KB801 for Neurotrophic Keratitis First Patient Dosed Update

July 2025

Forward Looking Statements and Disclosures

This presentation and the accompanying oral presentation contain forward-looking statements that involve substantial risks and uncertainties. Any statements about future expectations, plans, and prospects for Krystal Biotech, Inc. (together with its subsidiaries, the "Company"), including but not limited to statements about the Company's investigational product candidate, KB801, and the EMERALD-1 clinical trial evaluating KB801 for the treatment of NK; KB801 being well positioned to deliver significant benefit for the growing number of patients diagnosed with NK; the estimated number of NK patients the U.S.; the potential benefits of KB801 compared to Oxervate, including superior and sustained NGF exposure in the cornea and a significant reduction in dosing frequency; the versatility and breadth of the Company's redosable HSV-1 based platform and potential opportunities for front of the eye applications; the clinical development path for KB801 being relatively short and cost-effective with safety, efficacy, and CMC all significantly derisked; the possibility of expedited development and potential registrations in 2026 and 2027 for KB803 and KB801, respectively; the timing of data readouts from the Company's pipeline products in 2025; value creation opportunities and a path to building long-term growth and shareholder value, including the VYJUVEK franchise being poised for steady growth for years to come, the addition of KB803, if approved, being highly synergistic with VYJUVEK and driving further top-line and bottom-growth, and pipeline efforts in the lung and eye being springboards that could open up multi product opportunities in blockbuster markets; 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: uncertainties associated with regulatory reviews and the content and timing of regulatory authorities' decisions; uncertainties in the initiation and conduct of clinical trials and availability and timing of data from clinical trials; the availability or commercial potential of product candidates; and such other important factors as are set forth in the Company's filings with the SEC. The forward-looking statements represent the Company's views as of the date of this presentation and should not be relied upon as representing the Company's views as of any subsequent date. The Company specifically disclaims any obligation to update forward-looking statements.

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Other than VYJUVEK, all products described in this presentation are investigational therapies.

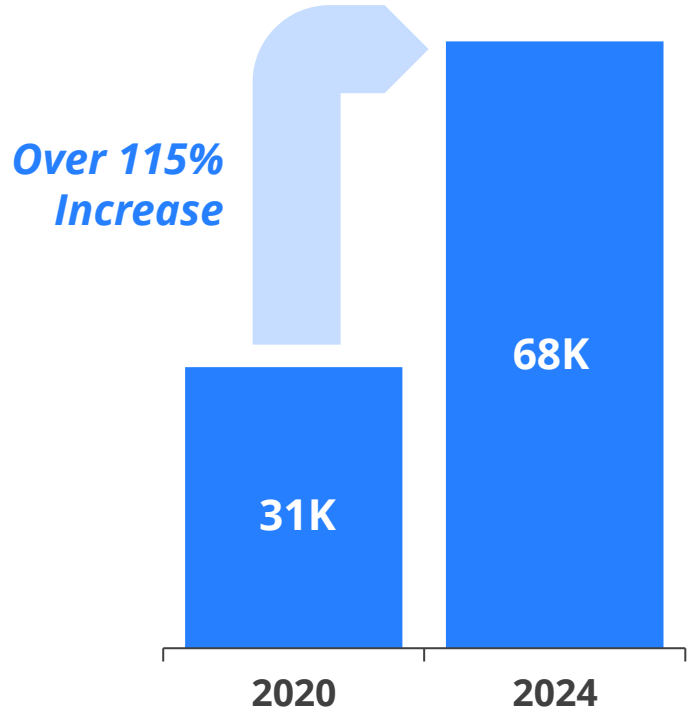
Agenda

About Neurotrophic Keratitis	Krish Krishnan; Chairman and CEO
Krystal's Platform for Front of Eye	Suma Krishnan, MS, MBA; President, Research & Development
Krystal's KB801 Program ▪ Preclinical Overview ▪ Phase 1/2 Clinical Trial Design ▪ Regulatory and Pipeline Outlook	 Trevor Parry, PhD; VP, Product Development David Sweet, MD, PhD; Director, Clinical Development Suma Krishnan, MS, MBA; President, Research & Development
Closing	Krish Krishnan, Chairman and CEO
Q&A	All Speakers

Neurotrophic Keratitis is a Degenerative, Vision-Threatening Disease

- NK is a degenerative disease of the cornea that occurs when corneal nerves are damaged and their roles in maintaining the corneal epithelium are compromised
- Corneal epithelial impact can range from punctate lesions to recurrent or persistent epithelial defects and ulcers, leading to stromal melting and corneal perforation
- All NK associated with some degree of vision impairment, severe cases lead to blindness
- Although rare, diagnosis rates are climbing rapidly as awareness grows
- There were an estimated **68K patients** in U.S. with at least one NK claim in 2024, more than double the number in 2020

Estimated Patients with NK Claim in the U.S.



