



Innovation in  
Ophthalmology

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**KPI – 012 Overview**

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November 15, 2021



# Safe Harbor and Disclaimer

This presentation contains forward-looking statements that involve substantial risks and uncertainties. Any statements in this presentation about our future expectations, plans and prospects, including but not limited to statements about our acquisition of Combangio, Inc. (the "Acquisition") and the other transactions contemplated by the Acquisition, and any other statements about future expectations, prospects, estimates and other matters that are dependent upon future events or developments, including statements related to our expectations with respect to the potential financial impact and benefits of the Acquisition, including our expectations with respect to milestone payments pursuant to the Agreement and Plan of Merger with Combangio, Inc., and expectations with respect to and potential advantages of KPI-012 or any other product candidate that we may acquire in connection with the Acquisition, the future development or commercialization of KPI-012, conduct and timelines of clinical trials, the clinical utility of KPI-012 for Persistent Corneal Epithelial Defect ("PCED"), plans for filing of regulatory approvals, the market opportunity for KPI-012 for PCED and other indications, plans to pursue research and development of KPI-012 for other indications, the sufficiency of our existing cash resources and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "likely," "will," "would," "could," "should," "continue," and similar expressions constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: our ability to realize the anticipated benefits of the Acquisition, including the possibility that the expected benefits, synergies and growth prospects from the Acquisition will not be realized or will not be realized within the expected time period or at all, negative effects of the announcement of the Acquisition on the market price of our common stock, significant transaction costs, unknown liabilities, the risk of litigation and/or regulatory actions related to the Acquisition, the uncertainties inherent in the initiation and conduct of clinical trials, availability and timing of data from clinical trials, whether results of early clinical trials or trials in different disease indications will be indicative of the results of ongoing or future trials, whether results of the Phase 1/2 clinical trial of KPI-012 will be indicative of results for any future clinical trials and studies of KPI-012, uncertainties associated with regulatory review of clinical trials and applications for marketing approvals, whether regulatory or commercial milestones are achieved, our ability to successfully integrate Combangio, Inc.'s business into our business, our ability to retain and hire key personnel, the risk that disruption resulting from the Acquisition may adversely affect our business and business relationships, including with employees and suppliers, the sufficiency of cash resources and need for additional financing and such other important factors as are set forth under the caption "Risk Factors" in our annual and quarterly reports and any other filings on file with the U.S. Securities and Exchange Commission. In addition, the forward-looking statements included in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.

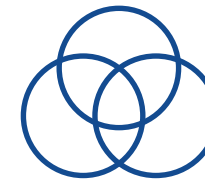
# KPI-012: Novel Clinical Stage Secretome Therapy With Multifactorial MoA Currently in Development for Persistent Corneal Epithelial Defect (PCED)

- Human bone marrow derived mesenchymal stem cell (MSC) secretome currently in development for PCED
  - Mixture of biologically active components secreted by human MSCs and processed into a simple solution formulation
  - Accelerated corneal wound healing in established preclinical models
  - Potential utility in other severe ocular surface diseases
- Encouraging Ph 1b results with BID dosing
  - Improvement in 7 of the 8 PCED patients
  - Complete healing of PCED in 6 of 8 patients, in most cases with 1 to 2 weeks of dosing
- Positive pre-IND meeting with FDA
  - Agreement on clinical requirements and endpoints for PCED
  - FDA open to a broad PCED indication
- Orphan drug designation granted by FDA for PCED
- Significant market potential for PCED and additional underserved rare disease segments – eg chemical/ thermal injury, corneal ulcer, graft vs host disease, limbal cell deficiency

## Applying Innovative Science to the Treatment of Serious Ocular Surface Diseases

**Cell-free  
regenerative  
therapy**

Secreted biologically active MSC factors critical for effective wound healing



Addresses the complex wound healing process involved in PCED and other ocular surface diseases via a multifactorial mechanism of action

