Krystal®

Genetic Medicines for High Unmet Medical Needs

May 2026

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Forward Looking Statements and Disclosures

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Disclosures

The Company is using the Aerogen Solo® Nebulizer System and Aerogen® Ultra in certain of its studies of its inhaled product candidates.

Other than VYJUVEK, all Company product candidates described in this presentation are investigational therapies.

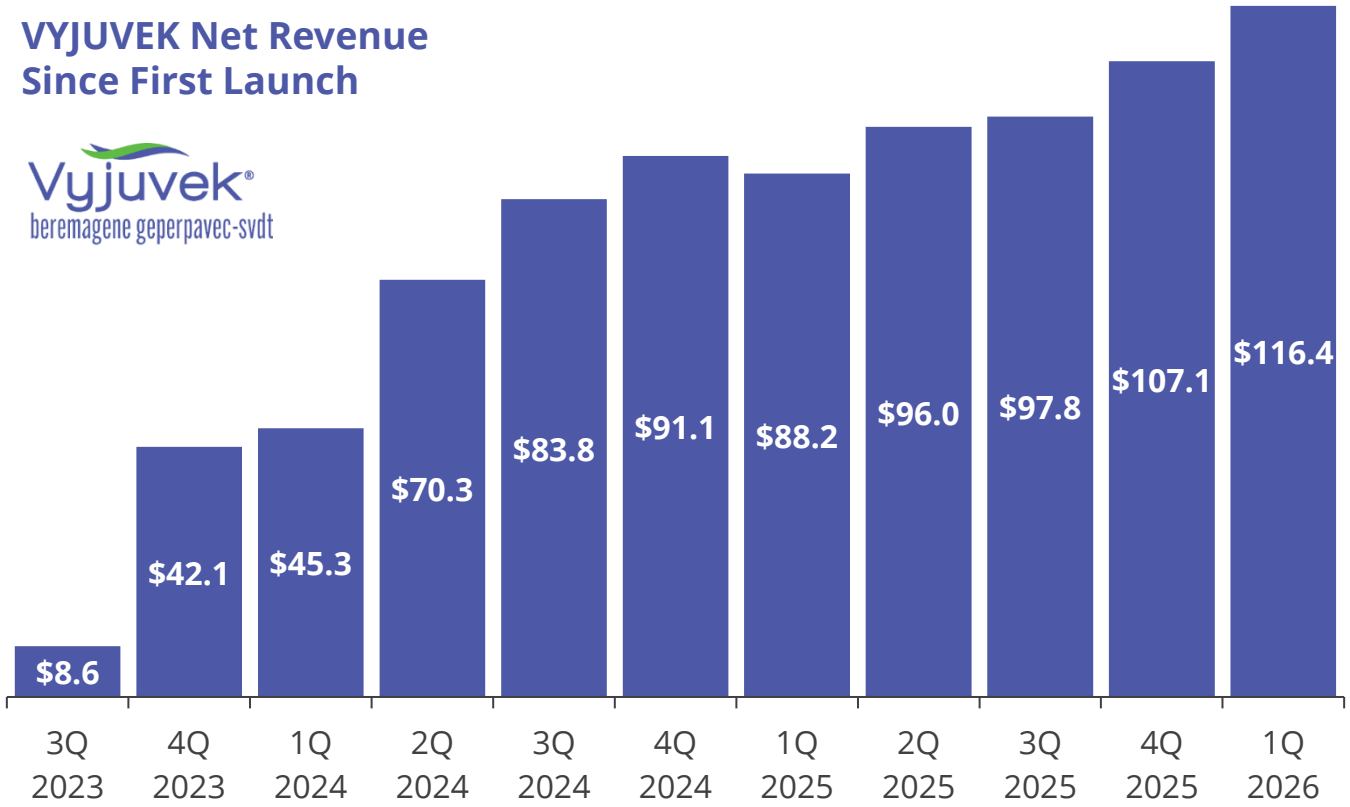
VYJUVEK® is a registered trademark of Krystal Biotech, Inc. TRIKAFTA® is a registered trademark of Vertex Pharmaceuticals Incorporated. OXERVATE® is a registered trademark of Dompé farmaceutici S.p.A.

Building a Global Leader in Redosable Genetic Medicines

Over $846M

VYJUVEK Net Revenue Since First Launch

Vyjuvek® beremagene geperpavec-svdt



Net Revenue ($M)

175K+ sq ft

Combined size of Krystal's two U.S. cGMP manufacturing facilities

ANCORIS: 20K+ sq ft

ASTRA: 150K+ sq ft

$1.017B

Cash and investments as of 1Q 2026

11

Consecutive quarters of positive EPS

cGMP, current good manufacturing practices; EPS, earnings per share; U.S., United States

VYJUVEK® for Dystrophic Epidermolysis Bullosa

Dystrophic Epidermolysis Bullosa

An ultra-rare genetic disease characterized by fragile skin, recurring and chronic wounds and serious complications

Monogenic Disease Caused by Mutations in *COL7A1* Gene

Mutations lead to absent or dysfunctional COL7 protein, without which the epidermis does not anchor to the dermis[1-3]

Heavy, Lifelong Burden on Patients and Caregivers

Recurring and chronic wounds are hallmarks of DEB causing significant pain, scarring, deformity, loss of function, limited mobility, and other complications with the oral cavity, eye, and gastrointestinal tract[1,4,5]

Costly and Time-Consuming Wound Care

Chronic wound management, bandages, pain and infection control, as well as surgical interventions lead to estimated **annual care costs of $200K-$400K**[6,7]

Increased Risk for Serious Complications and Cancers

DEB patients are at significantly higher risk of developing aggressive forms of squamous cell carcinoma[8-10]

Before VYJUVEK There Were No Treatments for Underlying Genetic Cause of DEB

1. Fine J-D, et al. *J Am Acad Dermatol*. 2014;70(6):1103-1126; 2. Fine J-D. *JAMA Dermatol*. 2016;152(11):1231-1238; 3. Bardhan A, et al. *Nat Rev Dis Primers*. 2020 Sep 24;6(1):78; 4. Has C, et al. *Br J Dermatol*. 2020;183(4):614-627; 5. Bardhan A, et al. *Nat Rev Dis Primers*. 2020;6(1):78; 6. Rashidghamat E., Mellerio J.E., Management of chronic wounds in patients with dystrophic epidermolysis bullosa: challenges and solutions, Chronic Wound Care Management and Research Volume 2017:4, 45-54; 7. GENEGRAFT Report Summary. (2015, February 16). Retrieved December 13, 2016, from http://cordis.europa.eu/result/rcn/156078_en.html 8. Condorelli A, et al. *Int J Mol Sci.* 2019;20(22):5707; 9. Montaudié H, et al. *Orphanet J Rare Dis*. 2016;11(1):117; 10. Fine J-D, Mellerio JE. *J Am Acad Dermatol*. 2009;61:367-384; 11. Krystal Biotech. Data on file

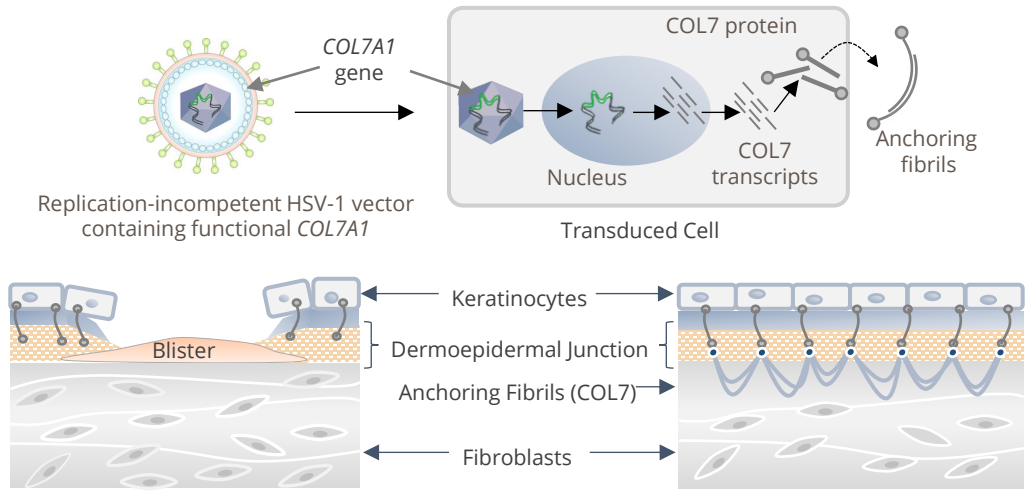
COL7, type VII collagen; COL7A1, collagen type VII alpha 1 chain; DEB, dystrophic epidermolysis bullosa

VYJUVEK is the First Corrective Therapy for DEB

Topically applied, VYJUVEK, is a gel designed to induce local COL7 expression and replace defective or missing gene

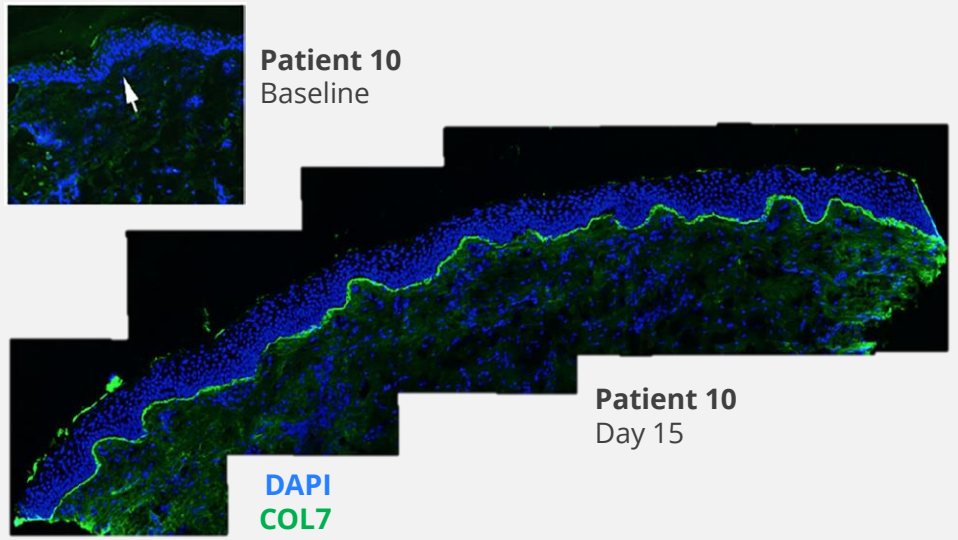
VYJUVEK Mechanism of Action

- When applied topically to the wound, VYJUVEK transduces local keratinocytes and fibroblasts and delivers *COL7A1* to the nucleus
- The *COL7A1* payload then persists episomally, enabling the transduced cell to produce and secrete functional COL7 protein without host genomic disruption
- Secreted COL7 assembles into anchoring fibrils, holding skin together



Clinical Evidence of Molecular Correction in Phase 1/2

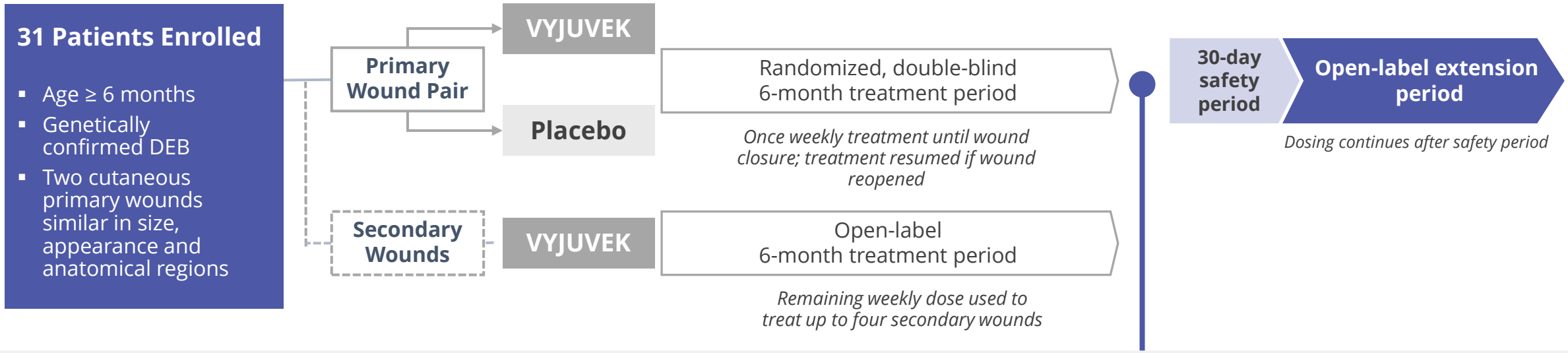
- Representative data from patient in Phase 1/2 study assessing COL7 deposition in the skin by immunofluorescence
- Strong, properly localized COL7 signal detected in treated skin
- Anchoring fibril formation also detected by electron microscopy



