protoKinetix

PKX-001 + Novel Treatment for Dry Eye Disease (DED)

Overview

What is Dry Eye Disease and Current Market Overview

What is Dry Eye Disease?

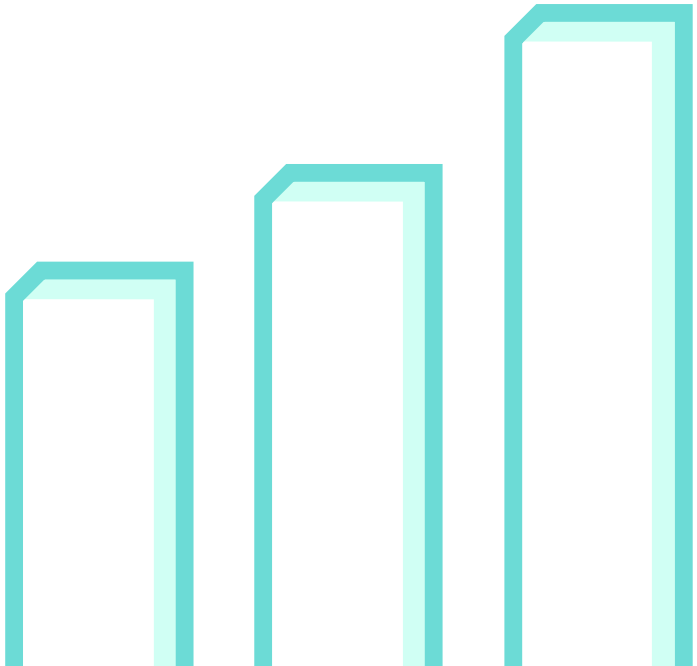
- Dry eye disease (DED) is a multifactorial disease of the ocular surface which results in a spectrum of symptoms and/or signs that affect 5–30% of the population.
- Dry eye symptoms include discomfort and visual disturbances that are described as eye dryness, foreign body sensation, grittiness, light sensitivity, and pain.
- Clinical signs include diminished tear volume, increased ocular surface staining, reduced tear break-up time, abnormal meibomian glands, tear hyperosmolarity, inflammation and ocular surface damage.
- While several approved and off-label treatments are available, there is clearly an unmet need for the safe and efficacious treatment for DED.

Consensus roadmap 2019-2025 developed by European Vision Institute states "Although significant progress has been made, several important unmet needs need to be addressed in the next 5 years" .

Cursiefen C. et al. Unmet needs in ophthalmology:
a European Vision Institute-consensus roadmap 2019-2025. Ophthalmic Res. 2019. 62(3):123-133

Market Overview

- Studies of the Dry Eye Disease market[1,2] indicated a value of ~USD 4.5 billion in 2018, and ~USD 6.2 billion by 2024, with an anticipated CAGR of 5.23%, during the forecast period (2019-2024).



- The growth of DED market include several factors:
  - Population aging
  - Decrease in the supportive hormone,
  - Systemic inflammatory disease,
  - Ocular surfaces diseases or surgeries affecting cholinergic nerves which stimulate tear secretion

1 - market research published by Mordor Intelligence LLP
2- https://www.prnewswire.com/news-releases/global-dry-eye-disease-market-2020-to-2025---growth-trends-and-forecasts-301096025.html

PKX-001

PKX-001: Novel Glycopeptide in clinical development as cytoprotective agent

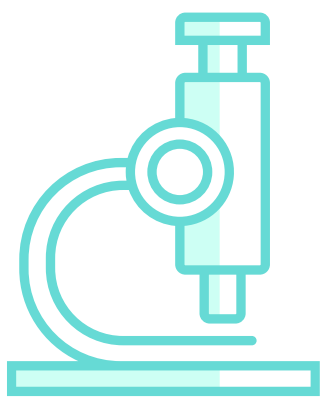
The Cell

Novel Glycopeptide in clinical development as cytoprotective agent

- Small, synthetic analog of the family of anti-freeze glycoproteins.
- Cytoprotective and anti-inflammatory activity in various cellular and animal models.
- Currently under investigation in patients with type 1 diabetes (effect on engraftment in clinical islet transplantation; ClinicalTrials.gov NCT03073577).