Komodo Healthcare Map, Estimated Patients with at Least One H1623* Code, 2020-2024

Sacchetti M, et al. *Clin Ophthalmol*. 2014. 8: 571-579; Bian Y, et al. *Ophthalmology*. 2022. 129: 1255-1262; Rama P, et al. *Orphanet*. Neurotrophic Keratopathy. 2017 [accessed Sept 28 2023]; Gablson EE et al. *Invest Ophthalmol Vis Sci*. 2018. 59: 1800; Komodo Health H16.23* Claims Analysis [June 2025]; Dana R, et al. *BMC Ophthalmol.* 2021. 21: 327

NK, neurotrophic keratitis; U.S., United States

KB801 Designed to Address Shortcomings of Only FDA Approved Therapy

- The only specific FDA approved therapy for NK is Oxervate®
- First approved in 2018, Oxervate is an ophthalmic formulation of recombinant human nerve growth factor (cenegermin-bkbj) for topical application as an eye drop
- Oxervate® targets underlying nerve defect and has been shown to improve healing
  - 4 week healing rates in the range of 50-60%
  - 8 week healing rates (primary endpoint) in the range of 65%-75%
- However, Oxervate **must be dosed 6x daily for 8 weeks** which is both highly burdensome and may lead to suboptimal outcomes
- Eye pain is the most common adverse event, compounding the problem of 6x daily dosing

Over $540M

2023 U.S. Medicaid and Medicare Spend on Oxervate

CMS – Medicare and Medicaid Spending Per Drug, query 'Oxervate', accessed June 2025

Over 410K

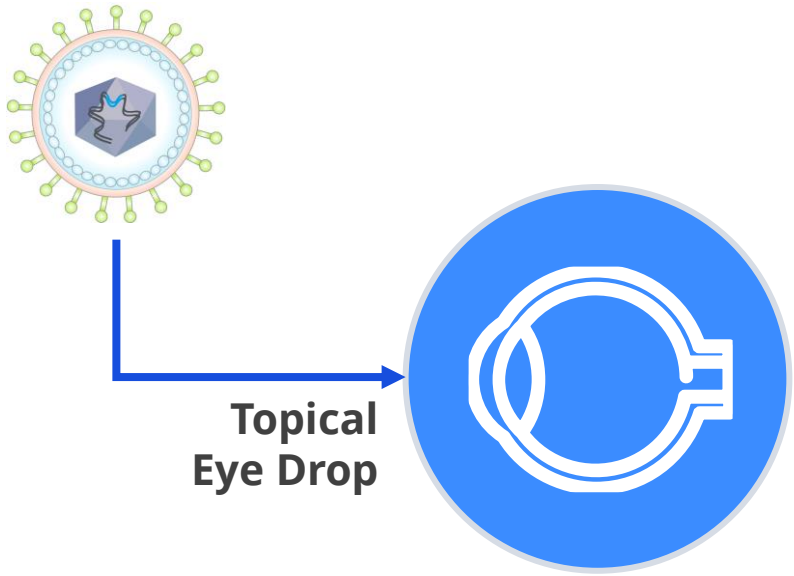
Estimated Days of Reimbursed Oxervate Therapy in US in 2024

Komodo Drug Projections Assuming 14 Day Supply per Projected Rx

CADTH Review – Cenegermin (Oxervate). 2022. Vol 2, Issue 9; Pflugfelder SC, et al. *Ophthalmology*. 2020. 127: 14-26; Bonini S, et al. *Ophthalmology*. 2018. 125: 1332-1343; Oxervate® 2019 FDA Label; Komodo Health Drug Projections [June 2025]

NK, neurotrophic keratitis; U.S., United States

Krystal's HSV-1 Platform Well Suited for Front of the Eye Applications



Rapid protein clearance and frequent cell turnover have to date limited potential of gene therapy and biologics in the front of the eye

Redosable HSV-1 based vector can overcome those challenges

- HSV-1 exhibits natural tropism for epithelial cells of the eye
- Vector is amenable to eye drop formulation and administration
- Safety and efficacy of repeat dosing with B-VEC eye drops already demonstrated under compassionate use in DEB patient
- Cargo capacity allows for delivery of wide variety and combinations of biologic payloads

Multiple development opportunities targeting genetic diseases as well as those where biologics would be beneficial but not feasible given rapid protein clearance rates

Sabater A et al., Poster # 787 - C0388. at the 2023 Association for Research in Vision and Ophthalmology Annual Meeting; Vetencourt AT, et al. *N Engl J Med*. 2024;390:530-535

B-VEC, beremagene geperpavec; DEB, dystrophic epidermolysis bullosa; HSV-1, herpes simplex virus type 1