Marinkovich MP, et al. Oral presentation at 2022 American Academy of Dermatology (AAD) Annual Meeting; Guide SV, et al. *N Engl J Med.* 2022;387(24):2211-9; Gurevich I et al. *Nat Med* 2022; 28:780-788

COL7, type VII collagen; COL7A1, collagen type VII alpha 1 chain; DEB, dystrophic epidermolysis bullosa

GEM-3 Pivotal Study Evaluated Weekly Dose of VYJUVEK or Placebo in DEB



Demographics

- 31 patients, each with one primary wound pair were enrolled and included in the ITT analysis
- Enrolled patients ranged from 1 year old to 44 years old at baseline; 61% of the patients enrolled were pediatric (≤18 years old)

Study conducted across 3 sites

Primary Efficacy Endpoints

- Complete wound healing† at Week 22 and Week 24; or at Week 24 and Week 26 (6-months)

Secondary Efficacy Endpoints

- Complete wound healing† at Week 8 and Week 10, or at Week 10 and Week 12 (3-months)
- Mean change in pain severity (VAS or FLACC-R Scale) associated with wound dressing changes

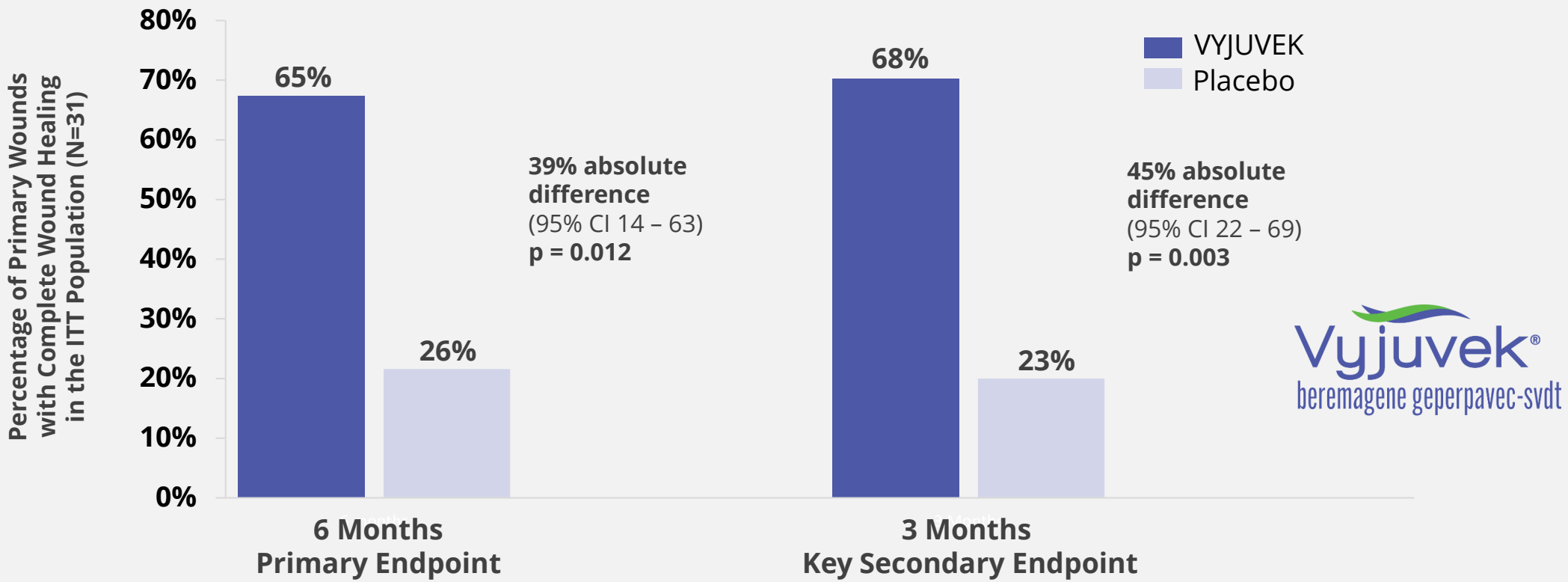
Guide SV, et al. *N Engl J Med.* 2022; 387(24):2211-9

DEB, dystrophic epidermolysis bullosa; FLACC-R Scale, Face, Legs, Activity, Cry and Consolability Revised scale; ITT, intent-to-treat; VAS, Visual Analogue Scale

†Complete wound healing defined as 100% wound closure from the exact wound area at baseline, specified as skin re-epithelialization without drainage

Significantly Higher Proportion of Wounds Closed with VYJUVEK

VYJUVEK impact on closure rates similar at both primary endpoint of 6 months and secondary endpoint of 3 months



Krystal Biotech. Data on file

Data shown on this slide is based on the data handling methodologies requested by FDA during labeling negotiations, with missing data for 1 subject replaced with remote assessments captured during COVID-19 pandemic and worst-case scenario* applied for other 2 subjects with missing data. In the *New England Journal of Medicine* (Guide SV, et al. *N Engl J Med.* 2022; 387(24):2211-9), missing data for 3 subjects was handled with multiple imputation method as prespecified in Statistical Analysis Plan for Phase 3. *Worst-case scenario assumes that the placebo-treated wound achieved complete wound closure whereas the VYJUVEK-treated wound did not.

CI, confidence interval; FDA, U.S. Food and Drug Administration; ITT, intent-to-treat

VYJUVEK Well Tolerated and Demonstrated Strong Safety Profile

Adverse Events	Total Patients (n=31)
Total number of adverse events (AEs)	45
Patients with ≥ 1 AE, n (%)	18 (58.1)
Serious AEs	3 (9.7)
Severe AEs	2 (6.5)
Drug-related AEs	1 (3.2)
AE leading to treatment discontinuation	0 (0)
Death	0 (0)

- Majority of AEs were mild or moderate; no AEs led to treatment discontinuation or death
- The most common side effects (>5%) were itching, redness, rash, cough, and runny nose
- One AE, mild erythema, was considered possibly related to study drug as assessed by the investigator
- Three patients experienced a total of five SAEs during the study: cellulitis, anemia (two events), diarrhea, and positive blood culture
  - ✓ None were considered related to study drug
- No clinically significant immunologic reactions were reported during the study
- Treatment response to VYJUVEK was not associated with HSV-1 serostatus at baseline or with COL7 seroconversion

Guide SV, et al. *N Engl J Med.* 2022;387(24):2211-9

AE(s), adverse event(s); COL7, type VII collagen; HSV-1; herpes simplex virus type 1; SAEs, serious adverse events

Strong VYJUVEK Launch in the United States Continues

Vyjuvek®
beremagene geperpavec-svdt

✓ **First DEB treatment approved by FDA in 2023, label expanded in 2025**

- Now indicated for the treatment of wounds in DEB patients of all ages
- Approved for recessive and dominant DEB with no restrictions on use by wound type

✓ **High demand and strong nationwide access underpin long-term growth outlook**

- **Over 695** patients have received reimbursement approvals for VYJUVEK in the U.S.
- Strong prescribing trends reflect high underlying demand
- Broad coverage and positive access policies for DEB patients of all ages and genetic subtypes

✓ **Dosing flexibility highly valued by patients and improved with updated label**

- Now approved for application by patient, caregiver, or HCP, either in clinic or at home
- Updated label also provides for greater flexibility with wound dressing changes
- Patients value convenience with vast majority already receiving VJYUVEK at home

Building on VYJUVEK's leadership position as the most flexible and convenient corrective therapy for DEB

DEB, dystrophic epidermolysis bullosa; FDA, United States Food and Drug Administration; HCP(s), healthcare professionals; U.S., United States

Global VYJUVEK Expansion Underway

Vyjuvek®
beremagene geperpavec-svdt

2023

First launch in the United States

2H 2025

Approval and launch in France, Germany, and Japan

Over 1.2K
Identified DEB Patients in the United States*

*Estimated Total U.S. DEB Population of 3K

Over 1.3K
Identified DEB Patients Across All Three Markets

+ expanding specialty distributor network

DEB, dystrophic epidermolysis bullosa; U.S., United States

VYJUVEK is Changing the Treatment Paradigm in DEB

Follow-On Opportunity to Address DEB Ocular Complications

A cause of progressive vision loss with no specific therapy available

Ocular Complications of Dystrophic Epidermolysis Bullosa (DEB)[1-3]

- A significant proportion of DEB patients suffer from ocular complications related to local COL7 deficiency in the eye
- Corneal abrasion, scarring, and pannus are among the most commonly cited issues, as well as eyelid ectropion, blisters
- Can lead to progressive vision loss and even blindness

No Specific FDA-Approved Therapy[1-3]

- There is no corrective therapy available to treat ocular complications of DEB
- Standard of care includes recurring surgical intervention to separate eyelid from the eye and clear occlusions from cornea; burdensome and no assurance of durable benefit

Over 50%

Proportion of RDEB patients with ocular complications[1,2]

750

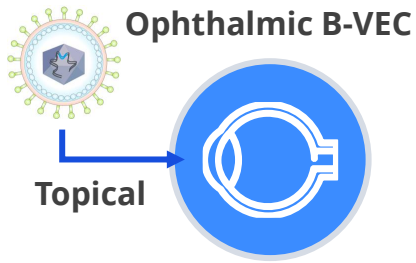
Estimated Patients in U.S.*

2K+

Estimated Patients WW*†

* Assuming 50% of DEB patients have RDEB of which at least 50% have ocular complications[1-4]

† Reimbursable markets only



KB803, a new ophthalmic formulation of B-VEC, is in development to restore local *COL7A1* expression and eye function in DEB patients

1. Tang JY, et al. *Orphanet J Rare Dis.* 2021;16(1):175; 2. Tong L, et al. *Br J Ophthalmol.* 1999; 83(3):323-326; 3. Chen VM, et al. *Ocul Surf.* 2020; 18(4):912-919; 4. Krystal Biotech. Data on File

B-VEC, beremagene geperpavec; COL7, type VII collagen; COL7A1, collagen type VII alpha 1 chain; DEB, dystrophic epidermolysis bullosa; FDA, United States Food and Drug Administration; RDEB, recessive dystrophic epidermolysis bullosa; U.S., United States; WW, worldwide

Significant Improvement in Eye of DEB Patient Treated with B-VEC

Well-tolerated and associated with full corneal healing and visual acuity improvement to 20/25

Compassionate Use of Ophthalmic B-VEC in Eye of DEB Patient

- 13-year-old male with DEB and bilateral cicatrizing conjunctivitis
- History of repeated symblepharon lysis surgeries with posterior recurrence, and bilateral limbal stem cell deficiency
- Surgical symblepharon lysis of right eye was performed followed with regular topical applications of B-VEC (5×10^9 PFU/mL)
- Regular applications eventually declining to weekly frequency were performed until corneal epithelium was healed, followed by monthly topical applications

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

Ophthalmic B-VEC well-tolerated and associated with corneal healing, epithelization, and continuing visual acuity improvement

Now evaluating KB803 in registrational study for the treatment and prevention of corneal abrasions in DEB patients

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; HM, hand motion; PFU, plaque forming unit

Top-Line Data from Registrational KB803 Study IOLITE Expected This Year

Intra-patient, double-masked, decentralized, placebo-controlled study in DEB patients with history of corneal abrasions

Objectives

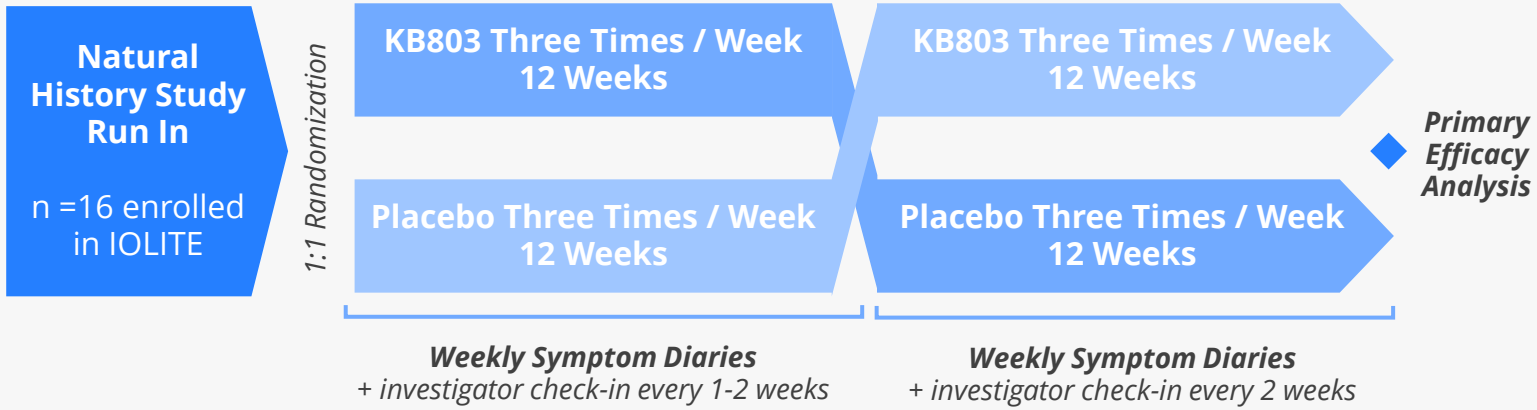
Evaluate safety and efficacy of three doses weekly of KB803 for the treatment and prevention of corneal abrasions in DEB patients

Primary Efficacy Assessment

Change from baseline in average number of days per month with corneal abrasion symptoms

Study Population

Patients 6 months of age or older with genetically confirmed diagnosis of DEB and corneal abrasion symptoms in natural history study 12 week run-in period



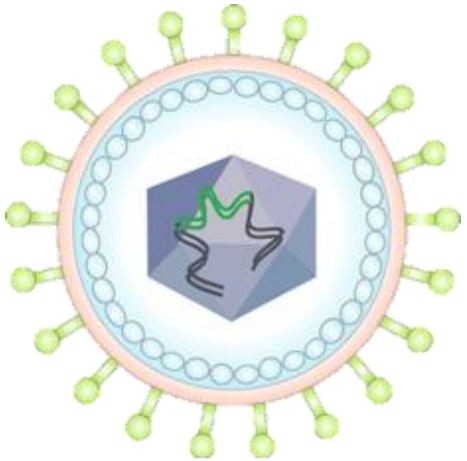
Fully enrolled IOLITE in April 2026 and top-line data expected in 4Q 2026

Krystal Biotech, Data on File.

