)–drug-eluting contact lenses created from the combination of an FDA-cleared drug and an FDA-cleared contact lens that leverages existing high-speed manufacturing with the MediPrint process. This innovation is in phase 3 development.[9]

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of efficacy and required one more trial proving benefit. Initial phase 3 trials proved statistical improvement in ocular redness, dry eye symptom scores, and Schirmer testing. Additional data released in 2024 have shown effective reduction in ocular discomfort compared with vehicle at the 80- to 100-minute mark ($P < .004$). The FDA has accepted the re-submitted NDA and a prescription Drug User Fee Act (PDUFA) date has been set for April 2, 2025.

Acoltremon

AR-15512 (Acoltremon, Alcon) is thought to activate transient receptor potential melastatin 8 (TRPM8). It's proposed mechanism of action is the stimulation of cold receptors on the corneal surface while also naturally stimulating tear production and providing immediate comfort.[2-4] This protein is located on corneal nerves and regulates basal tear production in response to temperature changes. Studies have found warming of the cornea reduces basal tearing rate while cooling increases it.[5,6] Alcotremon mimics this activation and increases tear production while also creating a cooling sensation to reduce dryness and irritation.

Acoltremon bypasses immune modulation, offering a novel approach for patients seeking fast, effective relief. With twice

Figure courtesy of Alcon

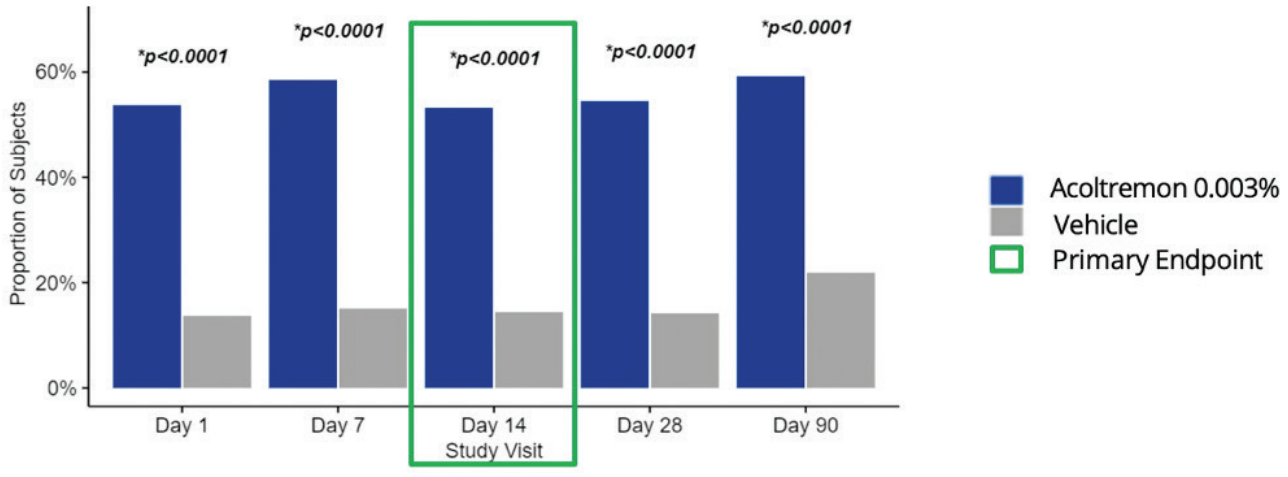

Figure 1. A significantly higher proportion of participants achieved at least a 10-mm increase in unanesthetized Schirmer test scores at day 14, the primary endpoint, and at days 1 and 90, which were secondary endpoints.

Image courtesy of Orasis Pharmaceuticals.