Ophthalmology Expansion Already Well Underway with KB803 Phase 3

KB803 for Ocular Complications of DEB

- ✓ Repeat administration of B-VEC eye drops under compassionate use previously shown to be well tolerated and associated with full corneal healing as well as significant visual acuity improvement
- ✓ Natural history study initiated last year and ongoing
- ✓ IND cleared and **first patient dosed in Phase 3 IOLITE study in 2Q 2025**

Patient Outcomes from B-VEC Eye Drop Compassionate Use Case

Treated Eye

Baseline

6 Months

Visual Acuity in Treated Eye

Time		Visual Acuity
Baseline / Prior to Surgery		HM
After Surgery	1 Week	20/400
	1 Month	20/200
	2 Months	20/150
	3 Months	20/100
	4 Months	20/80-2
	5 Months	20/80-1
	6 Months	20/70
	7 Months	20/40
	8 Months	20/25

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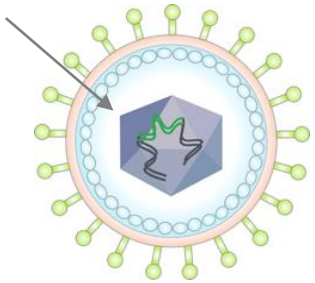
B-VEC, beremagene geperpavec; DEB, dystrophic epidermolysis bullosa; HM, hand motion

KB801 is Designed to Achieve Superior NGF Exposure in the Cornea With Significantly Reduced Dosing Frequency

KB801

2 x *NGF* genes



Replication-incompetent HSV-1 vector containing functional human *NGF*

Data Summary

- ✓ **Transduces primary human corneal epithelial cells *in vitro* leading to dose-dependent expression and secretion of mature NGF**
- ✓ **Functionality of secreted NGF confirmed using growth factor starved cell proliferation assay**
- ✓ **Topical administration to wounded murine corneas was well tolerated and resulted in localized NGF expression**
- ✓ **NGF expression was sustained, achieving higher peak levels than recombinant protein comparator and remaining elevated days after**
- ✓ **Safety and efficacy of HSV-1 vector redosing as an eye drop already demonstrated with B-VEC eye drop compassionate use case**

Data package strongly supportive of progression to the clinic for the treatment of neurotrophic keratitis

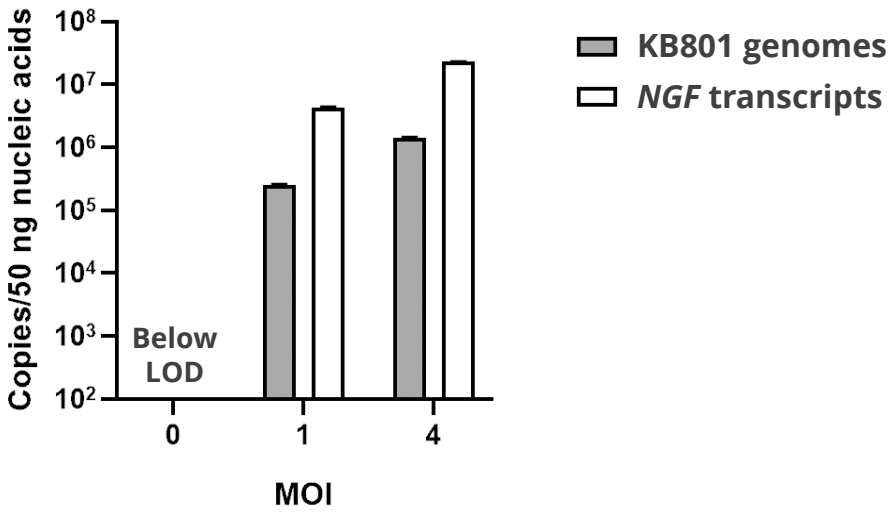
B-VEC, beremagene geperpavec; HSV-1, herpes simplex virus 1; NGF, nerve growth factor

KB801 Transduces Corneal Epithelial Cells *In Vitro* For Secretion of Mature NGF

KB801 transduces clinically relevant cells *in vitro*

- Primary corneal epithelial cells transduced with KB801 at MOI of 1 or 4
- Cells were collected after 24 hours for nucleic acid isolation and qPCR
- High levels of vector genomes and transcripts detected at both MOIs, with no vector-specific toxicity by MTT assay (not shown)

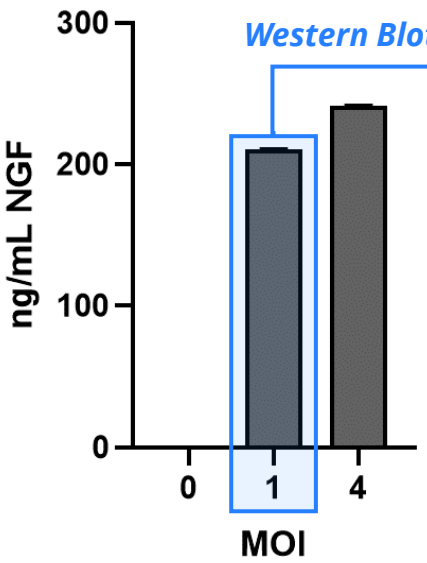
DNA / RNA Levels in Cell Lysates at 24 Hours