DEB, dystrophic epidermolysis bullosa

Platform and Pipeline

Krystal's Redosable HSV-1 Platform



Krystal's engineered, replication-incompetent HSV-1 vectors

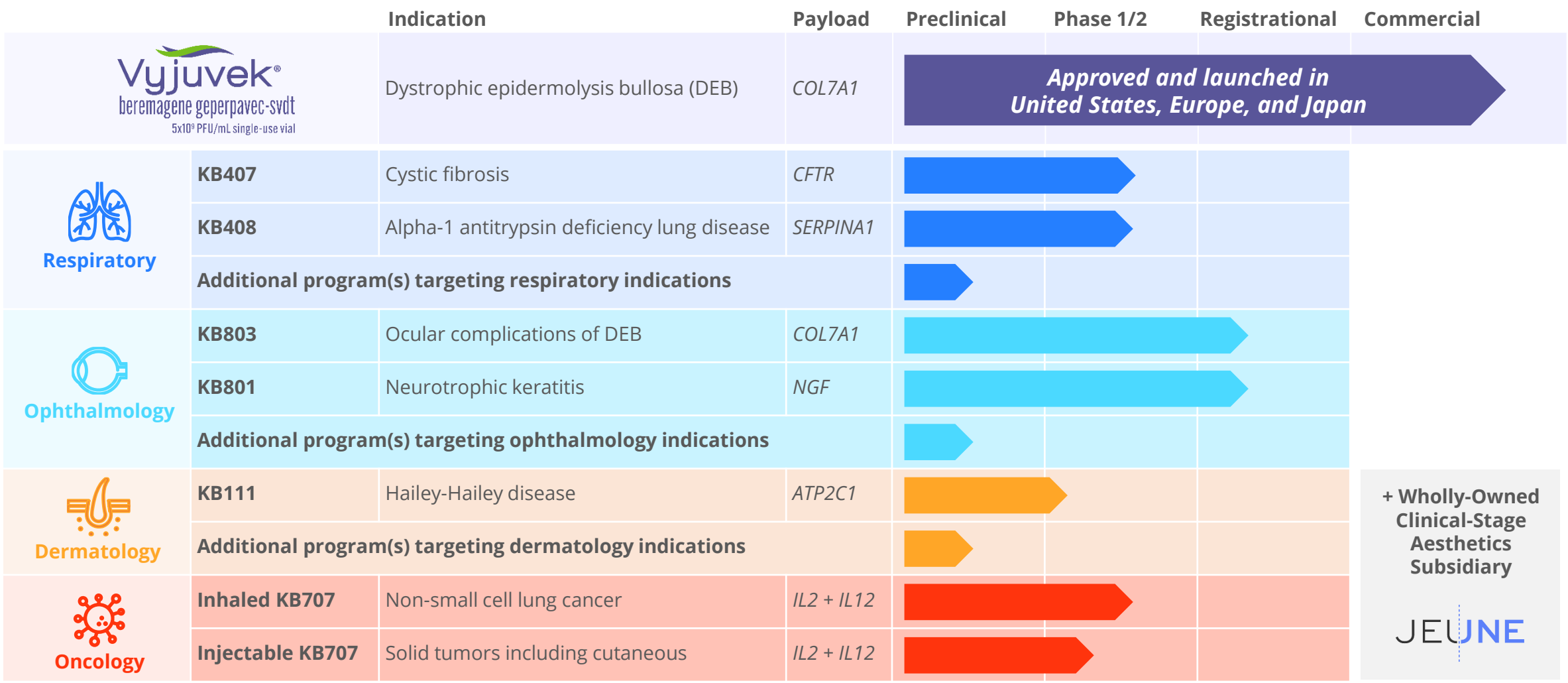
Optimally suited for non-invasive gene delivery to high turnover tissues including the lung, skin, and eye

- ✓ Large cargo capacity
- ✓ Broad cellular tropism
- ✓ Flexible administration options
- ✓ Redosable
- ✓ Low immunogenicity and no integration risk
- ✓ Scalable manufacturing

Three Krystal pipeline programs now benefiting from platform technology designation granted by the FDA

FDA, U.S. Food and Drug Administration; HSV-1, herpes simplex virus 1

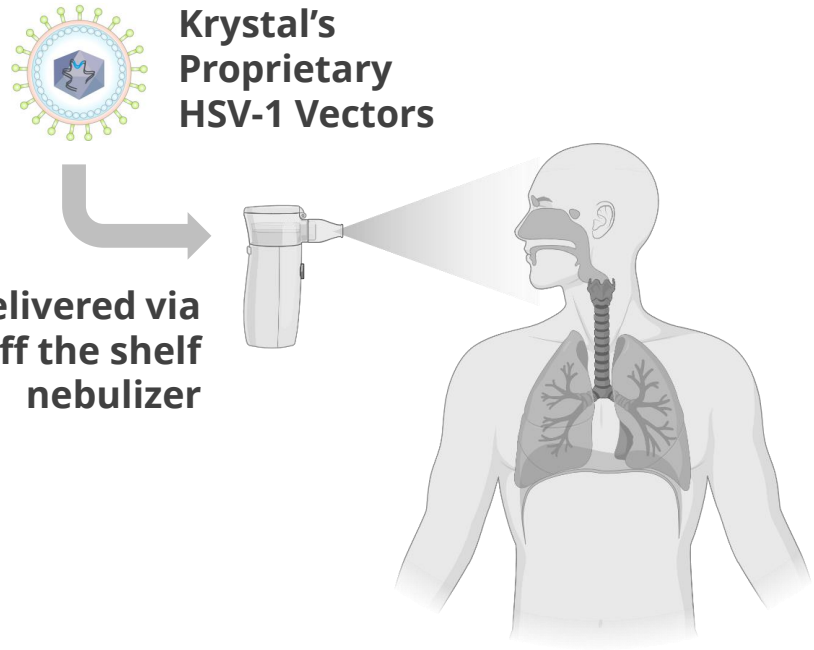
Deep Pipeline of Genetic Medicines Built on Krystal's HSV-1 Platform



ATP2C1, ATPase secretory pathway Ca2+ transporting 1; CFTR, cystic fibrosis transmembrane conductance regulator; COL7A1, collagen type VII alpha 1 chain; DEB, dystrophic epidermolysis bullosa; HSV-1, herpes simplex virus 1; IL-12, interleukin-12; IL-2, interleukin-2; NGF, nerve growth factor; SERPINA1, serpin family A member 1

Respiratory Pipeline

Krystal's Redosable HSV-1 Platform for Lung Gene Delivery



Lead Rare Respiratory Disease Programs

KB407
For Cystic Fibrosis

KB408
For AATD Lung Disease

Historical Challenges with Inhaled Gene Therapy

- Inhaled gene therapy has been explored for decades, with little success
- Focus to date has been on adenovirus, AAV, and non-viral approaches
- Multiple challenges including cargo limitations, low efficiency of gene transfer, toxicity, product instability, and burdensome delivery

HSV-1 Platform Has Potential to Overcome Historical Challenges

- Clinically validated vector; tolerated and redosable in Phase 3 for DEB
- Large cargo capacity to load in full genes, including *CFTR* for cystic fibrosis
- Ability to redose and/or adjust dose over time as lung cells turnover
- Broad cellular tropism and efficient transduction of airway epithelium
- Short expected nebulization time using off-the-shelf nebulizer

Lung delivery via inhalation now demonstrated for both KB407 and KB408 as well as lung cancer program KB707

Vu A, et al. *Human Gene Therapy* 2020;31(17-18):921-939

AAV, adeno-associated virus; CFTR, cystic fibrosis transmembrane conductance regulator; DEB, dystrophic epidermolysis bullosa; HSV-1, herpes simplex virus 1

Urgent Unmet Need Remains for Many Patients with Cystic Fibrosis

Over 100K

CF Patients Worldwide

10K

Modulator Ineligible CF Patients

20K

CF Patients with Suboptimal Modulator Responses

- Cystic fibrosis (CF) is progressive lung disease caused by mutations in the *CFTR* gene and loss of CFTR-mediated ion transport
- Life-span limiting disease characterized by airway obstruction and inflammation, cough, shortness of breath, and infection
- CFTR modulators, first approved in 2012 and now used in combination, are emerging as standard of care for eligible patients
- Unfortunately, many patients either have mutations that are not amenable to modulator therapy or are otherwise underserved by currently available modulators

New corrective therapies are urgently needed

U.S. Cystic Fibrosis Foundation – About Cystic Fibrosis, accessible at: About Cystic Fibrosis | Cystic Fibrosis Foundation (cff.org); U.S. Cystic Fibrosis Foundation – 2022 CFF Patient Registry Highlights; O'Sullivan BP, et al. *Lancet* 2009;373:1891-904; Elborn JS, et al. *Lancet* 2016; 388:2519-31; Sanders DB, et al. *Pediatr Clin North Am.* 2016;63:567-84; Stoltz DA, et al. *N Engl J Med*. 2015, 372 (4): 351-362; Hapnadak SG, et al. *J Cyst Fibros.* 2020;19(3):344-354;

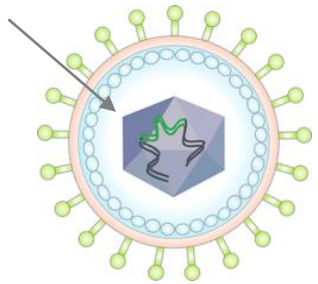
Modulator ineligible CF patients estimated based on CFF Patient Registry 2019, ECFS Patient Registry 2018; CF patients with suboptimal modulator responses estimated based on Middleton PG, et al. *N Engl J Med*. 2009;381:1809-1819; Heijerman HG, et al. *Lancet* 2019;394:1940-1948; Trikafta® FDA Label, Revised 10/2021