Identity	**PKX-001; Anti-aging glycopeptide™ (AAGP™)**
Physical Form:	White to off-white powder
Molecular Weight:	544.5 Da (free peptide)
Sequence:	H-Lys(Gal(OH)CF_2)-Ala-Ala-OH
Molecular Formula:	$C_{20}H_{34}F_2N_4O_{11}$

Test Results



PKX-001 demonstrates strong cytoprotective activity in *in vitro* and *in vivo* models

In Vitro & In Vivo Models

- PKX-001 increased survival of various cells [human and mouse fibroblasts, human peripheral blood mononuclear cells, Jurkat cells, mouse embryonic stem cells, human and mouse islets, and rat cardiomyocytes] incubated under conditions of:
  - Oxidative stress
  - Low temperatures
  - Low serum concentrations
  - Freezing
  - Varying pH
  - Stress conditions simulating cardiomyopathy

Additional information and study reports available under CDA

In Vitro & In Vivo Models

- PKX-001 increased *in vivo* survival and functional activity of transplanted cells (human islets and photoreceptor precursor cells) following their *in vitro* pre-treatment with PKX-001.

- *In vitro* tests suggest that PKX has anti-oxidative Activity and anti-Inflammatory activity.

PKX-001 Shows Efficacy in Murine DED Model: Proof-of-Concept Study

Study conducted by EyeCRO LLC, Oklahoma City, OK ,USA. Additional information and study report available under CDA

Murine DED Model

Proof of Concept Study

- *Murine model of desiccating stress (induced by low humidity, constant airflow and injections of scopolamine).*
- *5% PKX-001 formulated in BSS (Ocular sterile irrigating solution) and delivered topically QID.*
- *Results for CD4 + T-cell infiltration upcoming*

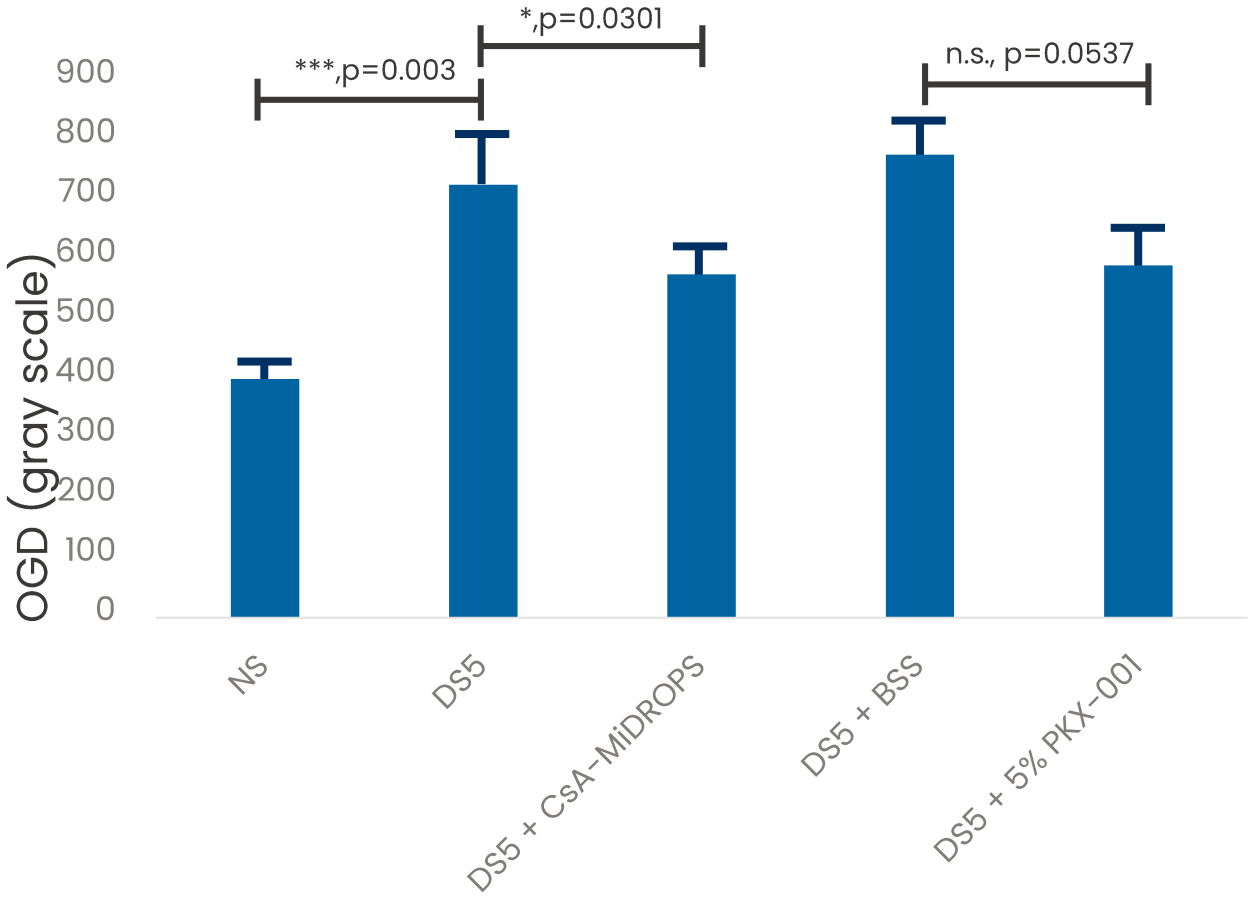
Study conducted by EyeCRO LLC, Oklahoma City, OK ,USA. Additional information and study report available under CDA