KB801 transduced cells secrete mature NGF

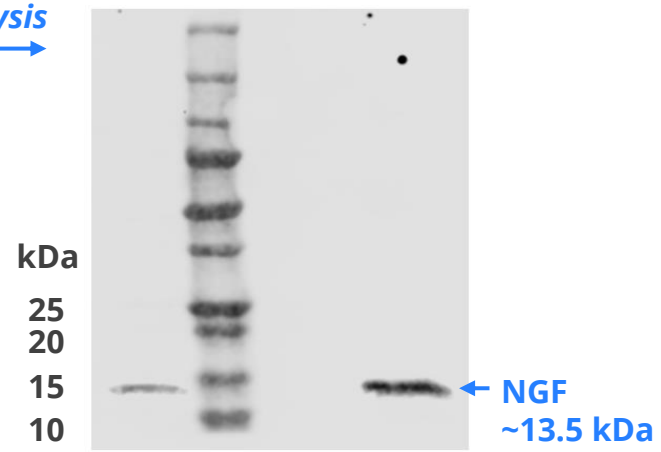
- Primary corneal epithelial cells were transduced at an MOI of 1 or 4
- Cell supernatants were collected at 48 hours for assessment of NGF protein expression and secretion via ELISA and western blot
- NGF levels in mock transduced cells were below limit of detection
- **Dose dependent increases in mature NGF levels were detected in KB801 transduced cell supernatants with over 95% of secreted protein cleaved**

NGF Protein Levels in Supernatant at 48 Hours by ELISA



Cell Supernatants

Western Blot Analysis



Functionality confirmed in TF-1 assay

Cartwright HN, et al. Poster #2467 at the 2025 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting; Krystal Biotech. Data on File.

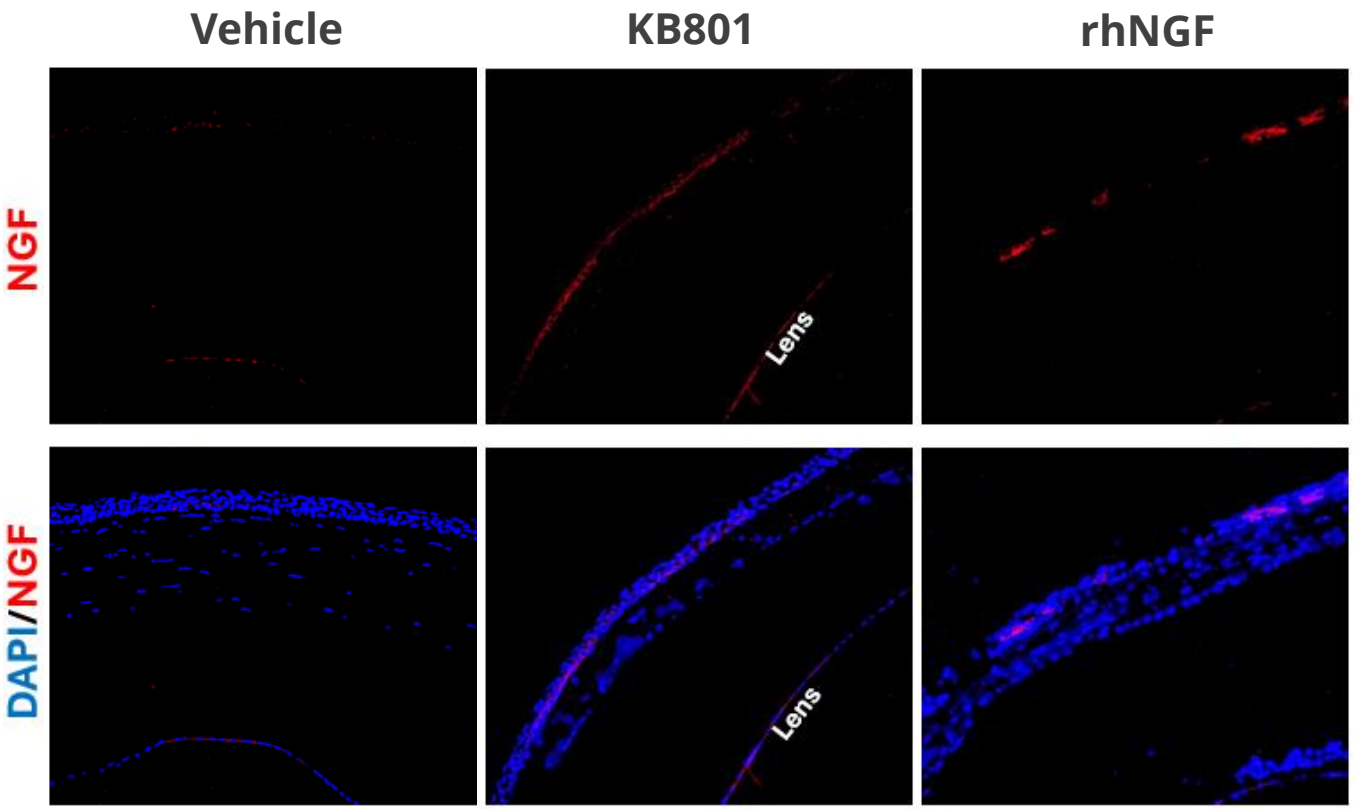
DNA, deoxyribonucleic acid; ELISA, enzyme linked immunosorbent assay; LOD, limit of detection; MOI, multiplicity of infection; MTT, Mosmann's tetrazolium toxicity; NGF; nerve growth factor; qPCR, quantitative polymerase chain reaction; rhNGF, recombinant human nerve growth factor; RNA, ribonucleic acid