CF, cystic fibrosis; CFTR, cystic fibrosis transmembrane conductance regulator

Inhaled Candidate KB407 Designed to Fill Cystic Fibrosis Treatment Gap

KB407

2 x *CFTR* genes



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

Preclinical Summary

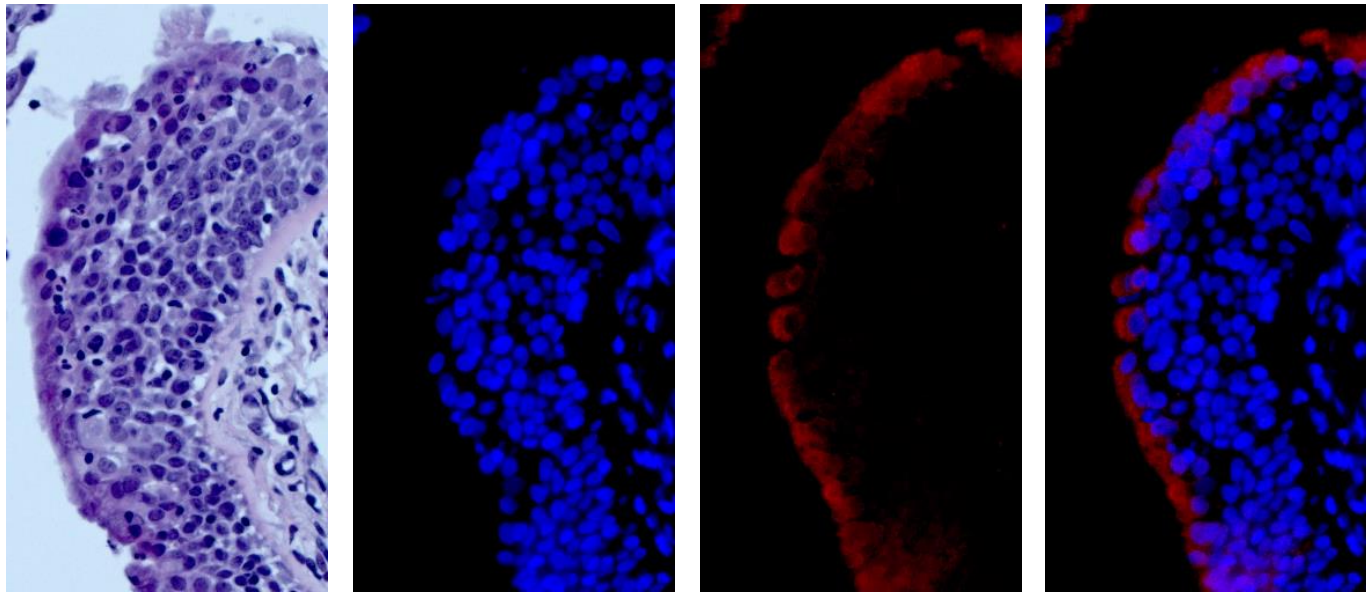
- ✓ **Cellular Tropism:** KB407 efficiently transduces human primary airway epithelial cells leading to dose dependent CFTR expression
- ✓ **Full-Length Payload:** CFTR protein expressed in KB407 transduced cells is full-length, properly localized, and glycosylated
- ✓ **Functionality:** Encoded CFTR has shown functionality in both *in vitro* CF patient model and *in vivo* rodent model
- ✓ **Tolerability:** KB407 well tolerated in multiple preclinical studies including in GLP IND-enabling repeat dose toxicology study in NHPs
- ✓ **Broad and Sustained *In Vivo* Expression:** KB407 well disseminated throughout NHP lungs via inhalation and human *CFTR* detected at least 28 days after last dose

KB407 clinical program first sanctioned by CFF in 2025

CF, cystic fibrosis; CFF, Cystic Fibrosis Foundation; CFTR, cystic fibrosis transmembrane conductance regulator; GLP, good laboratory practices; HSV-1, herpes simplex virus 1; IND, investigational new drug; NHP, non-human primate

Confirmed CFTR Delivery and Expression with KB407 in Phase 1 CF Study

Representative Image



H&E | DAPI | CFTR | Merge

29% to 42%

Conducting Airway Cells Transduced with KB407 (n = 6 CF patients)

✓ **Broad airway distribution**

All usable biopsies (n =31) were positive for CFTR and/or viral marker of KB407 transduction

✓ **Exceeded transduction target**

Over 29% of conducting airway cells transduced in all six patients, including four patients which were modulator-ineligible with baseline $ppFEV_1$ < 70%

✓ **Apical CFTR expression pattern**

Suggestive of appropriate post-translational modification and CFTR localization

✓ **CFTR protein expression for at least 96 hours**

Positive indicator for potential weekly or better dosing

Krystal Biotech, Data on File.

CF, cystic fibrosis, CFTR, cystic fibrosis transmembrane conductance regulator; $ppFEV_1$, percent predicted forced expiratory volume in 1 second

Next Steps and Accelerating The Path to Potential Registration of KB407

- Working with CFF, TDNCC, and FDA on innovative registrational study design leveraging natural history datasets prospectively collected by CFF and TDNCC
- Also initiating an open label, single-arm study to evaluate safety of repeat dose KB407 for 24 weeks in five patients with CF
  - Patients must be ineligible for, not tolerate, or not benefit from modulator therapy to enroll in the study
  - KB407 to be administered 4x in first week and once weekly thereafter at the same dose where CFTR expression was confirmed by bronchoscopy
- First patient to be dosed in May 2026 and data expected before year end
- Expecting to align with FDA on registrational study design in 2H 2026

✓ **Platform technology designation**

Granted by FDA for KB407 program in 2Q 2026

Expect repeat dose data later this year followed by registrational study start in 2027

CF, cystic fibrosis; CFF, Cystic Fibrosis Foundation; CFTR, cystic fibrosis transmembrane conductance regulator; FDA, United States Food and Drug Administration; TDNCC, CF Therapeutics Development Network Coordinating Center at Seattle Children's Research Institute

Alpha-1 Antitrypsin Deficiency (AATD)

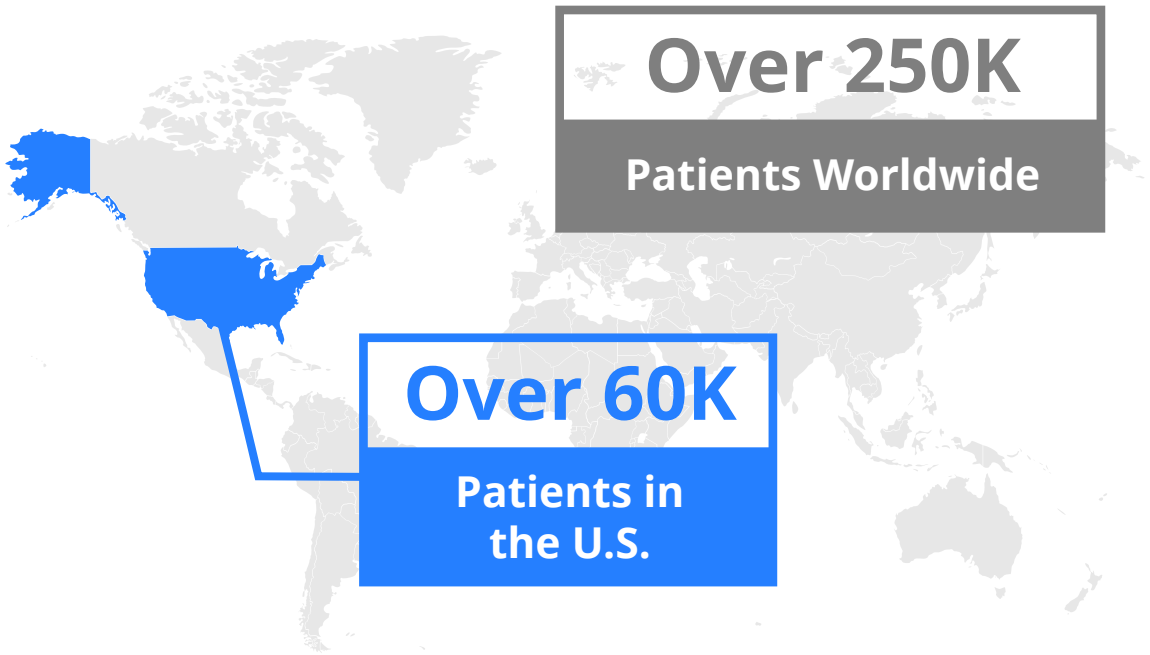
Monogenic disorder that leads to progressive lung disease

- Alpha-1 antitrypsin (AAT) is a key regulator of protease activity, in particular neutrophil elastase in lungs[1]
- AATD is an autosomal co-dominant inherited genetic disorder resulting from mutations in *SERPINA1* gene encoding AAT, misfolding mutations Pi*ZZ and Pi*SZ are the most common
- Genetic deficiency of AAT can result in unopposed neutrophil elastase activity and progressive pulmonary impairment

Unproven and Limited Treatment Options[1,2]

- There is no cure available for patients with AATD
- Standard of care is weekly IV infusions of AAT but treatment is burdensome on patients and clinical benefit not well defined

Severe AATD Prevalence[3-5]*



1. Greene CM, et al. *Nat Rev Dis Primers* 2016;2:16051; 2. Brantly ML, et al. *Int J Chron Obstruct Pulmon Dis.* 2019;6:100–114; 3. Aboussouan LS, et al. *Respir Med.* 2009;103:335-341; 4. Stoller JK, et al. *Int J Chron Obstruct Pulmon Dis.* 2013;10:26-24; 5. Blanco I, et al. *Int J Chron Obstruct Pulmon Dis.* 2017;12:561-569;

*Severe AATD defined as patients with Pi*ZZ genotype

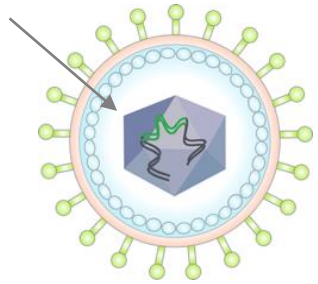
AAT, alpha-1 antitrypsin; AATD, alpha-1 antitrypsin deficiency; IV, intravenous; SERPINA1, serpin family A member 1; U.S., United States

Inhaled Candidate KB408 for AATD Lung Disease

Genetic medicine designed to achieve sustained, local AAT expression is supported by robust preclinical data package

KB408

2 x *SERPINA1* genes



Replication-incompetent HSV-1 vector containing functional human *SERPINA1*

Preclinical Summary

- ✓ Transduces human airway cells *in vitro* leading to dose-dependent expression and secretion of functional AAT
- ✓ AAT secreted from KB408 transduced cells is functional as demonstrated by binding to target neutrophil elastase
- ✓ Airway administration to wild-type or *SERPINA1* deficient mice yielded robust AAT expression detected by multiple independent assessments
- ✓ Vector platform shown to be amenable to nebulization with broad airway transduction and tolerability in non-human primates ***– KB407 data***
- ✓ Repeat KB408 dosing well-tolerated in murine GLP IND-enabling toxicology study with only mild findings and NOAEL of top dose

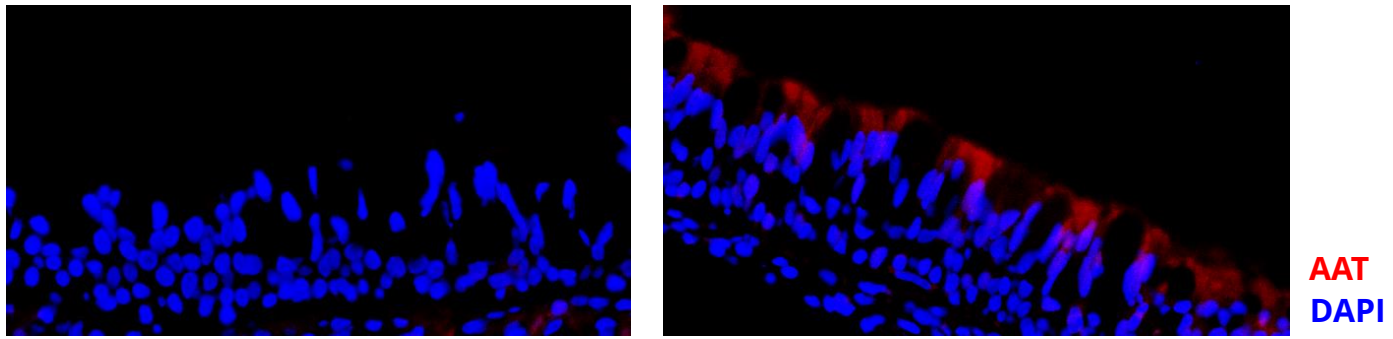
Data package strongly supportive of KB408 progression to the clinic

AAT, alpha-1 antitrypsin; AATD, alpha-1 antitrypsin deficiency; GLP, good laboratory practices; HSV-1, herpes simplex virus 1; IND, investigational new drug; NOAEL, no observed adverse effect level; SERPINA1, serpin family A member 1

Confirmed AAT Delivery and Functionality with KB408 in Phase 1 AATD Study

Single dose KB408 well tolerated in all AATD eight patients dosed with payload expression confirmed in all three patients with bronchoscopy data

Representative Patient 07 Images



Baseline

After KB408

Functionality of KB408-encoded AAT confirmed based on reduction in % free neutrophil elastase in lung ELF

Patient 07	Patient 08*
97.2% At Baseline	79.3% At Baseline
40.2% After Single KB408 Dose	52.1% After Single KB408 Dose

