Phase 2 Trial Results of Topically Administered ILYX-002, a Novel Immune Modulator for Inflammatory and Autoimmune Dry Eye Disease

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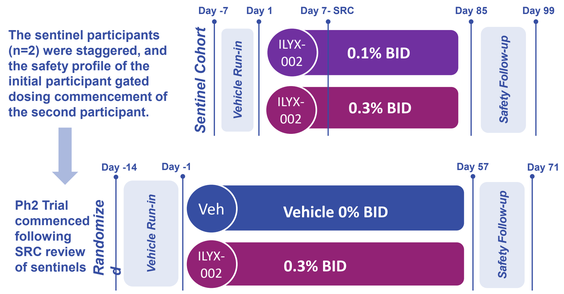
Background and Rationale

- The traditional classification of dry-eye disease (DED) is based on predominant, but overlapping, etiologies of evaporative and aqueous-deficient dry eye; regardless of etiology, inflammation plays a key role in the pathophysiology of DED.[1]
- Clinically, DED negatively impacts overall quality of life by causing pain and irritation; impacting both ocular and general health, as well as visual function and performance.[2]
- Patients with moderate to severe DED that is not controlled with other therapies may respond to short-term courses of topical corticosteroids,[3] but longer-term therapies are required for most patients as there is no curative treatment for aqueous-deficient DED.
- ILYX-002 is a potent immune modulator formulated as a sterile, preservative-free suspension, administered as a single-use eye drop; a Phase 2 trial (ILYX-002-201) was designed to evaluate safety and tolerability and explore the therapeutic effects of ILYX-002.
- The trial aimed to focus on the inflammatory mechanisms of DED and underscore the role of immune-related ocular complications in systemic conditions like Sjogren's syndrome, lupus, and rheumatoid arthritis where inflammation is a central factor.

Materials and Methods

- ILYX-002-201 was a Phase 2, multicenter, randomized, double-masked, vehicle-controlled trial designed for participants with moderate to severe DED with underlying autoimmune disease and included a 14-day vehicle run-in, 8 weeks of randomized treatment, and a 14-day safety follow-up; participants were randomized in a 1:1 ratio to ILYX-002 0.3% or vehicle control administered twice daily (BID) (**Figure 1**).
- As this was a first-in-human (FIH) trial, a sentinel cohort (n=2) was conducted as a single-masked, non-controlled, staggered-dosing design to evaluate the safety of low- (0.1%) and high-dose (0.3%) ILYX-002 for a minimum of 7 days that gated initiation of the randomized portion of the Phase 2 trial (**Figure 1**). Sentinel participants continued dosing BID to day 85 and were monitored closely for safety.
- The primary endpoints of safety and tolerability of ILYX-002 were assessed by ocular and nonocular adverse events, intraocular pressure, best-corrected visual acuity, slit-lamp biomicroscopy, and ophthalmoscopy.

Figure 1: ILYX-002-201 Study Design



Results

Sentinel Participants

- There were 2 sentinel participants. Participant 1 (male, 49 years-of-age) received a low dose of ILYX-002 (0.1% BID) to day 85, and Participant 2 (female, 68 years-of-age) received a high dose (0.3% BID) to Day 85.
- Both participants were monitored for key safety parameters; based on the positive safety outcomes, the randomized portion of the trial commenced.

Randomized Participant Demographics

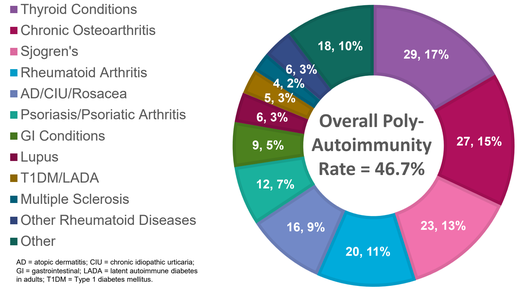
- An overview of the randomized participant demographics (N=105) at baseline are included in **Table 1**.
- A range of autoimmune diseases were allowed, with the most frequent being thyroid conditions, chronic osteoarthritis, Sjogren's, and rheumatoid arthritis, with 175 reported autoimmune diseases among participants (N=105) (**Figure 2**).

Table 1: ILYX-002-201 Participant Demographics

	Statistic	ILYX-002 (0.3%) (N=53)	Vehicle (N=52)	Overall (N=105)
Age (Years)*	N	53	52	105
	Mean	60.0	59.7	59.9
	Median	64.0	65.0	65.0
	SD	13.2	15.3	14.0
	Minimum	30.0	19.0	19.0
	Maximum	81.0	62.0	82.0
Race	Asian	6 (11.3)	7 (13.5)	12 (12.4)
n (%)**	Asian, White	1 91.9)	0	1 (1.0)
	White	44 (83.0)	43 (82.7)	87 (82.9)
	Native Hawaiian or Other Pacific Islander	0	1 (1.9)	1 (1.0)
	Other	2 (3.8)	1 (1.9)	3 (2.9)
Ethnicity	Not Hispanic or Latino	51 (96.2)	50 (96.2)	101 (96.2)
n (%)**	Hispanic or Latino	2 (3.8)	2 (3.8)	4 (3.8)
Sex	Female	45 (84.9)	37 (71.2)	82 (78.1)
n (%)**	Male	8 (15.1)	15 (28.8)	23 (21.9)

SD: standard deviation; *Age at screening visit; ** Percentages based on the number of participants in the relevant population with non-missing data.