NGF Expression and Corneal Localization Confirmed in Pilot Mouse Study

Pilot Study

- Study conducted in BALB/c mice, 6-10 weeks of age, with eyes wounded using crosshatch technique
- Test conditions, each administered as 3 µL eyedrop
  - KB801: 4.6 x 10^7 PFU
  - Mouse eye weight adjusted HED rhNGF: 1.6 ng (not shown)
  - Mouse eye area adjusted HED rhNGF: 11 ng*
  - Saline vehicle control
- Eyes collected 24 hours after administration for qPCR, ELISA, or immunofluorescence and histology (n = 2 / endpoint)

Immunofluorescence in Cornea @ 24 Hours



Uniform distribution of NGF along corneal epithelium similar to that achieved with recombinant protein

Cartwright HN, et al. Poster #2467 at the 2025 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting; Krystal Biotech. Data on File.

* Assuming single eye drop of Oxervate® is 35 uL and contains 700 ng of rhNGF, and adjusting for eye surface area assuming 24 mm diameter in human eye and 3mm diameter in mouse eye (64x adjustment factor)

ELISA, enzyme-linked immunosorbent assay; HED, human equivalent dose; NGF, nerve growth factor; PFU, plaque forming unit; qPCR, quantitative polymerase chain reaction; rhNGF, recombinant human nerve growth factor

No Evidence of Adverse Inflammation or Histological Abnormalities

Pilot Study

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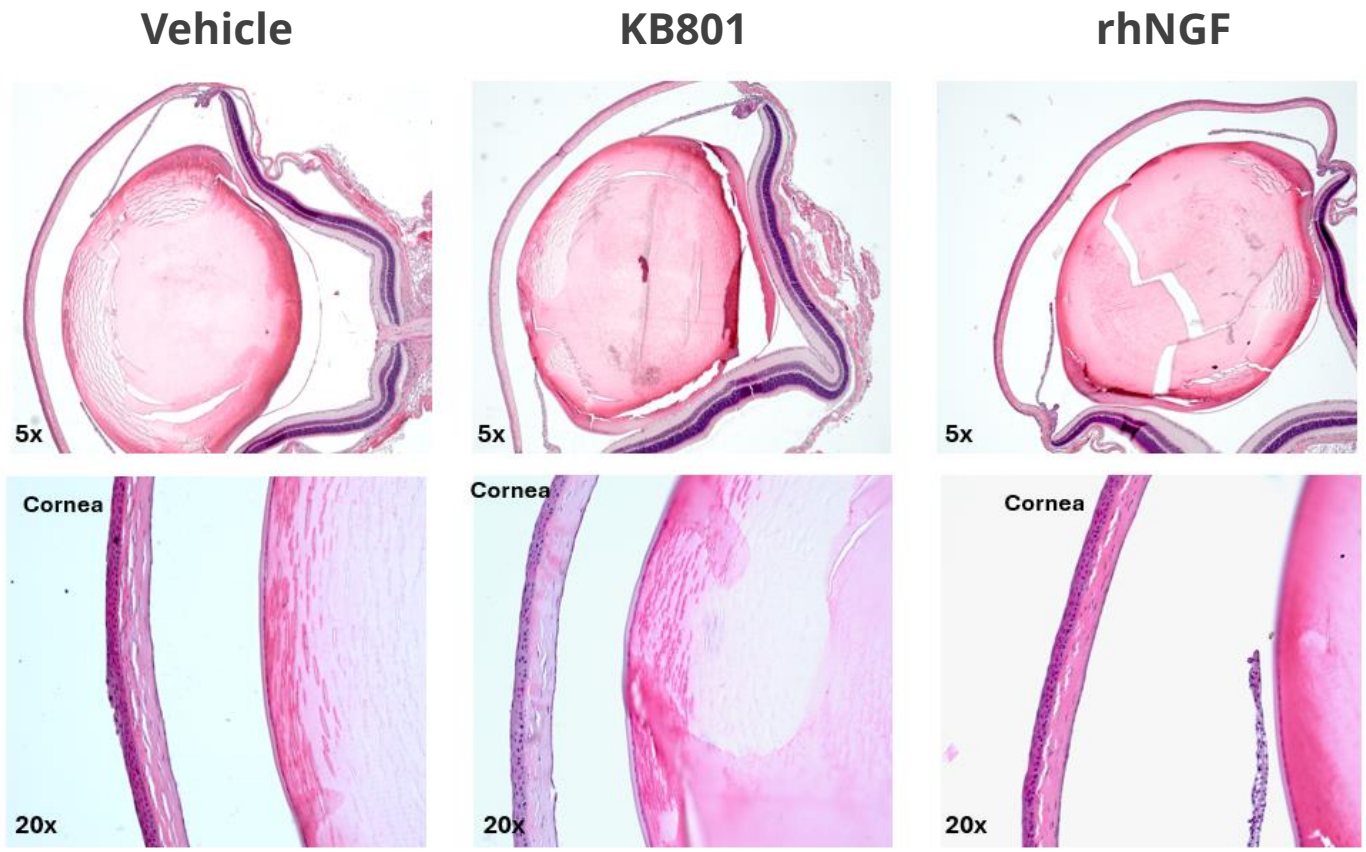
Histology @ 24 Hours