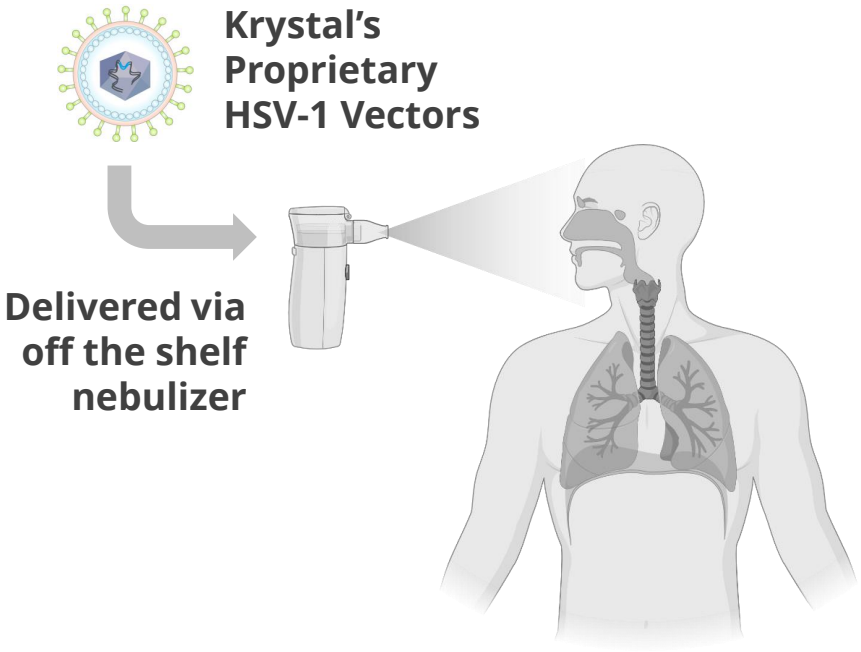
Now enrolling in repeat dose cohort with interim data expected later this year

* On background augmentation; **Based on quantification of DAPI positive and DAPI + AAT co-positive cells lining the conducting airways of the lung by immunofluorescence; 3-4 biopsies assessed for post-dose DAPI + AAT co-positive cell quantification, total cell counts > 300 per patient, all imaging conducted at 40x magnification, post-dose biopsies harvested 24-48 hours after nebulization

AAT, alpha-1 antitrypsin; DAPI, 4',6-diamidino-2-phenylindole; ELF, epithelial lining fluid; SERPINA1, serpin family A member 1

All imaging conducted at 40× magnification
Post-dose biopsies harvested 24-48 hours after nebulization

Working Towards a Highly Differentiated Respiratory Franchise



Lead Rare Respiratory Disease Programs

KB407
For Cystic Fibrosis

KB408
For AATD Lung Disease

- Krystal's HSV-1 vectors are well-tolerated in multiple patient populations with underlying lung disease
- Successfully delivered to the lung using commercially available nebulization technology ***– off the shelf, non-invasive therapy***
- Functionality of vector-encoded cargo confirmed in AATD patients
- Redosability provides opportunity to build on efficacy over time
- Platform technology designation derisks and accelerates development

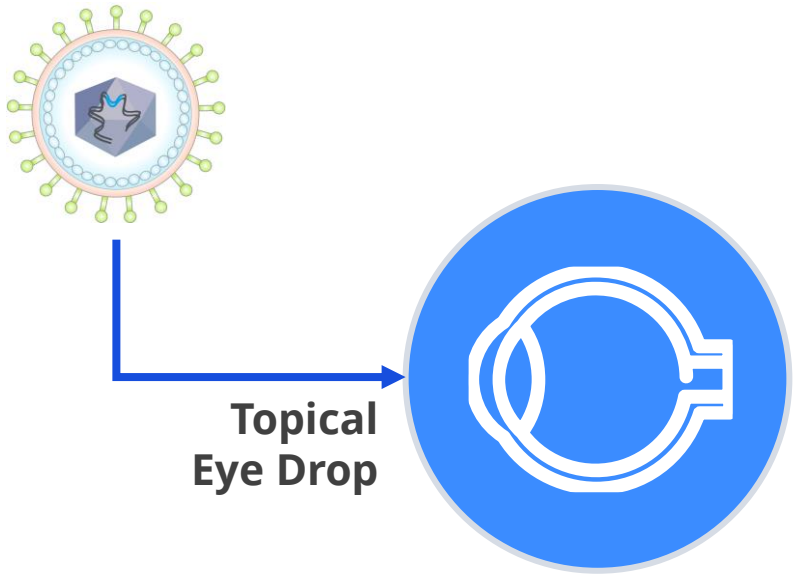
Milestones Expected Later This Year

- ❑ KB407 and KB408 repeat dosing data updates
- ❑ Alignment with FDA on KB407 registrational study design

AATD, alpha-1 antitrypsin deficiency; HSV-1, herpes simplex virus 1

Ophthalmology Pipeline

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

Krystal's ophthalmology pipeline now includes two late clinical-stage programs: KB803 for corneal abrasions in DEB and KB801 for NK

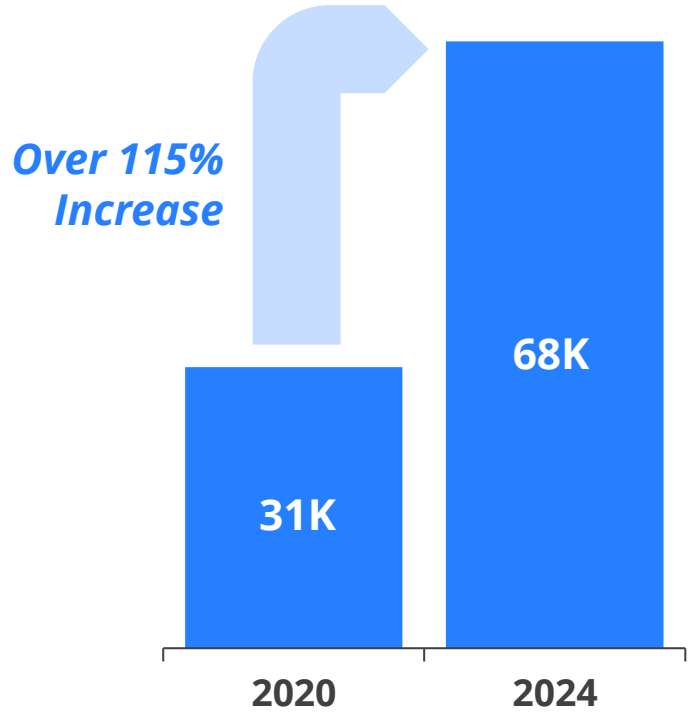
Sabater A et al., Poster # 787 - C0388. at the 2023 Association for Research in Vision and Ophthalmology Annual Meeting; Vetencourt AT, et al. *N Engl J Med*. 2024;390:530-535

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

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 U.S. in 2024

Komodo Drug Projections Assuming 14 Day Supply per Projected Rx

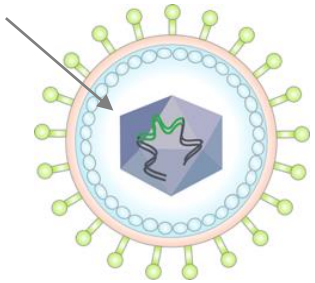
CADTH Review – Cenegermin (Oxervate). 2022. Vol 2, Issue 9; Pflugfelder SC, et al. *Ophthalmology*. 2020. 127: 14-26; Bonini S, et al. *Ophthalmology*. 2018. 125: 1332-1343; Oxervate® 2019 FDA Label; Komodo Health Drug Projections [June 2025]

FDA, United States Food and Drug Administration; NK, neurotrophic keratitis; U.S., United States

Strong Preclinical Data Package Highlights Potential Benefits of KB801

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

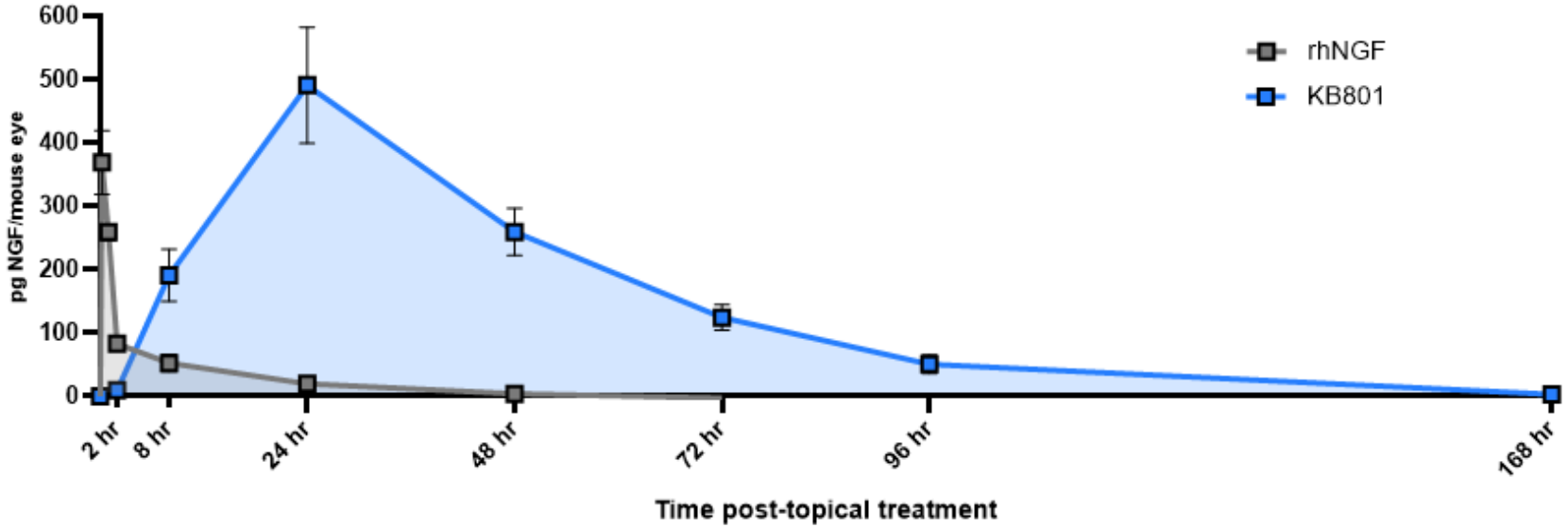
B-VEC, beremagene geperpavec; HSV-1, herpes simplex virus 1; NGF, nerve growth factor

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)

NGF Protein Levels



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

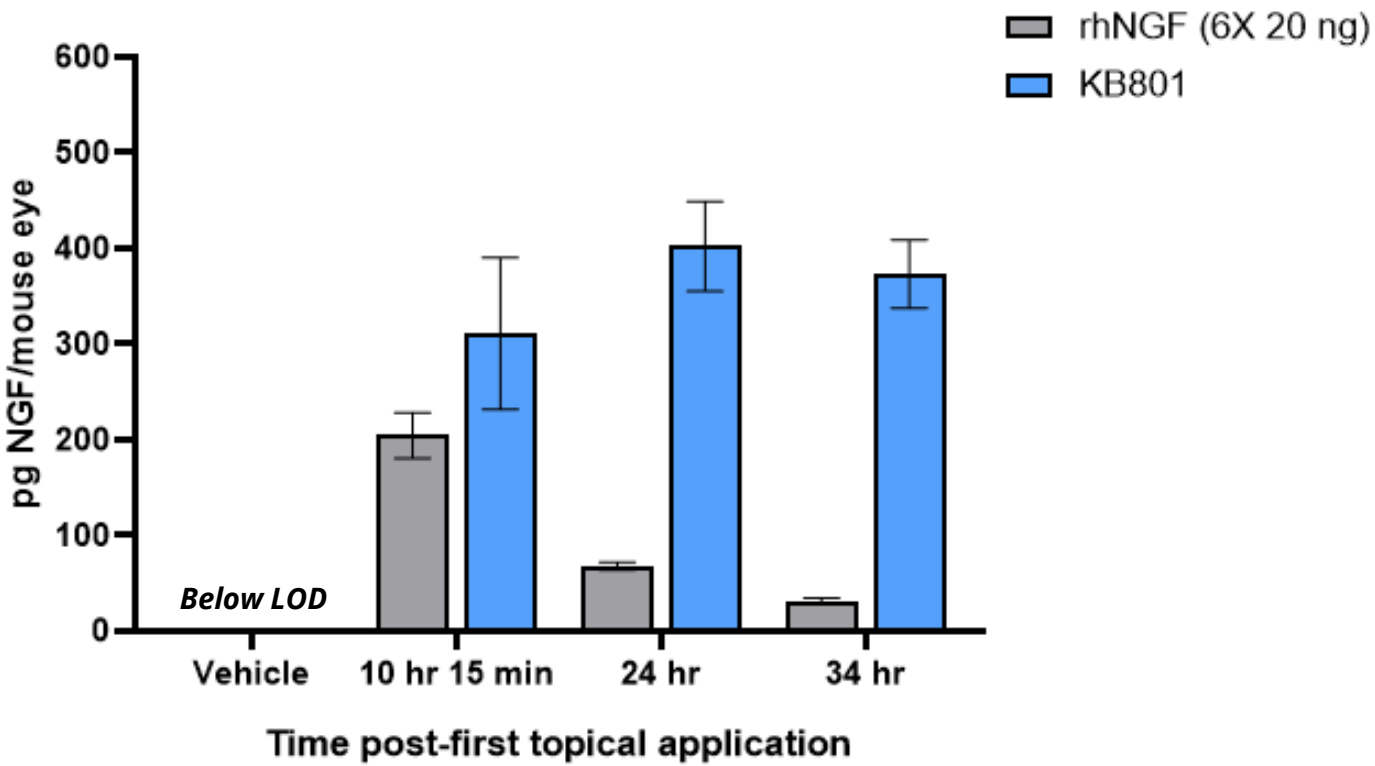
NGF; nerve growth factor; ELISA, enzyme-linked immunosorbent assay; PFU, plaque forming unit; PK, pharmacokinetics; rhNGF, recombinant human nerve growth factor