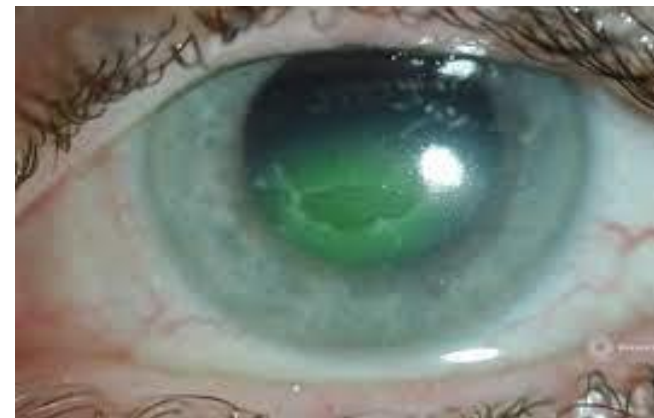


Simple convenient topical solution formulation to improve patient experience

**KPI-012 Has Potential To Treat PCEDs of Multiple Etiologies as Well as Other Severe Ocular Surface Diseases**

# Persistent Corneal Epithelial Defect (PCED) is a Significant Unmet Need

- PCED – persistent non-healing corneal defect that is refractory to conventional treatments
- Clinical symptoms include pain, foreign body sensation, redness, photophobia and tearing
- Clinical signs include non-healing epithelial defect, stromal scarring and stromal thinning
- Can lead to infection, corneal perforation and vision loss
- Estimated incidence of approximately 100,000 patients in the US and 238,000 in the US, EU and Japan combined
- Underserved market – only approved Rx product (Oxervate™) has limited indication
  - Indicated for neurotrophic keratitis (NK) which is estimated to be the underlying etiology for only ~ 1/3 of all PCED
  - Contains a single growth factor (NGF)
  - Dosed 6 times/day at 2-hr intervals for 8 weeks
  - Often requires repeat treatment



**PCED is driven by various potential etiologies, including:**

- Neurotrophic keratitis
- Surgical epithelial debridement
- Microbial/viral keratitis
- Corneal transplant
- Limbal stem cell deficiency
- Mechanical trauma

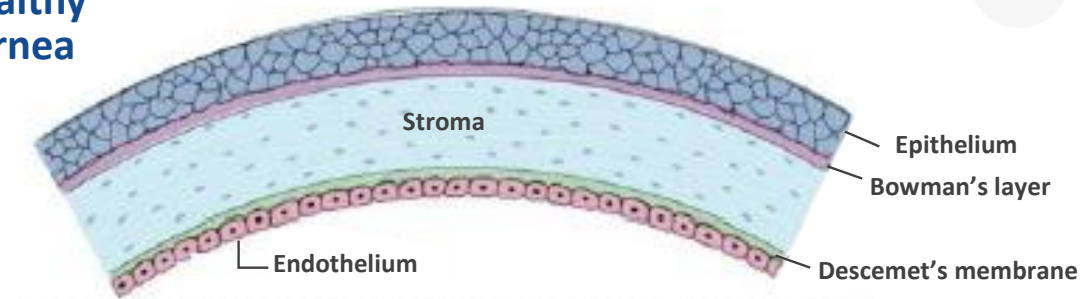
**PCED patients often have more than one underlying etiology**

**There Are Currently No Effective Treatments for Many of the Etiologies of PCED**

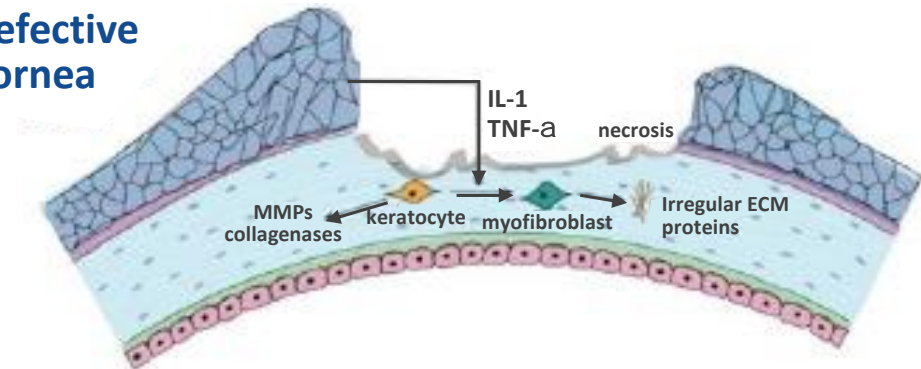
# PCED is a Disease of Impaired Corneal Healing