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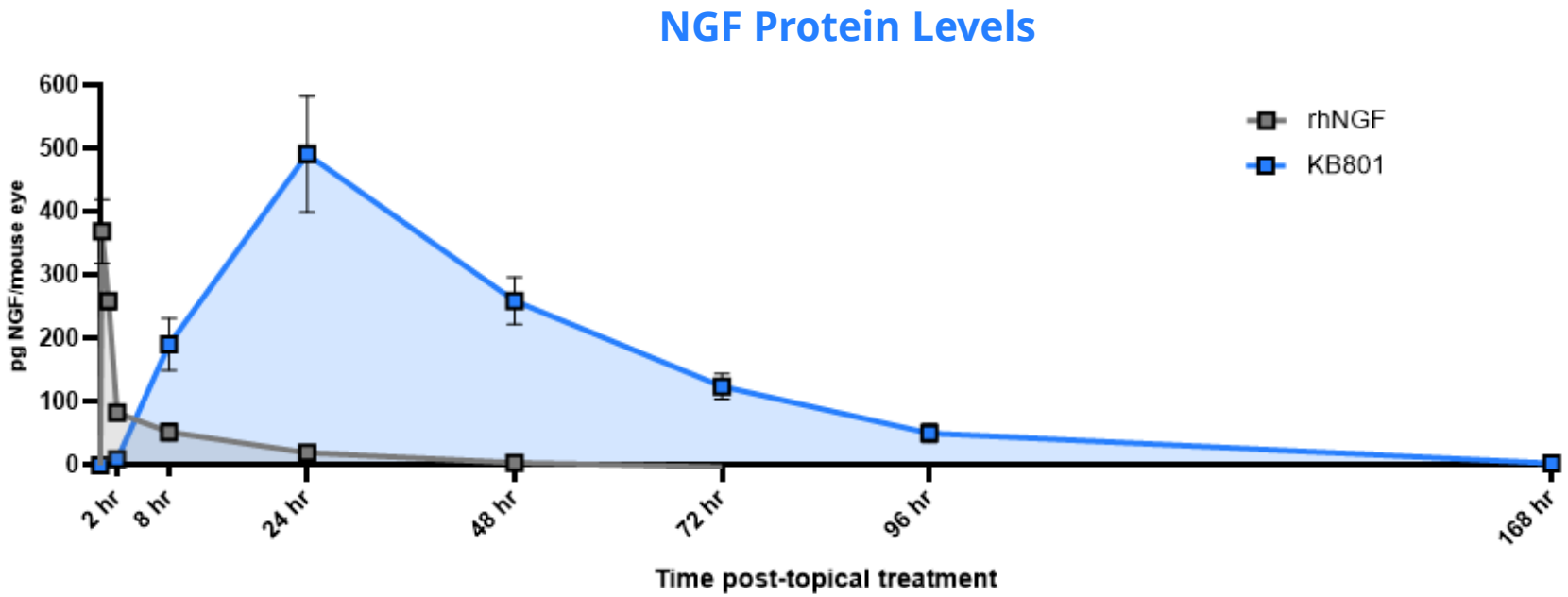
Clear Durability Advantage with KB801 in Head to Head Mouse PK Study