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



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

ELISA, enzyme-linked immunosorbent assay; LOD, limit of detection; NGF; nerve growth factor; PFU, plaque forming unit; PK, pharmacokinetic; rhNGF, recombinant human nerve growth factor

KB801 in Registrational Study and One of Two Registrational Readouts Expected This Year in Ophthalmology

KB801 for treatment of neurotrophic keratitis

EMERALD-1 Study Design

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

Primary Efficacy Endpoint

Complete healing of corneal epithelium **at 8 weeks**

Status

Enrolling

Top-line data expected before end of year

+

KB803 for treatment and prevention of corneal abrasions in DEB patients

IOLITE Study Design

Intra-patient, double-masked, decentralized, placebo-controlled study with crossover design in DEB patients with history of corneal abrasions

Primary Efficacy Endpoint

Change in average number of days per month with corneal abrasion symptoms, assessed after 12 weeks on KB803 and 12 weeks on placebo

Status

Fully enrolled

Top-line data expected in 4Q 2026

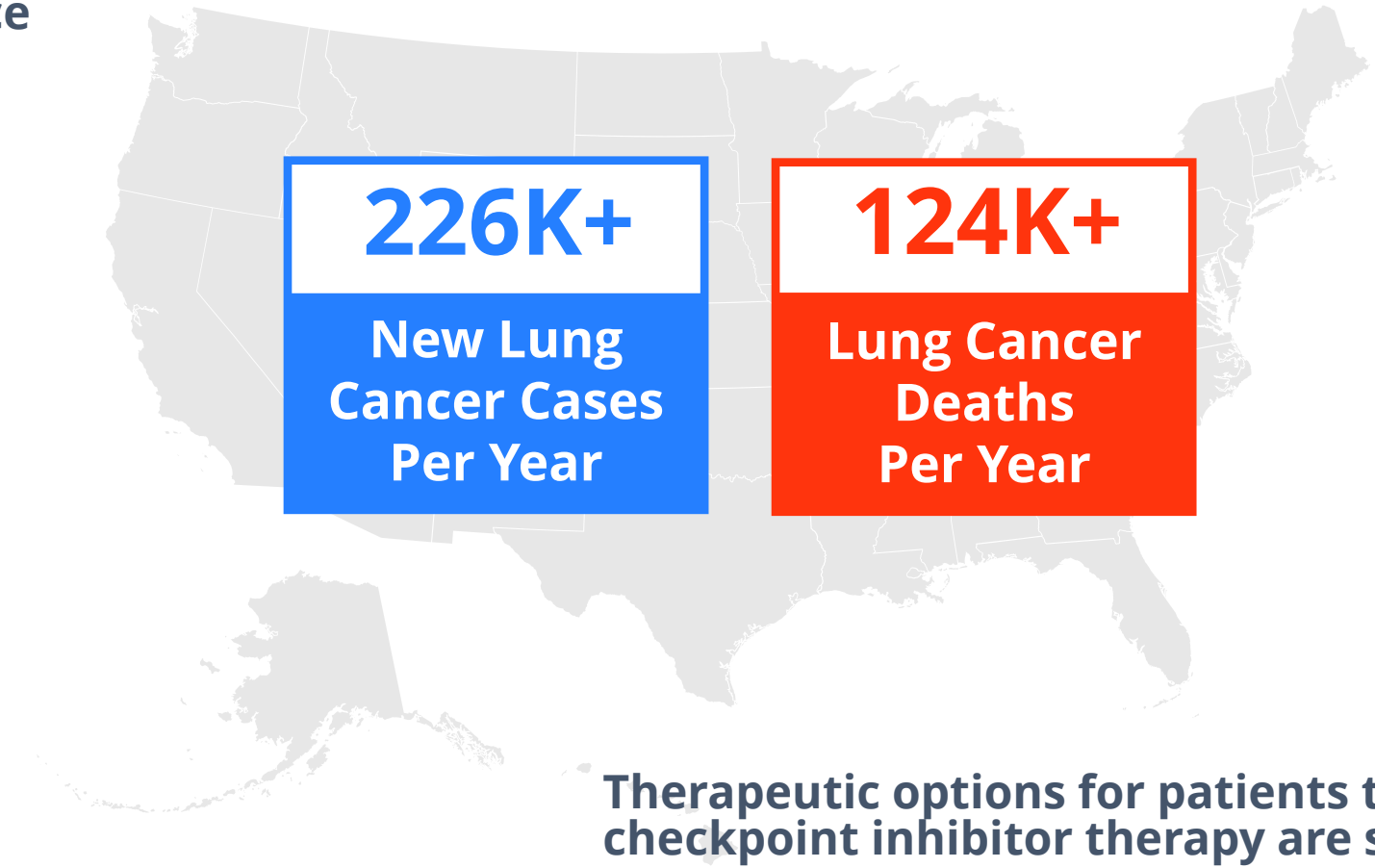
NK, neurotrophic keratitis

Oncology Pipeline

Lung Cancer Remains Deadliest Cancer in the U.S. and an Urgent Unmet Need

Lung Cancer Incidence and Mortality in U.S.

2025 SEER Estimates



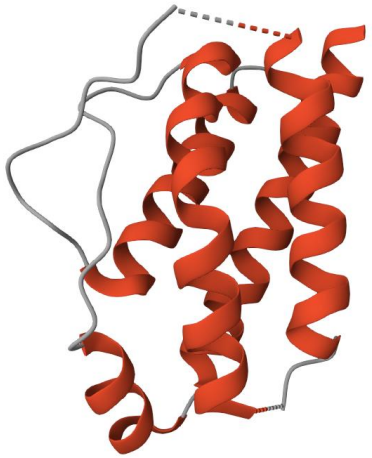
Therapeutic options for patients that have failed checkpoint inhibitor therapy are severely limited

NCI SEER. 2025: https://seer.cancer.gov/statfacts/html/common.html [accessed October 29 2025], estimates for incident cases and deaths from cancers of the lung and bronchus

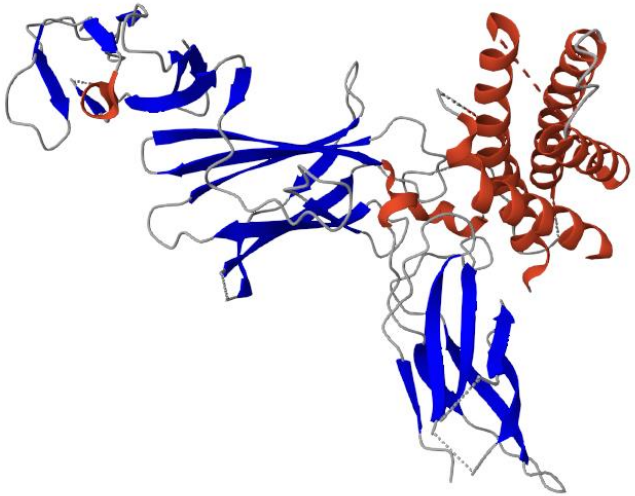
SEER; Surveillance, Epidemiology, and End Results Program; U.S., United States

Using Krystal's HSV-1 Platform to Unlock the Potential of Cytokine Therapy

IL-2



IL-12



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Expand and Activate Lymphocyte Population

Well-characterized NK and T cell activator with known roles inducing T cell proliferation and promoting NK and T cell cytotoxic functions

Reinforce Cytotoxic Effector Functions

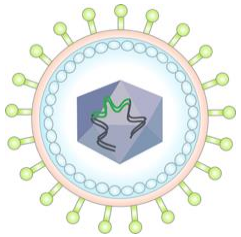
Complementary cytokine known to promote lymphocyte effector functions and IFN-gamma secretion

Cytokines with synergistic functions and therapeutic potential

IL-2 image from the RCSB PDB (RCSB.org) of PDB ID 1M47 [image generated July 20 2023]; Jiang T, et al. *Oncoimmunology*. 2016; 5(6):e1163462; Morgan DA, et al. *Science*. 1976; 193(4257):1007-1008; IL-12 image from the RCSB PDB (RCSB.org) of PDB ID 1F45 [image generated July 20 2023]; Lasek W, et al. *Cancer Immunol Immunother*. 2014; 63:419-35

HSV-1, herpes simplex virus 1; IL-12, interleukin-12; IL-2, interleukin-2; NK, natural killer

KB707 Designed to Drive Sustained, Localized Cytokine Expression



KB707

Replication-incompetent HSV-1 vector encoding functional human IL-12 and IL-2

Optimal vector platform to maximize cytokine expression and immune activation while limiting systemic toxicity

- ✓ Efficiently transduces wide variety of cell types enabling robust expression within and around the tumor
- ✓ DNA payload persists in transduced cells extending the window of cytokine expression
- ✓ Non-replicating vector avoids premature lytic cell death or host cell shutdown
- ✓ Redosability to further boost local cytokine expression
- ✓ Safety profile suitable for administration via multiple routes including inhalation

Krystal Biotech, Data on File.

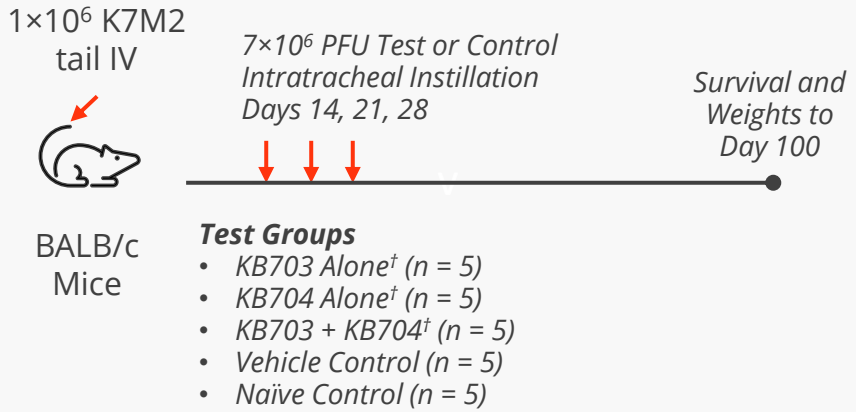
DNA, deoxyribonucleic acid; HSV-1, herpes simplex virus 1; IL-12, interleukin-12; IL-2, interleukin-2

Clear Benefit with HSV-1 Encoded IL-2 + IL-12 in Lethal Osteosarcoma Model

Metastatic K7M2 Osteosarcoma Model

- K7M2 is an osteoblast cell line derived from bone of mouse with spontaneous osteosarcoma[1]
- Considered highly aggressive with pulmonary metastatic rate of over 90% in mice[1]
- Previously shown to be non-responsive to PD-1/PD-L1 targeting therapies, partial benefit from combo therapies[2]

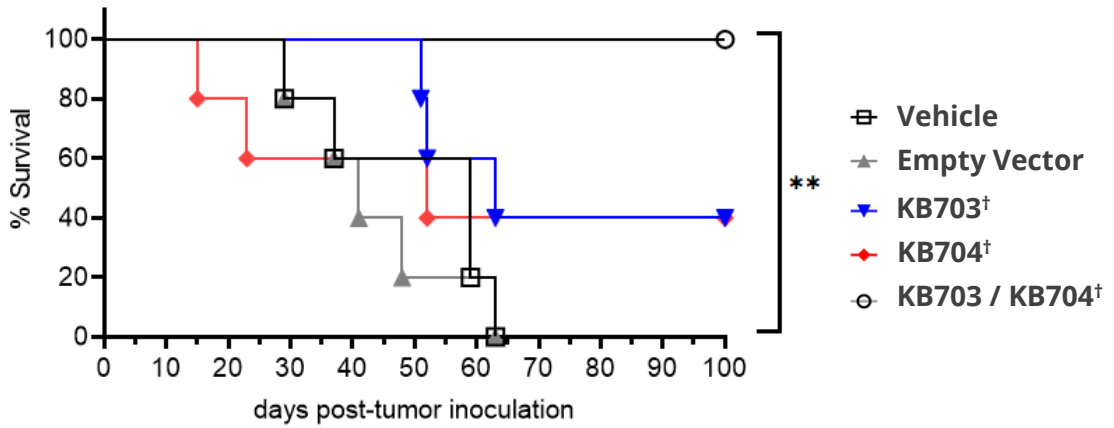
Study Design



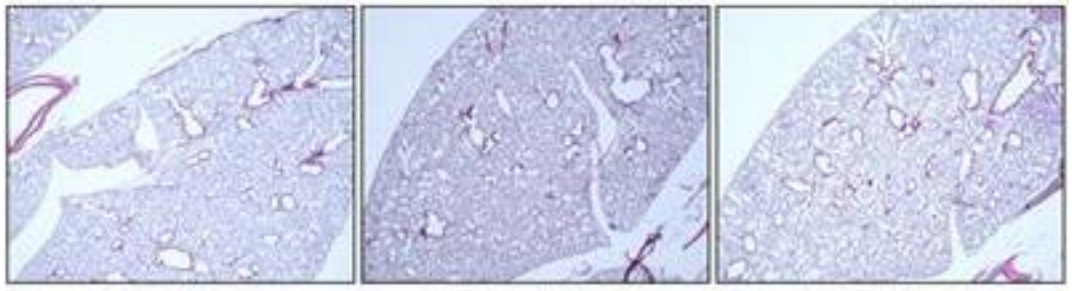
Test Groups

- *KB703 Alone† (n = 5)*
- *KB704 Alone† (n = 5)*
- *KB703 + KB704† (n = 5)*
- *Vehicle Control (n = 5)*
- *Naïve Control (n = 5)*