Figure 2: Types of Autoimmune and Inflammatory Diseases (# reported, %)



AD = atopic dermatitis; CIU = chronic idiopathic urticaria; GI = gastrointestinal; LADA = latent autoimmune diabetes in adults; T1DM = Type 1 diabetes mellitus.

Results (continued)

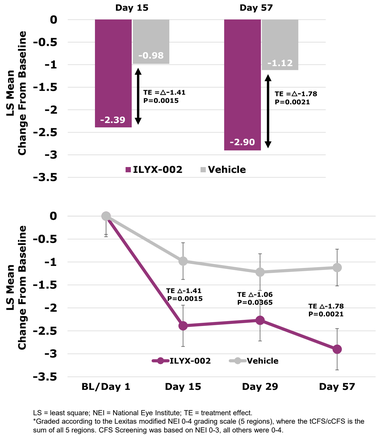
Safety and Tolerability

- There were no serious adverse events (SAEs) related to ILYX-002 study treatment.
- The majority of treatment-emergent adverse events (TEAEs) were mild or moderate, with 3 severe TEAEs among 2 participants (1.9%).
  - There was 1 severe instance of instillation site irritation in a participant in the ILYX-002 arm that resolved and did not affect treatment dosing.
  - There was 1 severe instance of migraine and 1 severe instance of headache in 1 participant in the ILYX-002 arm that were considered possibly related to the trial treatment and resulted in withdrawal of trial treatment.
- Intraocular pressure and other ocular safety assessments were stable throughout the trial and similar for participants in both the ILYX-002 and vehicle arms.
- ILYX-002 was well tolerated with improvement in ocular tolerability Visual Analogue Scale (VAS) scores over time.

Total Corneal Fluorescein Staining (tCFS)

- The mean tCFS score (±SEM) in the ILYX-002 treatment group decreased from 6.61±0.276 at baseline to 3.61±0.379 at Week 8, with a change of -2.90±0.420 and a statistically significant difference of -1.78 (P=0.0021) compared with vehicle (**Figure 3**).
- The onset of action was rapid, with an LS mean change by Day 15 of -2.39 in the treatment arm and a statistically significant difference of -1.41 (P=0.0015) compared with vehicle (**Figure 3**).

*Figure 3: ILYX-002 Total Corneal Fluorescein Staining Scores Change from Baseline Compared With Vehicle at Week 8 (Day 57) and Over Time**



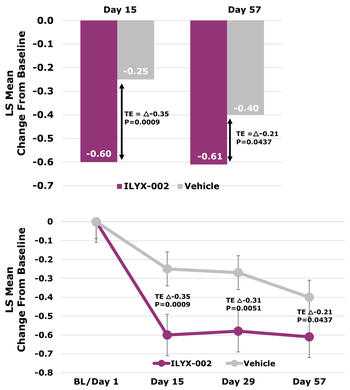
LS = least square; NEI = National Eye Institute; TE = treatment effect.
*Graded according to the Lexitas modified NEI 0-4 grading scale (5 regions), where the tCFS/cCFS is the sum of all 5 regions. CFS Screening was based on NEI 0-3, all others were 0-4.

Results (continued)

Central Corneal Fluorescein Staining (cCFS)

- The mean cCFS score (±SEM) in the ILYX-002 treatment group decreased from 0.98±0.118 at baseline to 0.36±0.074 at Week 8 with a statistically significant difference of -0.21 (P=0.0437) compared with vehicle (**Figure 4**).
- Onset of action was rapid with an LS mean change of -0.60 from baseline and statistically significant difference of -0.35 (P=0.0009) at Day 15 (**Figure 4**) compared with vehicle.

*Figure 4: ILYX-002 Central Corneal Fluorescein Staining Scores Change from Baseline Compared With Vehicle at Week 8 (Day 57) and Over Time**



Conclusions

- This trial was designed to address the unmet need for effective immunomodulatory treatment in DED patients with underlying autoimmune disease.
- ILYX-002 was well tolerated with safety results similar to those of vehicle.
- Based on tCFS and cCFS results, ILYX-002 has the potential to provide therapeutic benefit with a favorable safety profile.

References

1. **Craig JP, et al.** TFOS DEWS II definition and classification report. Ocul Surf. 2017;15(3):276-283.
2. **Stapleton F, et al.** TFOS DEWS II epidemiology report. Ocul Surf. 2017;15(3):334-365.
3. **Jones L, et al.** TFOS DWS II management and therapy report. Ocul Surf. 2017;15(3):575-628.

Acknowledgments

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