Murine DED Model

Proof of Concept Study

Corneal Permeability

- 5% PKX-001 improved corneal permeability to similar extent as Positive control (Cyclosporin CsA-MiDROPS™).



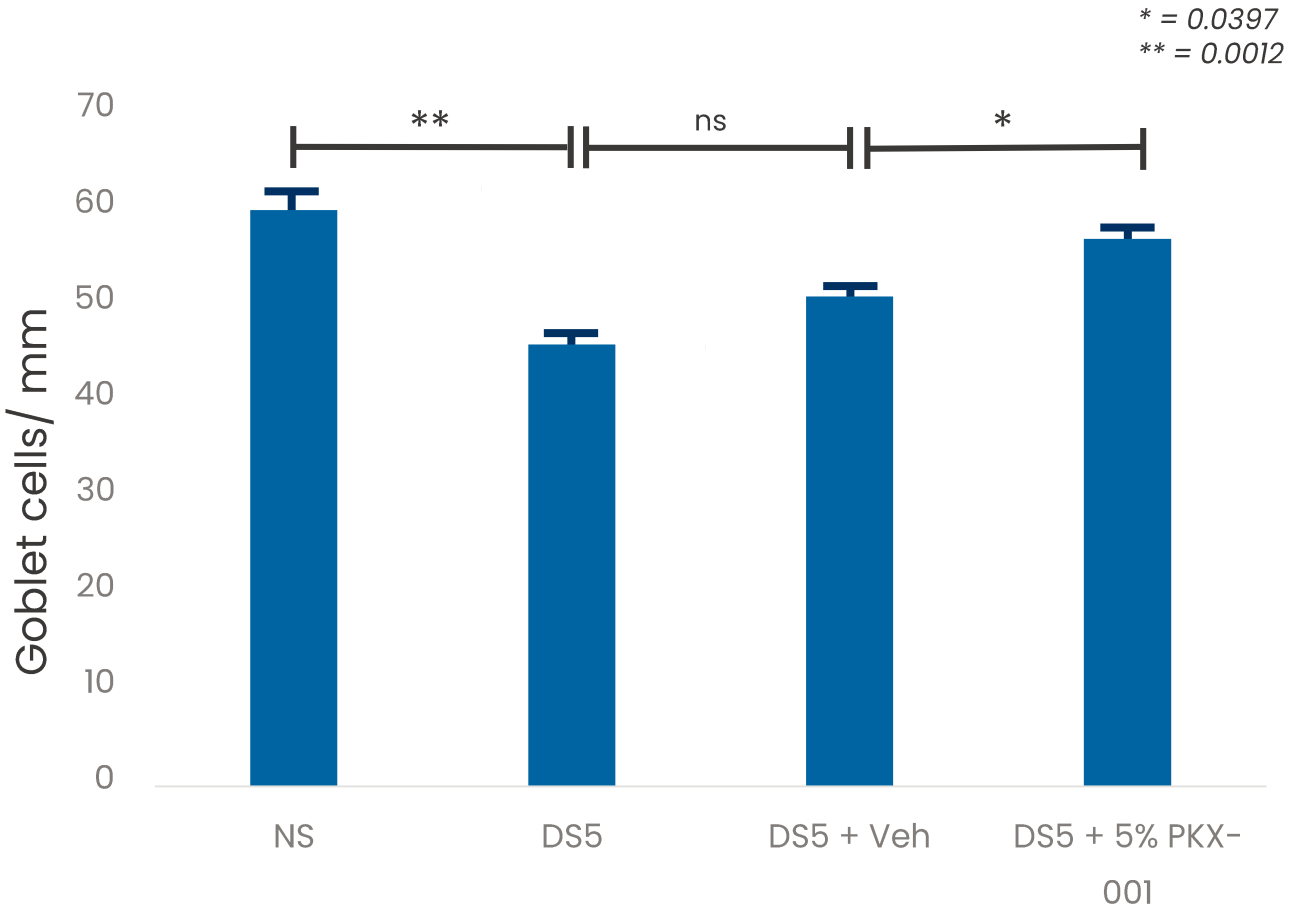
Study conducted by EyeCRO LLC, Oklahoma City, OK ,USA. Additional information and study report available under CDA