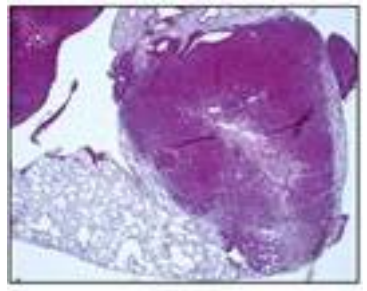
Survival



Lung H&E, Day 100



KB703 / KB704†
Representative images
from n = 3 of 5 survivors



KB703 Alone†
Representative image
from n = 1 of 2 survivors

1. Khanna C, et al., *Clin Exp Metastasis*. 2000;18(3):261-271; 2. Lussier DM et al. *J Immunother Cancer* 2015;3(21);

Krystal Biotech, Data on File; Previte DM et al., Poster # 1066 at the 2025 Society for Immunotherapy of Cancer (SITC) Annual Meeting

† KB703 encodes murine IL-12, KB704 encodes murine IL-2, and KB703 + KB704 is murine equivalent to KB707

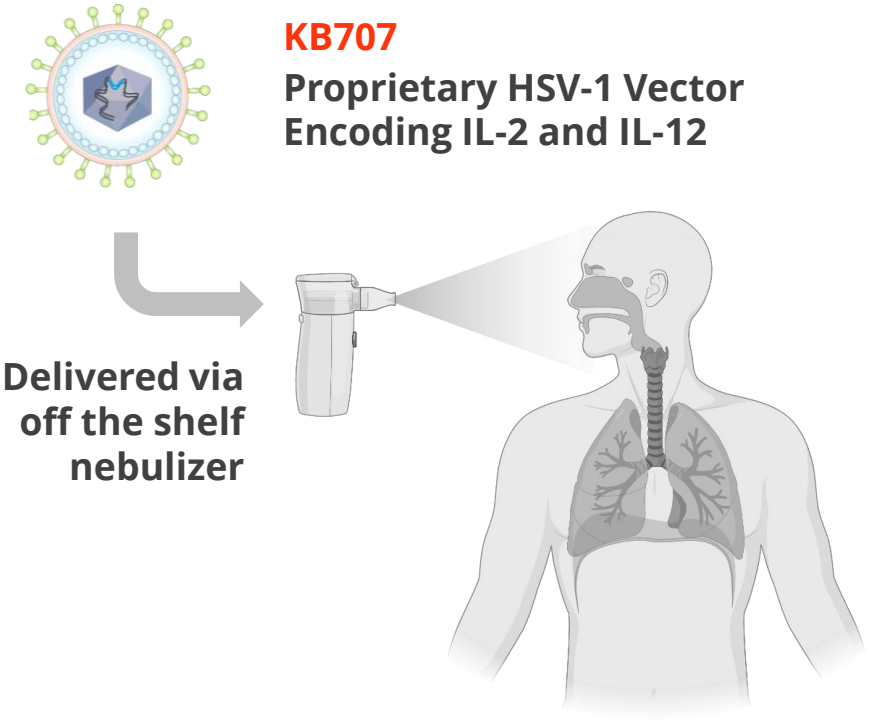
H&E, hematoxylin and eosin; IL-12, interleukin-12; IL-2, interleukin-2; IV, intravenous; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PFU, plaque forming unit

**p<0.01

Currently Evaluating Inhaled KB707 in KYANITE-1 Phase 1/2 Study

Study Design

- Open-label, multicenter, dose escalation and expansion study evaluating inhaled KB707, as monotherapy or in combination, for treatment of **solid tumors of the lung**
- Broad initial enrollment criteria including patients with primary lung cancers (*e.g.* NSCLC) or lung metastases, heavily pre-treated
- KB707 administered via inhalation weekly for first three weeks, then once every three weeks
- Doses of 10^8 PFU and 10^9 PFU inhaled KB707 were evaluated in dose escalation and 10^9 PFU selected for dose expansion
- Trial objectives include evaluation of safety, tolerability, and tumor response measured using RECIST v1.1 criteria



Reported interim clinical updates on monotherapy dose escalation and expansion cohorts in 4Q 2024 and at ASCO 2025

Krystal Biotech, Data on File.

HSV-1, herpes simplex virus 1; IL-12, interleukin-12; IL-2, interleukin-2; NSCLC, non-small cell lung cancer; PFU, plaque forming unit

Latest KYANITE-1 Update Showcases Potential of Inhaled KB707 Monotherapy

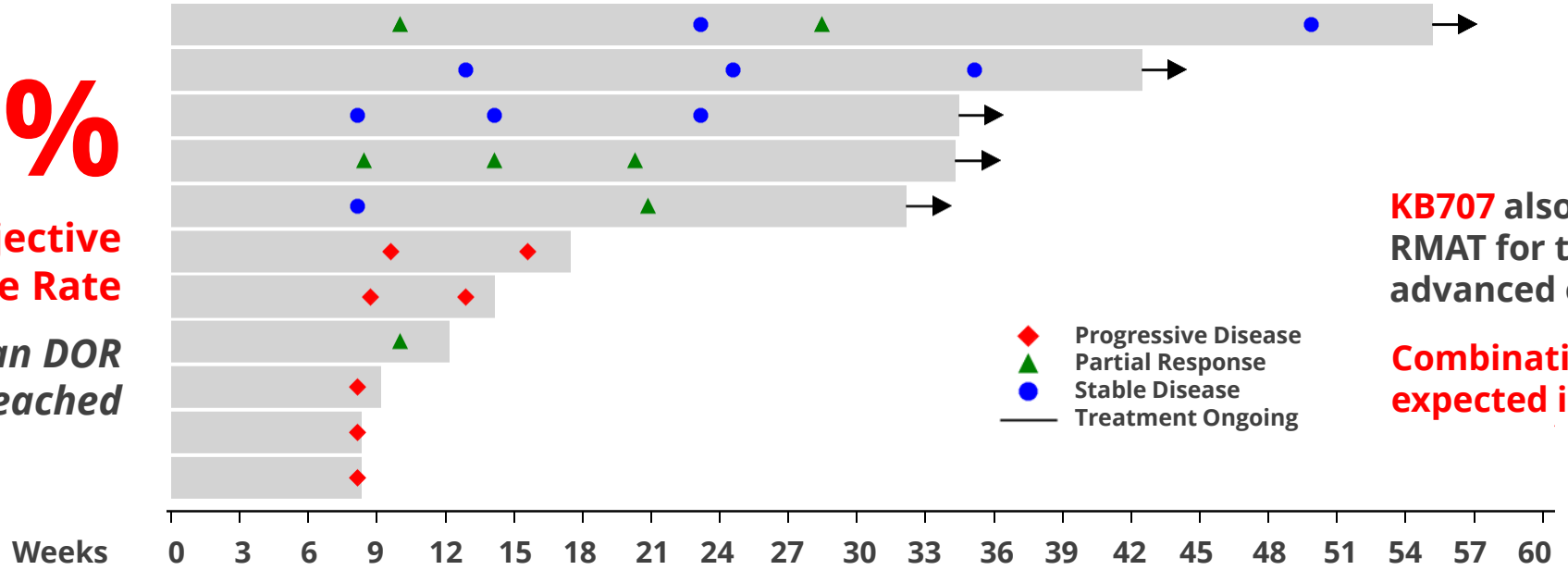
- KB707 safe and generally well tolerated across diverse, heavily pre-treated patient population (n = 39)
- Durable monotherapy responses detected in efficacy cohort patients with advanced NSCLC (n = 11)*
- All patients in efficacy cohort had received at least one prior line of immunotherapy, median four lines prior therapy

36%

Objective Response Rate

with median DOR and PFS not reached

Time on therapy and response in advanced NSCLC efficacy cohort



KB707 also recently granted RMAT for the treatment of advanced or metastatic NSCLC

Combination cohort data expected in 2026

Ma WW et al., Abstract #2575 at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting
Data cutoff date of April 15, 2025

DOR, duration of response; IL-12, interleukin-12; IL-2, interleukin-2; NSCLC, non-small cell lung cancer; PFS, progression free survival; RMAT, Regenerative Medicine Advanced Therapy

* Efficacy analysis conducted in all evaluable NSCLC patients with at least one radiographic scan and RECIST v1.1 evaluation as of data cutoff

Dermatology Pipeline

Krystal's Rare Skin Program KB111 for Hailey-Hailey Disease

- Hailey-Hailey disease (HHD) is a rare monogenic disease characterized by painful rash and blistering in skin folds
- Prevalence not well characterized and may be underreported, estimated at 1 per 50,000
- HHD patients report high levels of psychological distress and severe impacts on quality of life, intimacy issues, as well as pain, itch, burning, body odor, and infections
- Disease is linked to mutations in the *ATP2C1* gene and low expression levels of calcium-transporting ATPase ATP2C1 in keratinocytes
- **No** specific therapy approved by the FDA or EMA for the treatment of HHD
- KB111 builds on Krystal's know-how and VYJUVEK experience in skin gene delivery to increase ATP2C1 levels in skin cells after topical administration to HHD lesions
- Delivery of functional ATP2C1 confirmed preclinically and IND cleared in October 2025
- Initiating open-label study HALITE-1 in May 2026 to evaluate safety of repeat dose KB111 in HHD patients with data update **expected later this year**
- Also developing HHD-specific scale and expecting to submit both scale and registrational study design to FDA in 2H 2026 to enable registrational study start in **2027**

✓ **KB111 granted Fast Track Designation for the treatment of HHD**

✓ **Also granted platform technology designation**

10K-15K

Estimated HHD Patients in the U.S. and Europe*

*Based on 1:50K prevalence estimates

Nmezi B et al., Poster #0554 at the 2025 Society for Investigative Dermatology (SID) Annual Meeting; Krystal Biotech, Data on File.

Konstantinou MP, et al. StatPearls [Internet]. 2022. https://www.ncbi.nlm.nih.gov/books/NBK585136 [accessed October 30 2025]; Micaroni M, et al. *Cell Death Dis*. 2016. 7: e2259; Hu Z, et al. *Nat Genet*. 2000. 24: 61-65; Sudbrak R, et al. *Hum Mol Genet*. 2000. 9: 1131-1140; Shibata A, et al. *Acta Derm Venereol*. 2013. 93: 719-720; Fairclough RJ, et al. *J Invest Dermatol*. 2004. 123: 67-71; Foggia L, et al. *Am J Med Genet C Semin Med Genet*. 2004. 131C: 20-31

ATP2C1, calcium-transporting ATPase type 2C member 1' EMA, European Medicines Agency; FDA, United States Food and Drug Administration; IND, investigational new drug; U.S., United States

Aesthetics Pipeline

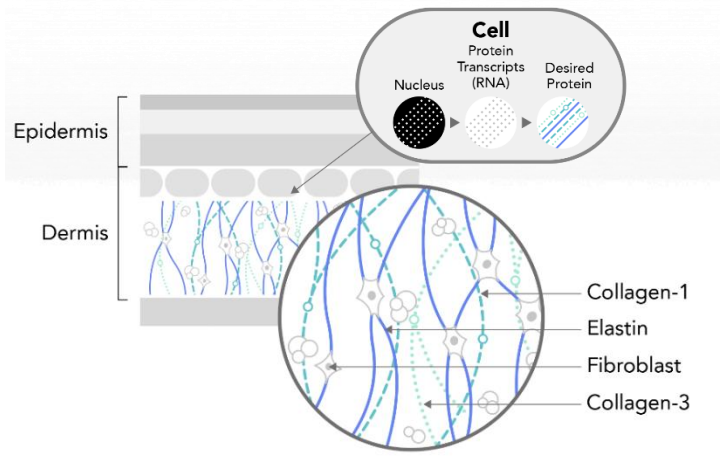
JEUNE

A wholly owned subsidiary of Krystal Biotech, Inc.