- PCED – multifactorial pathophysiology leads to impaired corneal wound healing
- Normal corneal healing follows a highly regulated multifactorial process
  - Involving growth factors, cell signaling, epithelial proliferation/migration, and extracellular matrix remodeling
- Healing process impaired in PCED and similar diseases
  - Imbalance of the the key biomolecules that orchestrate normal wound healing
  - Leads to significant inflammation, impaired innervation and disruption of the protective epithelial and stromal layers of the cornea
- We believe that addressing the imbalance of key biomolecules is critical for effective treatment of diseases involving impaired healing

## Healthy Cornea



## Defective Cornea



**Effective Treatment of PCED and Other Ocular Diseases of Impaired Healing May Require a Multifactorial Mechanism of Action**

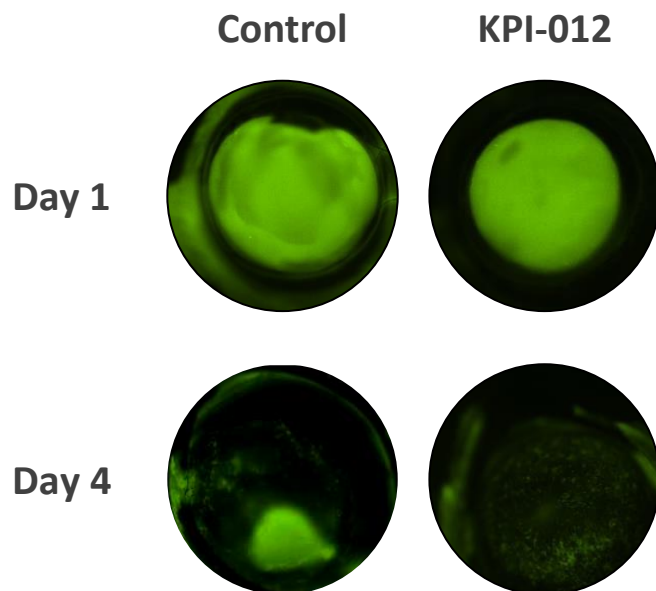
# Multifactorial Mechanism of Action to Address Impaired Healing in PCED and Other Ocular Surface Diseases of Impaired Healing

Key KPI-012 Components	Ocular Surface Wound-Healing Function
Protease Inhibitors (TIMP-1, TIMP-2, Serpin E1)	Inhibition of destructive proteases that degrade matrix in the wound bed
Matrix Proteins (Collagen)	Construction of a molecular scaffold in the wound bed for cells to migrate and adhere to
Growth Factors (HGF)	Suppression of inflammation and promotion of corneal epithelium repair
Neurotrophic Factors (PEDF)	Regeneration and maintenance and of neurons to support corneal health

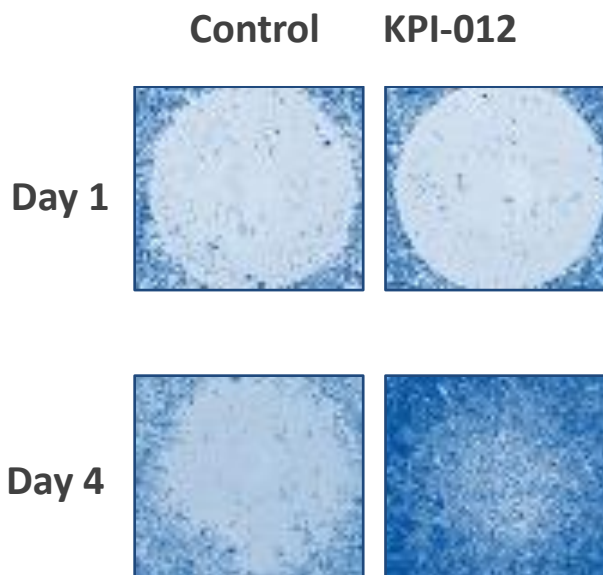
**KPI-012's Mechanism of Action Offers Promise for the Treatment of PCED and Other Ocular Surface Diseases of Various Etiologies**