Head to Head PK Study #1

- Study conducted in BALB/c mice, 6-10 weeks of age, with eyes wounded using crosshatch technique
- Test conditions, each administered as 3 µL eyedrop
  - KB801: 4.6 x 10^7 PFU
  - Dilution factor matched rhNGF: 20 ng*
  - Saline vehicle control
- Eyes collected at specified time points for ELISA (n = 3)



Cartwright HN, et al. Poster #2467 at the 2025 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting

* Based on 1/30 dilution of intended human dose of KB801

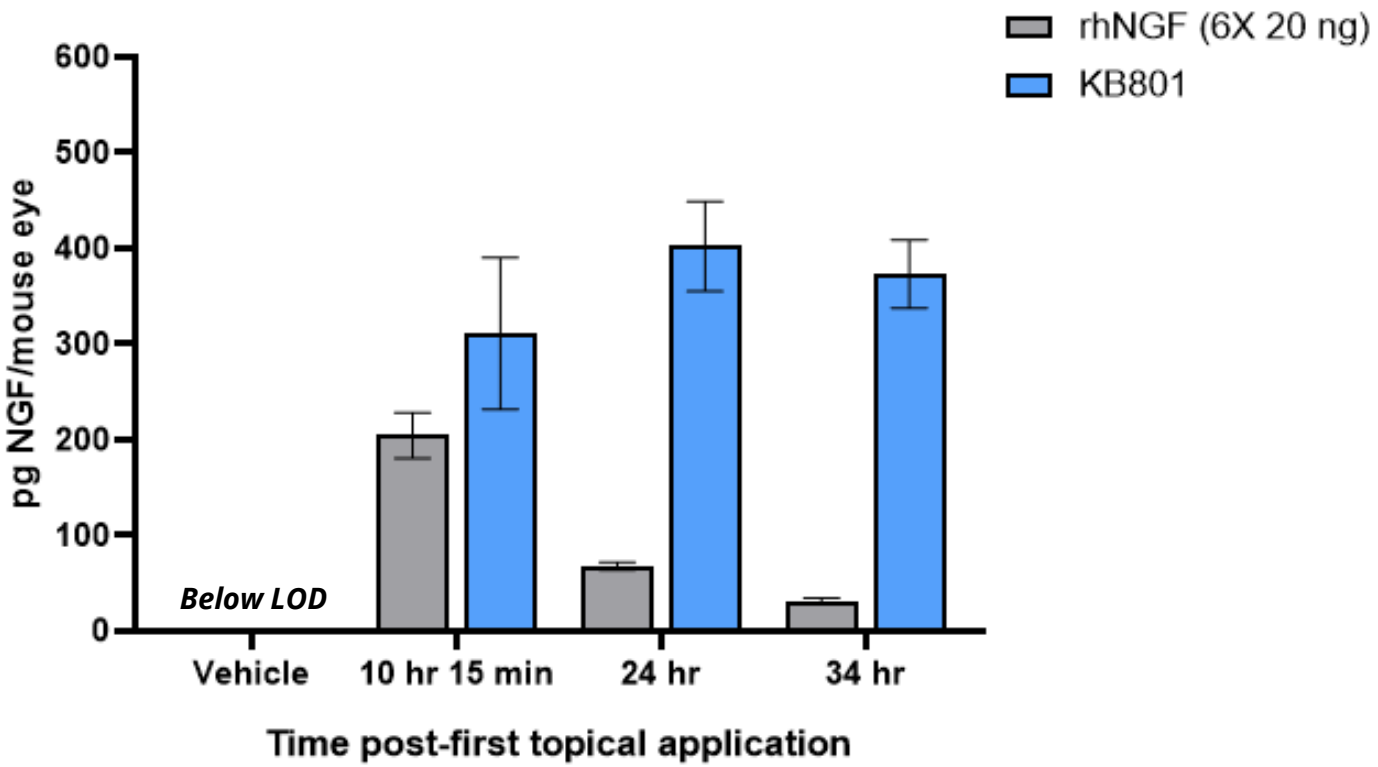
NGF; nerve growth factor; ELISA, enzyme-linked immunosorbent assay; PFU, plaque forming unit; rhNGF, recombinant human nerve growth factor

Superior PK Profile Confirmed Even Against Intensive Recombinant Dosing

Head to Head PK Study #2

- Study conducted in BALB/c mice, 6-10 weeks of age, with eyes wounded using crosshatch technique
- Test conditions, each administered as 3 µL eyedrop
  - KB801: 4.6 x 10^7 PFU
  - Dilution factor matched rhNGF: **6 x 20 ng***
  - Saline vehicle control
- Eyes collected at specified time points for ELISA (n = 3)

NGF Protein Levels



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KB801 Phase 1/2 Study EMERALD-1