Murine DED Model

Proof of Concept Study

Conjunctival Goblet Cell Density

- PKX-001 treatment normalized conjunctival goblet cell density.



Study conducted by EyeCRO LLC, Oklahoma City, OK ,USA. Additional information and study report available under CDA

PKX-001 Shows Efficacy in Murine DED Model: Confirmatory Study

Study conducted by EyeCRO LLC, Oklahoma City, OK ,USA. Additional information and study report available under CDA

Murine DED Model

Confirmatory Study

- Murine model of desiccating stress (induced by low humidity, constant airflow and injections of scopolamine).
- 2-5% PKX-001 formulated in BSS and delivered topically under different treatment schedules.
- PKX-001 protective activity confirmed (Table below).
- PKX-001 effects under various treatment regimens determined (Results available under CDA).

	Study 1	Study 2
Treatment	**% reduction of elevated corneal permeability**	
5% PKX-001, QID	51.1% (p=0.0537)	69.5% (p<0.01)
5% PKX-001, BID	Not done	54.8% (p<0.01)

Study conducted by EyeCRO LLC, Oklahoma City, OK ,USA. Additional information and study report available under CDA

PKX-001 is Not Genotoxic and Has Beneficial Safety Profile *in vivo*

Study conducted by EyeCRO LLC, Oklahoma City, OK ,USA. Additional information and study report available under CDA

Beneficial Safety Profile *in vivo*

- Rabbit eye irritation study (2-10% PKX-001, single ocular administration): not considered an eye irritant.

- Mouse eye irritation study (5% PKX-001, QID ocular administration, 5 days): well tolerated and not considered an eye irritant.

Studies conducted by

- *ITR Laboratories Canada, Montreal, Canada (Rabbit eye irritation and genotoxicity)*
- *EyeCRO LLC, Oklahoma City, OK ,USA (Mouse eye irritation)*
- *Charles River Laboratories, Montreal, Canada (Rabbit ocular tolerance)*
- *BRI Biopharmaceutical Research, Vancouver, Canada (Acute toxicity)*

Additional information and study reports available under CDA

Beneficial Safety Profile *in vivo*

- Rabbit ocular tolerance and PK study (5% PKX-001, BID or QID, 14 days): well tolerated at all dose levels.
  - No difference between Control and PKX-001 groups for clinical signs, body weight, food consumption, gross ocular evaluations for local ocular irritation, or ophthalmology examinations. Ocular histopathology results upcoming.
- Genotoxicity (GLP): negative in bacterial reverse mutation assay and did not induce chromosomal damage in micronucleus test in Chinese hamster ovary cells.
- Acute toxicity: maximum tolerated dose (MTD) >500 mg/kg, single intravenous administration, mice