# Broad Wound Healing Activity in Preclinical Models

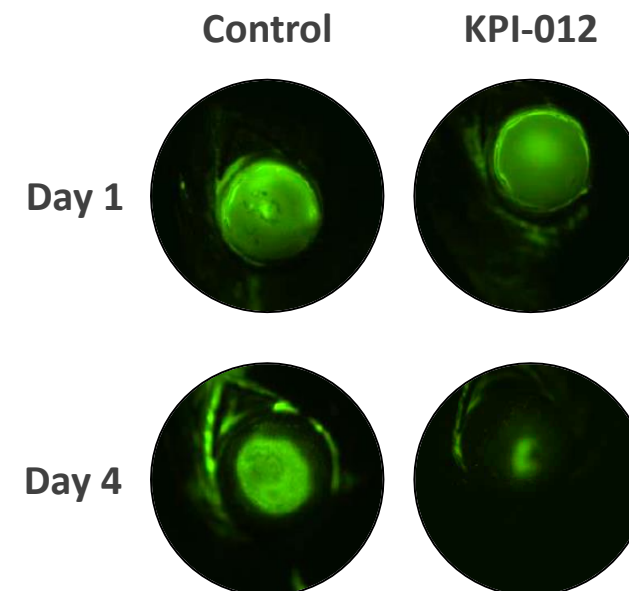
## Rat Alkali Injury Model (*in vivo*)



## Human Corneal Epithelial Cells (*in vitro* cell culture)



## Mouse Mechanical Wound Model (*in vivo*)



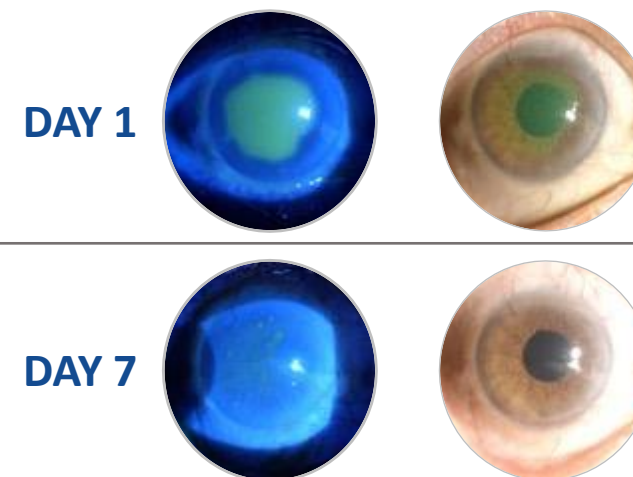
Positive Results Across Various Models Suggest Potential Benefit in PCED and Other Ocular Surface Diseases

# Promising Results in PCED With BID Dosing in Phase 1b Clinical Trial

- Prospective single arm trial at 2 sites in Mexico City
  - Initial safety cohort of 3 subjects without corneal disease dosed BID for 1 week showed no tolerability or safety issues
  - Efficacy cohort consisted of 8 PCED patients dosed BID for 1 to 8 weeks and followed for up to 19 weeks
  - Key efficacy endpoint – healing of PCED based on corneal staining photographs
- Top line results in efficacy cohort
  - 7 of 8 patients showed improvement in PCED
  - 6 of 8 patients had complete healing of PCED
    - 4 of the 6 completely healed after 1 week
    - 1 of the 6 healed after 2 weeks; the other after 4 weeks
  - All healed patients remained healed through end of follow-up
  - KPI-012 well-tolerated with no safety issues observed