Treatment Related Adverse Events		
	QLOSI™ N=308 n (%)	**Vehicle** N=305 n (%)
Non-Ocular TRAEs		
Headache	21 (6.8%)	2 (0.7%)
Eye/facial pain	6 (1.9%)	1 (0.3%)
Nausea	4 (1.3%)	
Ocular TRAEs		
Instillation site pain	18 (5.8%)	1 (0.3%)
Vision blurred	11 (3.6%)	2 (0.7%)
Conjunctival hyperemia	5 (1.6%)	1 (0.3%)
Installation site pruritis	3 (1.0%)	1(0.3%)
Visual impairment	3 (1.0%)	

*All TRAEs ≥ 1% ; Suspected Treatment Related Adverse Event means any adverse event for which there is a reasonable possibility that the drug caused the adverse event.

- 1.3% (n=4) of all Qlosi™ participants reported moderate treatment related adverse events
- All other treatment related adverse events were mild (no severe)
- No serious treatment related adverse events occurred with Qlosi™

Table. Pooled days 1, 8, and 15. Note: The majority of adverse events were mild, transient, and self-resolving.

daily dosing, a phase 2b trial met the primary endpoint of 10 mm improvement in unanesthetized Schirmer score with > 10 mm in improvement ($P < .001$). Secondary endpoints proved improvement as early as day 1 and through 90 days.[7] Additional statistically significant improvements were noted for ocular staining, hyperemia, SANDE score, and QoL-VAS, tested at multiple points through the 12-week trial. Phase 3 trials confirmed an improvement in Schirmer score (Figure 1). A current trial is looking at long-term safety with data expected no later than March 31, 2025. With phase 3 trials complete, a PDUFA date is expected May 30, 2025.

PRESBYOPIA

Are we ready to "accommodate" a second wave of presbyopia drops? Newer options aim to tap into that near vision fountain of youth while limiting side effects such as blurred distance vision, headache, conjunctival hyperemia, and risk of retinal tear/detachment that are possible with available options.

Pilocarpine 0.4%

Pilocarpine HCl ophthalmic solution 0.4% (Qlosi, Orasis Pharmaceuticals) is a cholinergic agonist that activates the iris sphincter, leading to pupil constriction and an extended depth of focus. This drop is recommended for twice daily dosing for the treatment of presbyopia and has an efficacy of approximately 8 hours.[8] Results from phase 3 trials (NEAR-1 and NEAR-2) showed significant 3-line or greater gain in distance-corrected near visual acuity, and no loss of 1-line or more in distance visual acuity.[8]

As you likely recall, there's another pilocarpine product already on the market for presbyopia, but at a higher concentration—1.25% (Vuity, AbbVie). The lower concentration drug looks to offer an effective pilocarpine presbyopia treatment with less frequent, milder side effects to improve patient comfort and satisfaction (see Table).

The FDA approved 0.4% pilocarpine HCl for the treatment of presbyopia in October 2023; however, a launch date has yet to be announced by Orasis.

Aceclidine

Another emerging treatment for presbyopia is 1.75% aceclidine ophthalmic solution (LNZ-100, Lenz Therapeutics). Aceclidine is a parasympathomimetic drug that causes pupil constriction through contraction of the iris sphincter muscle while sparing the ciliary muscle.[9] Dosed once daily, 1.75% aceclidine ophthalmic solution has a duration of up to 10 hours. According to findings from the phase 3 CLARITY study, participants experienced improved near vision without losing 1 or more lines of clarity for distance vision. At 30 minutes after instillation, 84% of participants exhibited 2-lines greater VA at near, and 69% of participants exhibited 3-lines greater VA at near (Figure 2). The drug was well tolerated and no serious adverse events related to the treatment were reported.[10]

Lenz Therapeutics submitted an NDA in August 2024 and has a goal PDUFA date of August 2025.

GLAUCOMA

The topical glaucoma therapy world continues to work on its age-old problem: inefficient therapies that require multiple daily drops. Sticking to the recent theme of "less drops," a new drug with this goal will be coming to market this year.