Studies conducted by

- *ITR Laboratories Canada, Montreal, Canada (Rabbit eye irritation and genotoxicity)*
- *EyeCRO LLC, Oklahoma City, OK ,USA (Mouse eye irritation)*
- *Charles River Laboratories, Montreal, Canada (Rabbit ocular tolerance)*
- *BRI Biopharmaceutical Research, Vancouver, Canada (Acute toxicity)*

Additional information and study reports available under CDA

PKX-001 Blood and Ocular Tissue Concentrations

Study conducted by EyeCRO LLC, Oklahoma City, OK ,USA. Additional information and study report available under CDA

Blood & Ocular Tissue Concentrations

- Rabbit ocular tolerance and PK study (5% PKX-001, BID or QID, 14 days).
- Blood samples collected at several time points post PKX-001 dosing.
- Ocular tissue samples collected after last PKX-001 dosing (conjunctiva, cornea, aqueous humor, vitreous humor, retina and RPE/choroid/sclera complex) and flash frozen.
- Results of PKX-001 concentration analysis in plasma and ocular tissues upcoming.

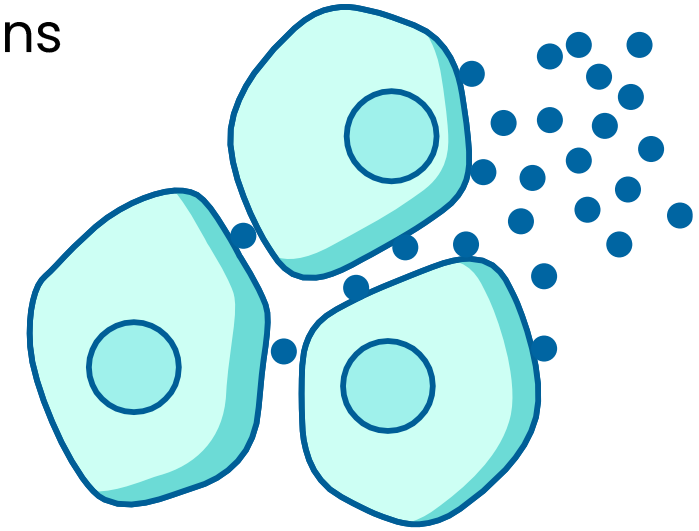
Study conducted by EyeCRO LLC, Oklahoma City, OK ,USA. Additional information and study report available under CDA

Secured CMO for cGMP Manufacturing

Study conducted by EyeCRO LLC, Oklahoma City, OK ,USA. Additional information and study report available under CDA

Secured CMO for cGMP Manufacturing

- Process development, analytical and manufacturing of PKX-001 lyophilized powder for clinical studies provided by experienced US-based Contract Manufacturing Organization
- PKX-001 powder (API) manufactured using proprietary synthetic manufacturing process, under cGMP conditions
  - Multiple large-scale batches successfully manufactured and utilized for nonclinical and clinical studies
  - Stability of PKX-001 powder confirmed for at least 2 years at -20° C
- Stability of 5% PKX-001 formulation in BSS confirmed for at least 28 days at room temperature



Formulation stability study conducted by AmbioPharm, North Augusta, SC, USA. Additional information and study report available under CDA

PKX-001 has strong IP protection status

Study conducted by EyeCRO LLC, Oklahoma City, OK ,USA. Additional information and study report available under CDA

Secured CMO for cGMP Manufacturing

- ProtoKinetix has patent coverage for the composition of matter (for the family of AAGP compounds including PKX-001).
- Method of use patent applications are pending for the use of PKX-001 in ocular setting. Specifically, for enhancing neurosensory precursor cells (NPC; e.g. photoreceptor precursor cells), and for the treatment of dry eye disease.
  - 3 pending patents applications for NPC: in the US, Europe and Canada
  - 1 pending US provisional patent application for the treatment of dry eye disease and other ocular inflammatory conditions
  - Expected U.S. market exclusivity to at least 2036 for NPC and 2040 for dry eye disease

Formulation stability study conducted by AmbioPharm, North Augusta, SC, USA. Additional information and study report available under CDA

Thank You!

from

protoKinetix

- Additional information on efficacy, safety and manufacturing of PKX-001 is available under CDA
- ProtoKinetix Inc. is seeking collaboration and licensing partners to further the development of PKX-001 for the treatment of dry eye disease.

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