Presentation Summary: Toward Scalable, Transplant-Free Treatment of Advanced Keratoconus: Development and Pre-clinical Validation of a Bioengineered Hydrogel Corneal Implant

Speaker: Dr. Shuo Li (Senior Scientist, ETH Zurich)

Event: VDCO Annual Conference (SICHT.KONTAKTE)

Key Topics Covered

- **The Clinical Bottleneck:** Limitations of current keratoconus treatments and donor tissue scarcity.
- **Implant Design Strategy:** Key properties required for a successful synthetic corneal implant.
- **Material Characterization:** Optical, mechanical, transport, and stability benchmarks.
- **Biological Compatibility:** *In vitro* human corneal cell response and long-term *in vivo* systemic safety.
- **Ocular Preclinical Validation:** Femtosecond laser-assisted implantation in *ex vivo* and *in vivo* models.

1. The Clinical Problem & Target

- **Current Limitations:** Advanced keratoconus leads to severe corneal thinning and astigmatism. Interventions like corneal cross-linking (CXL) stabilize progression but do not restore lost thickness or shape.
- **Supply Crisis:** Globally, only 1 donor cornea is available for every 70 needed, leaving millions without treatment options.
- **Why Historical Inlays Failed:** Previous synthetic corneal inlays failed due to nutrient blockade (causing stromal necrosis) and interface light scattering (causing haze), rather than chemical toxicity.

2. Design Principles & Material Properties

To avoid past failure modes, the implant is engineered as a **non-degradable, double-network hydrogel** designed to match native stromal properties:

- **Cornea-Matched Hydration & Optics:** Maintains a water content, visible light transmittance, and a refractive index identical to human corneal tissue.
- **Nutrient Permeability:** Allows rapid oxygen transport and glucose diffusion close to native tissue levels to prevent nutrient starvation and tissue melting.
- **Matched Biomechanics:** Matches native corneal stiffness to prevent mechanical stress concentration and tissue extrusion, while remaining highly elastic for injector delivery.
- **Anti-Fouling & Surface Recognition:** Features a specialized surface layer that prevents non-specific protein adsorption and haze while enabling healthy keratocyte integration.

3. Biological Safety & Preclinical Validation

- **In Vitro Cell Integration:** Human corneal keratocytes attach and maintain healthy spindle morphology with >95% cell viability over 20 days without losing optical clarity.

- **In Vivo Systemic Safety:** 24-week subcutaneous rat studies demonstrated full systemic biocompatibility with no fibrous capsule formation, chronic inflammation, or blood chemistry alterations.
- **Ex Vivo Surgical Feasibility:** Tested in porcine eyes using standard femtosecond laser platforms (SMILE/pocket creation), showing excellent optical clarity and smooth stromal integration on OCT.
- **In Vivo Ocular Performance:** Implantation in living rabbit models confirmed long-term corneal clarity, stable central positioning, healthy wound healing, and no sign of ocular inflammation or haze.

Key Takeaway for Clinicians

This bioengineered hydrogel platform provides a **scalable, off-the-shelf, donor-independent approach** for treating advanced keratoconus, offering a surgical bridge between conservative management and full donor corneal transplantation.