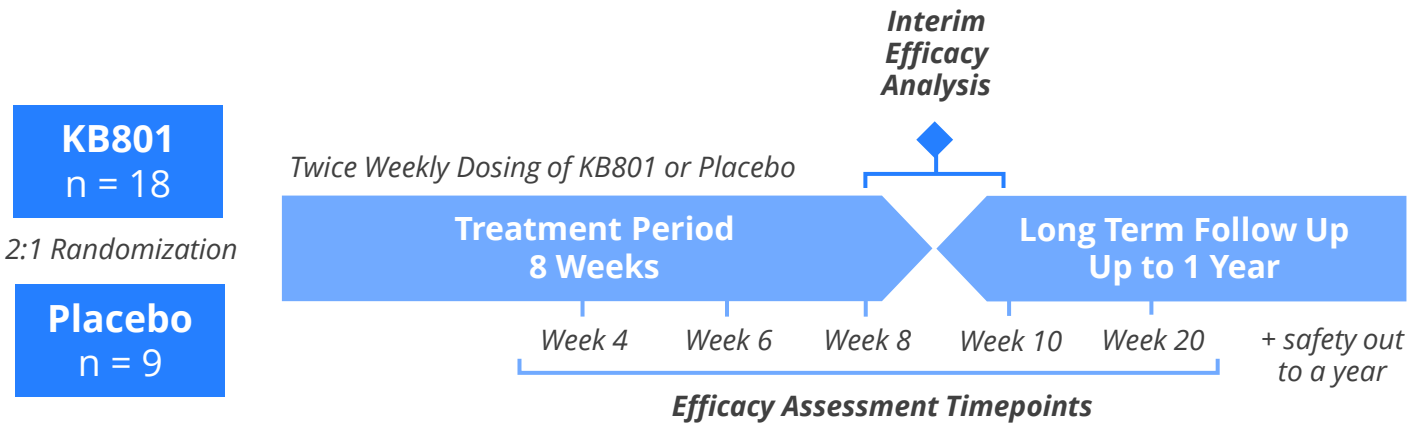
Double-masked, 2:1 randomized, placebo-controlled study in patients with moderate-to-severe NK

Study Objectives

- Evaluate safety and tolerability of twice-weekly KB801, as well as preliminary efficacy evaluation including:
  - Complete durable healing of the corneal epithelium at 8 weeks, defined as 0 mm fluorescein staining at 8 weeks and no residual staining at 10 weeks
  - Change from baseline in persistent corneal epithelial defect size at weeks 4, 6, 8, 10, and 20
  - Change from baseline in corneal sensitivity as assessed by Cochet-Bonnet esthesiometry at weeks 4, 8, and 20
  - Change from baseline in ocular tolerability numeric rating scale through week 10

Key Enrollment Criteria

- Age ≥ 18 years with stage 2 or 3 NK per Mackie criteria
- Persistent corneal epithelial defect for at least two weeks and at least 1 mm in length
- Decreased corneal sensitivity as assessed by Cochet-Bonnet esthesiometry
- Excluding patients with active infections, recent unrelated surgeries, concomitant therapies, defects over 8 mm



First patient dosed earlier this month

NK, neurotrophic keratitis;

Opportunity for Expedited Development on EMERALD-1 Success

Leveraging Prior Experience with Oxervate

- Extensive clinical and commercial experience with Oxervate derisks safety of KB801 payload
- Opportunity for efficient registrational study primarily focused on efficacy
- Endpoints and design well known with short time to readout

Upside: Krystal is Pursuing Platform Technology Designation with FDA

- HSV-1 platform is strong fit with FDA's recently announce Platform Technology Designation Program
- Potential for earlier, expanded, or accelerated FDA interactions
- Opportunity to leverage previous preclinical and clinical data to support streamlined development
- Possibility of FDA referencing prior CMC validation of the manufacturing process, release testing assays and stability for future marketing authorization

Clinical development path for KB801 expected to be relatively short and cost-effective with safety, efficacy, and CMC all significantly derisked

CMC, chemistry, manufacturing, and controls

Broadening the Scope of HSV-1 Platform with an Active Clinical Pipeline

Respiratory

- **KB407** Phase 1 Cohort 3 in cystic fibrosis patients
- **KB408** Phase 1 in patients with alpha-1 antitrypsin deficiency lung disease

Ophthalmology

- **KB803** Phase 3 in DEB patients with ocular complications
- **KB801** Phase 1/2 in patients with neurotrophic keratitis

Plus ongoing clinical programs in aesthetics, oncology, and rare dermatology indications

Clear Path to Delivering Long-Term Growth and Shareholder Value

- VYJUVEK franchise poised for multiple years of growth in U.S. and through global expansion
- Potential for efficient, near-term launch of KB803 highly synergistic with VYJUVEK
- Lung and eye are springboards targeting multiple blockbuster markets
- Significant value unlock and multi-product opportunity with success in either tissue

U.S., United States

Krystal®

Developing Genetic Medicines to Treat Diseases with High Unmet Medical Needs