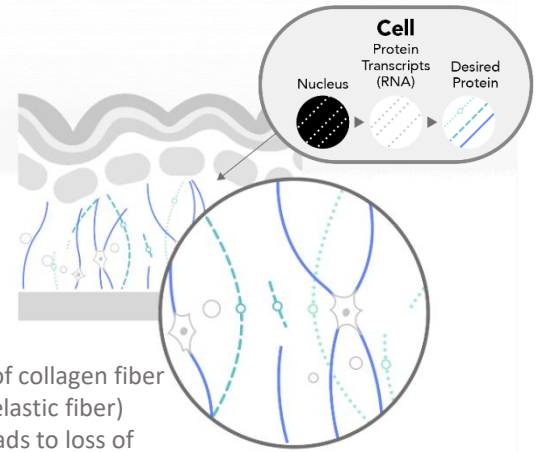
Characteristic Look of Aging Caused by Declining Levels of Key Proteins in Skin's Extracellular Matrix

- Skin aging is caused, in part, by a reduction of the skin's key proteins: collagen and elastin
- Impaired collagen and elastin synthesis leads to the degradation of the extracellular matrix, affecting overall skin quality and function
- The primary function of the extracellular matrix is to give skin its mechanical and biochemical properties

YOUNGER / HEALTHY

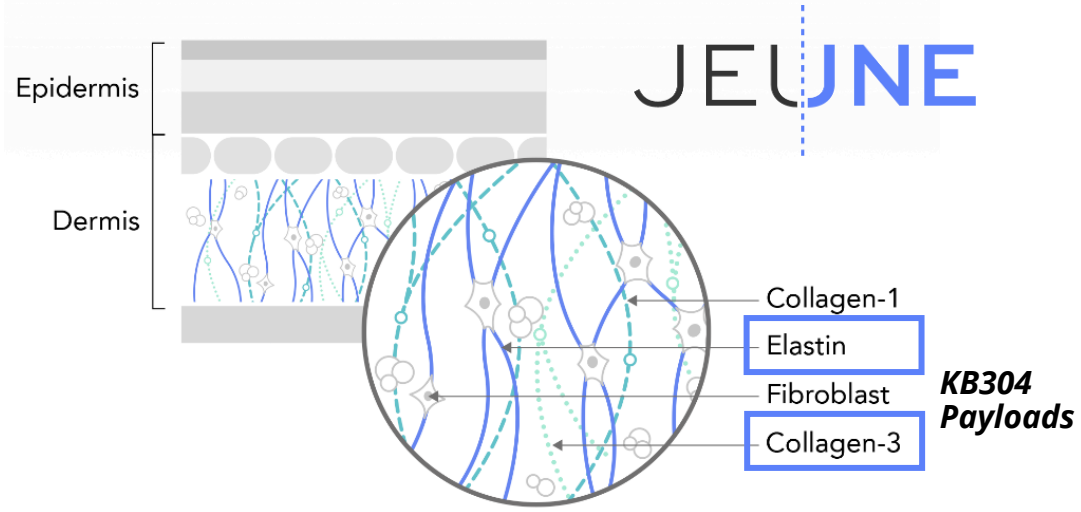


AGED / PHOTODAMAGED



Declining levels of collagen fiber and elastin (elastic fiber) production leads to loss of extracellular matrix integrity

Lead Program KB304 Designed to Increase Collagen and Elastin in Aging Skin



- Type III collagen (COL3) is the second most abundant protein in the skin but levels decline significantly with age
- COL3 has been implicated in both new collagen fibril formation as well as regulation of collagen fibril diameter, organization, and elasticity
- COL3 is indispensable for youthful, resilient skin and has been implicated in both new collagen fibril formation as well as regulation of collagen fibril diameter, organization, and elasticity
- Elastin is 1000 times more flexible than collagen giving skin elastic quality
- Elastin production peaks near birth and effectively ceases by adulthood
- Due to the low rate of turnover, elastin fibers are particularly prone to the accumulation of damage from aging
- Degradation of these key proteins leads to sagging and wrinkled skin

By delivering directly to the body's skin cells, KB304 has the potential to restore youthful collagen and elastin levels to naturally rejuvenate the skin

Varani J, et al. *Am J Pathol.* 2006. 168(6): 1861-1868; Singh D, et al. *Cardiol Cardiovasc Med*. 2023. 7(1): 5-16; Gosline J, et al. *Philos Trans R Soc Lond B Biol Sci.* 2002. 357(1418): 121-132; Shapiro SD, et al. *J Clin Invest*. 1991. 87: 1828-1834; Swee MH, et al. *J Biol Chem*. 1995. 270: 14899-14906

Meaningful Aesthetic Improvements Reported Following KB304 Treatment in Placebo Controlled Phase 1 Study PEARL-2

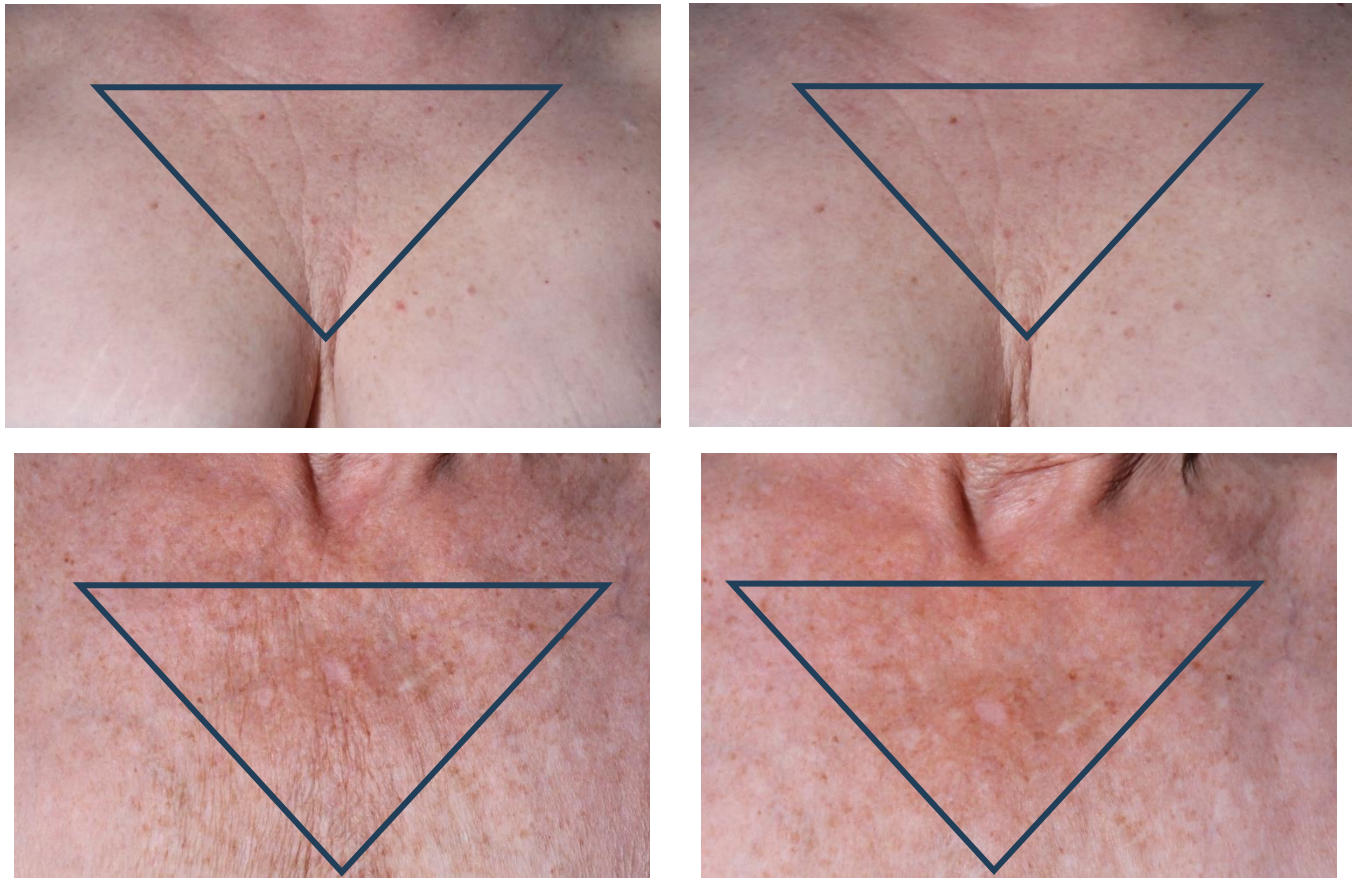
PEARL-2 Study Design

- 2:1 randomized, double-blind, placebo-controlled Phase 1 evaluating KB304 for the treatment of wrinkles of the décolleté
- Efficacy evaluation included investigator and subject assessments of aesthetic improvement on the 5-point GAIS scale; multiple skin attributes evaluated
- 19 subjects enrolled and 18 assessed through three month follow up, assessed subjects were all female with median age of 62 years (range 47-75)

✓ **Meaningful aesthetic improvements following KB304 treatment with clear and statistically significant advantages over placebo**

✓ **Safety profile consistent with prior clinical experience in KB301 and all adverse events were mild-to-moderate and transient**

Décolleté Before and After Images



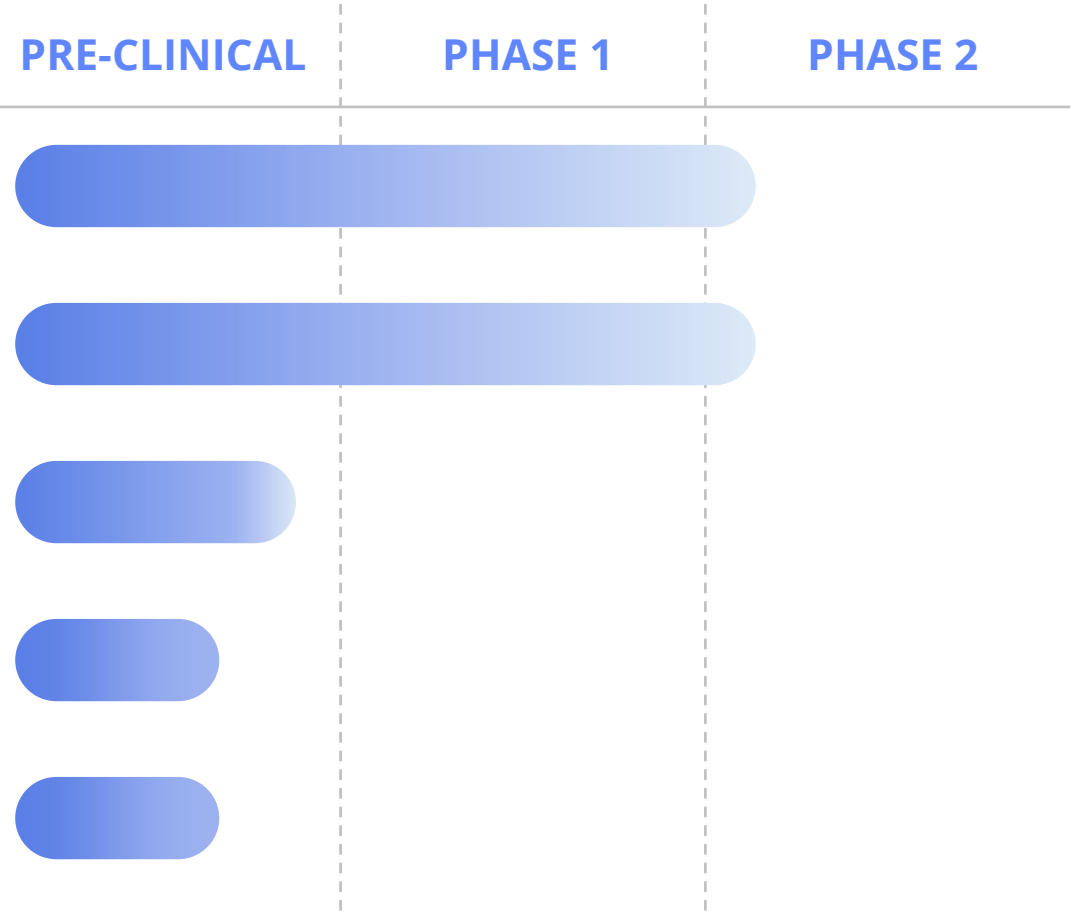
Baseline | **Three Month Follow Up**

Expecting to initiate Phase 2 study of KB304 in 2027

GAIS, Global Aesthetic Improvement Scale

Deep Pipeline Targeting Priority Skin Proteins as Fast Followers to KB304

PROGRAM	INDICATION	PAYLOAD
KB304	Dynamic Wrinkles of the Décolleté	Type III collagen (COL3) + elastin (ELN)
KB301	TBD	COL3
KB303	TBD	ELN
KB302	TBD	Type 1 collagen (COL1)
KB305	TBD	Type IV collagen (COL4)



JEUNE

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