## 6/8 Completely Healed PCED Patients

	Mean	Median
PCED Size at Baseline (mm x mm)	5.1 x 3.5	5.6 x 2.9
PCED Duration at Baseline (Days)	58	32
PCED Healing Time (Days) KPI-012, 2x/day	12	7

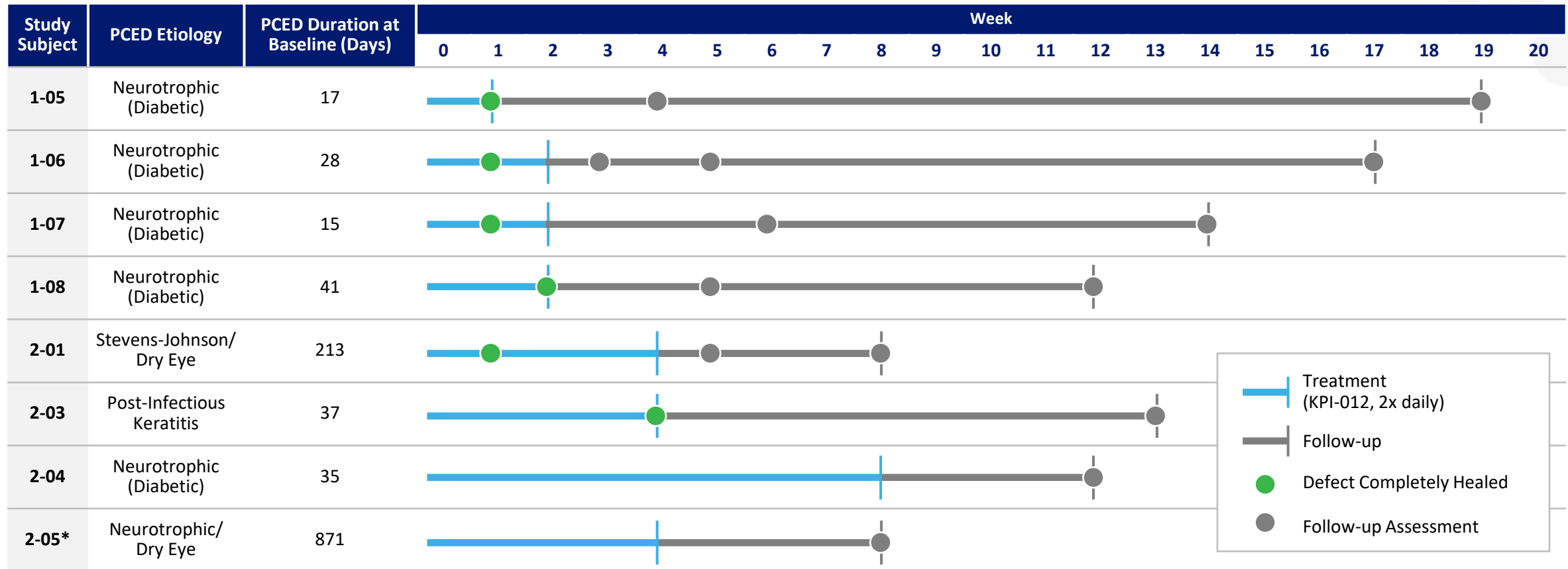


Representative images for a healed patient study eye

**Results Support Moving Directly to Phase 2/3 Clinical Trial**



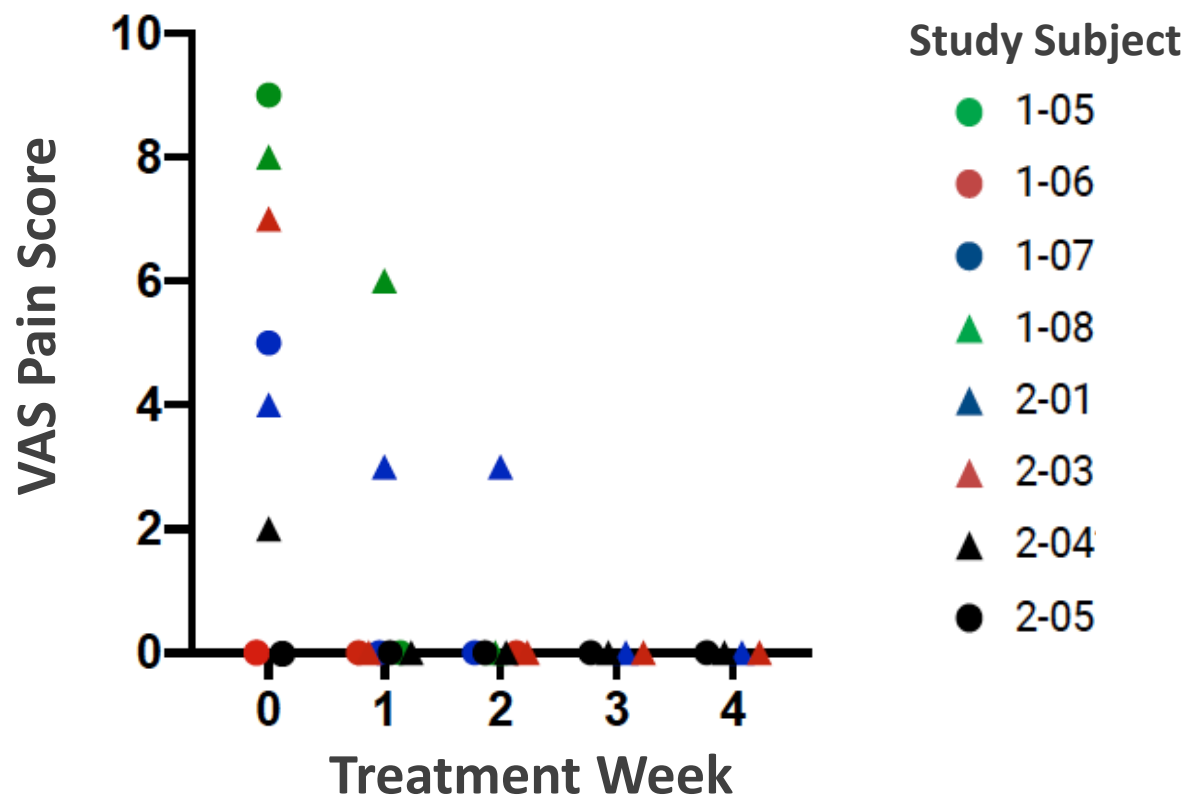
# Complete Healing in 6 of 8 PCED Patients After 1 - 4 Weeks of BID Treatment With KPI-021 in Phase 1b Clinical Trial



\*Improvement in the PCED was observed for subject 2-05 but did not achieve complete healing

**Rapid and Sustained Healing in Patients with Varying Etiologies and Duration of Disease Suggests Potential for Broad Efficacy in PCED**

## Significant Pain Relief Within 1 Week of Treatment in Phase 1b Trial



Of Patients Reporting Pain  
at Baseline (6 of 8):