PDP-716

The FDA in December 2022 accepted for filing Visiox Pharma's New Drug Application for once-daily

Figure courtesy of Lenz Therapeutics.

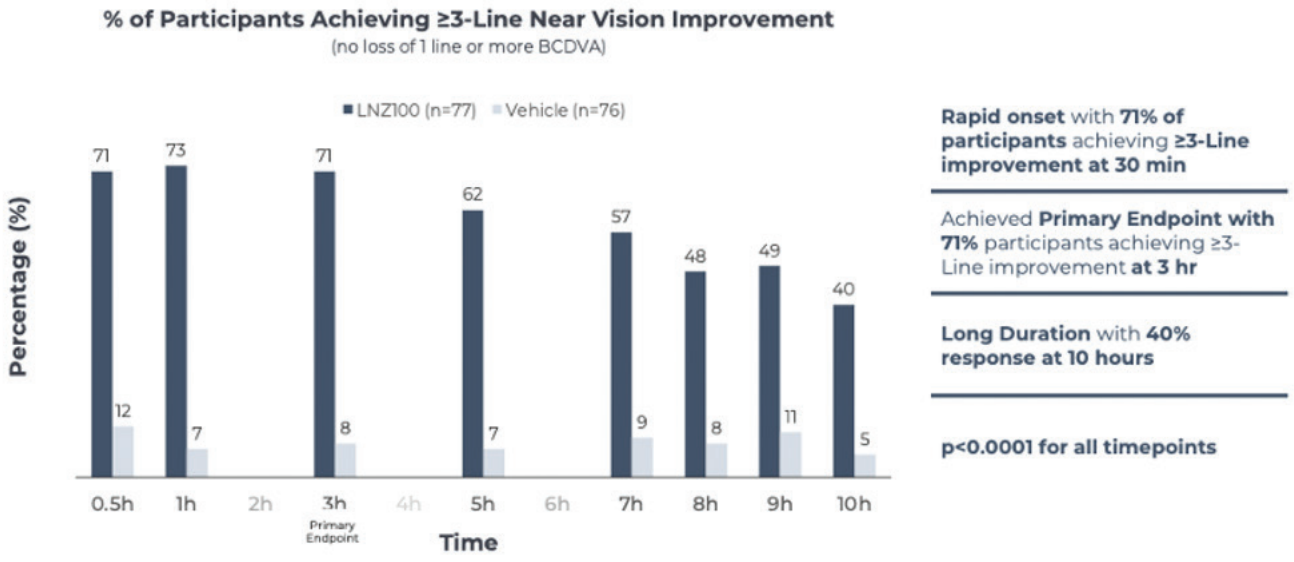

Figure 2. Clarity 2, day 1 results, full analysis set. Near visual acuity was assessed at 40 cm using monocular best-corrected distance visual acuity. LNZ-100 achieved rapid onset and potential for 10 hours duration with a single dose.

brimonidine tartrate 0.35% (PDP-716) for the treatment of glaucoma.[11,12] The alpha-adrenergic agonist lowers IOP by decreasing the production of aqueous humor and increasing outflow via the uveoscleral pathway. Contrary to existing topical brimonidine formulations (eg, 0.1%, 0.15%, or 0.2%) dosed three times daily, brimonidine 0.35% uses TearAct fine resin technology, which employs resin microparticles to extend the release of the medication. By decreasing the immediate exposure and achieving longer coverage for IOP control, patients can decrease dosing to once daily.

The FDA had assigned a PDUFA target action date of August 4, 2023, but there has been no update since from the company.

NEW THERAPIES IMPROVE OPTIONS

The common goal in eye care is to provide a safe, effective, and efficient therapy for patients struggling with an eye condition. We should be excited as new therapies come to market, as they increase our ability to tailor individual plans for our patients to effectively treat their conditions and maintain (or improve) their quality of life.

We aim to stay up to date with the latest and greatest therapies, and are excited for the year ahead, as some fantastic new options become available. ■

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