**100%** reported pain  
reduction at Week 1

**67%** reported 0 pain score  
at Week 1

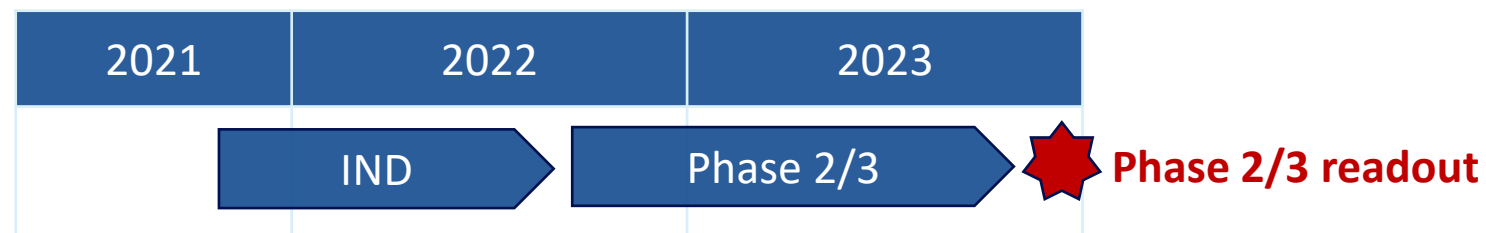
**100%** reported 0 pain score  
at Week 3

Rapid and Sustained Improvement in Pain in PCED Patients Treated with KPI-012

# KPI-012 Development Program for PCED

- Pre-IND meeting in 2020
  - FDA open to broad PCED indication and provided guidance on CMC, clinical trial design and endpoints
- US IND submission and initiation of Phase 2/3 clinical trial targeted for Q3 2022
  - Top line Phase 2/3 results expected by end of 2023
- If Phase 2/3 results positive, it could serve as the first of the two required trials to support a BLA submission

## Projected Timelines for PCED Development



**Straightforward PCED Clinical Development Program  
Clinical Program(s) for Additional Orphan Indications Being Evaluated**

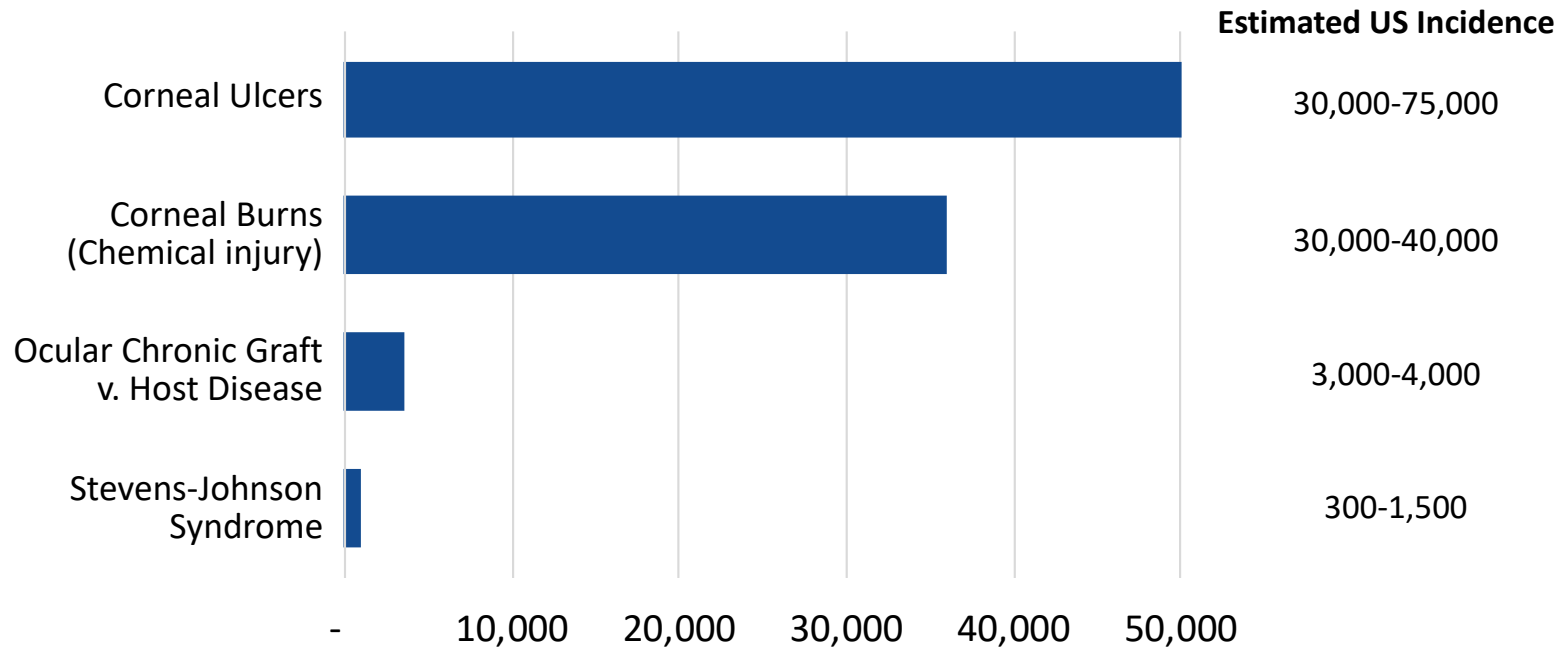
# KPI-012 – An Orphan Drug with Significant Global Market Opportunity

- PCED is a rare disease with substantial clinical burden and high unmet need - speed of healing, pain resolution, prevention of vision loss
  - No FDA-approved products for the treatment of PCED across multiple etiologies
  - KPI-012 granted orphan drug designation by FDA
  - KPI-012 has potential for broad efficacy across all PCED etiologies and BID dosing for 4-weeks with favorable safety and tolerability
  - Estimated ~100K patients in the U.S. and ~ 238K patients in US/EU/Japan combined; projected to grow annually through 2030<sup>1,2</sup>
  - One product approved to treat Neurotrophic Keratitis (Oxervate), an underlying etiology in only ~35% of all PCED cases
  - Oxervate priced at approximately \$100K per treatment
- KPI-012 Drug Substance manufacturing scaled up to the bioreactor scale needed for pivotal trials
  - Process design enables scaling to commercial bioreactor scale utilizing same quantity of working cell bank starting material
- Preservative-free unit dose blow-fill-seal vials for pivotal trials with planned commercial container closure
- PCED treated by small subset of ECPs, allowing for efficient rare disease commercial model

**KPI-012 Provides Significant Global Commercial Opportunity and Entry into Rare Disease Space**

# KPI-012 Has Potential Application in Other Orphan Ocular Surface Disease Segments as Well as Non-ocular Diseases

## Potential Orphan Disease Markets in Severe Ocular Surface Disease



Also evaluating severe Sjogren's syndrome (with chronic keratitis) and limbal cell deficiency as potential indications

## Potential Out-licensing Opportunities in Unmet Needs Outside of the Eye

- Diabetic Foot Ulcer
- Venous Leg Ulcer
- Oral Mucositis

**KPI-012 Could Have Significant Commercial Potential Beyond PCED**

# Patent and Regulatory Exclusivity

- Regulatory Exclusivity in the U.S.
  - If approved as a new biologic product under a BLA, KPI-012 should enjoy 12 years market exclusivity for each indication during which biosimilars of KPI-012 cannot be launched
  - 7-year orphan exclusivity on the treatment of PCED
- Patent Exclusivity
  - A worldwide patent portfolio related to KPI-012 and its use for the treatment of an ocular condition, such as PCED and other ocular surface diseases, has a 20-year patent term ending in 2040
  - If approval occurs after 2026, a patent term extension\* may be available in the U.S., which can extend the term beyond 2040
- KPI-012 should meet the criteria for FDA designations of Fast Track Status and Breakthrough Therapy

## Potential U.S. Regulatory Exclusivity and IP Protection Beyond 2040

\*While a maximum of 5 years of patent term extension is available, the total patent life with the patent term extension cannot exceed 14 years from the approval date. If the patent life after approval has 14 or more years, the product would not be eligible for patent term extension.

## Combango Acquisition Summary

- Meaningfully advances goal of **strengthening Kala's pipeline** for the treatment of front and back of the eye diseases
- Leverages **existing R&D and commercial expertise**
- Provides Kala entrée into **rare disease space**
- Provides potential **'Pipeline in a Product'** with opportunity for additional applications and indications across rare ophthalmic and other non-ocular diseases