Krystal®

Genetic Medicines for High Unmet Medical Needs

November 2023

Forward Looking Statements and Disclosures

Forward Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. Any statements in this presentation about future expectations, plans and prospects for Krystal Biotech, Inc. (together with or its subsidiaries and affiliates, the "Company"), including, but not limited to, statements about commercialization of VYJUVEK® in the United States; efforts and timelines to bring VYJUVEK to market in Europe, Japan and elsewhere; the market opportunity for and the potential market acceptance of VYJUVEK; estimated annual care costs for DEB patients; the B-VEC label expansion opportunity to address DEB ocular complications; the Company's in-house manufacturing capacity and expertise; the Company's technology platform, including its expected advantages; the development and commercialization of the Company's product candidates and pipeline expansion opportunities, including expected timing of upcoming milestones, and the conduct and timelines of preclinical and clinical trials; the preclinical and clinical utility of the Company's product candidates; plans for and timing of regulatory filings and meetings with regulators, including the U.S. Food and Drug Administration; the market opportunity for and the potential market acceptance of the Company's product candidates; the sufficiency of the Company's 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: the content and timing of decisions made by the U.S. Food and Drug Administration, European Medicines Agency and other regulatory authorities; 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 studies in different disease indications will be indicative of the results of ongoing or future trials; uncertainties associated with regulatory review of clinical trials and applications for marketing approvals; the availability or commercial potential of product candidates; the ability to retain and hire key personnel; the sufficiency of cash resources and need for additional financing; and such other important factors as are set forth in the Company's annual and quarterly reports and other filings on file with the U.S. Securities and Exchange Commission. In addition, the forward-looking statements included in this presentation represent the Company's views as of the date of this presentation. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this presentation.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Disclosures

The Company is using the Aerogen Solo® Nebulizer System and Aerogen® Ultra in its Phase 1 CORAL-1 study evaluating KB407 and plans to use those Aerogen products in its anticipated Phase 1 clinical trials evaluating KB408 and inhaled KB707.

VYJUVEK Approved and Launched in U.S.

Strong commercial launch driven by high demand among patients, caregivers, and HCPs for first-in-kind therapy

Vyjuvek®

beremagene geperpavec-svdt

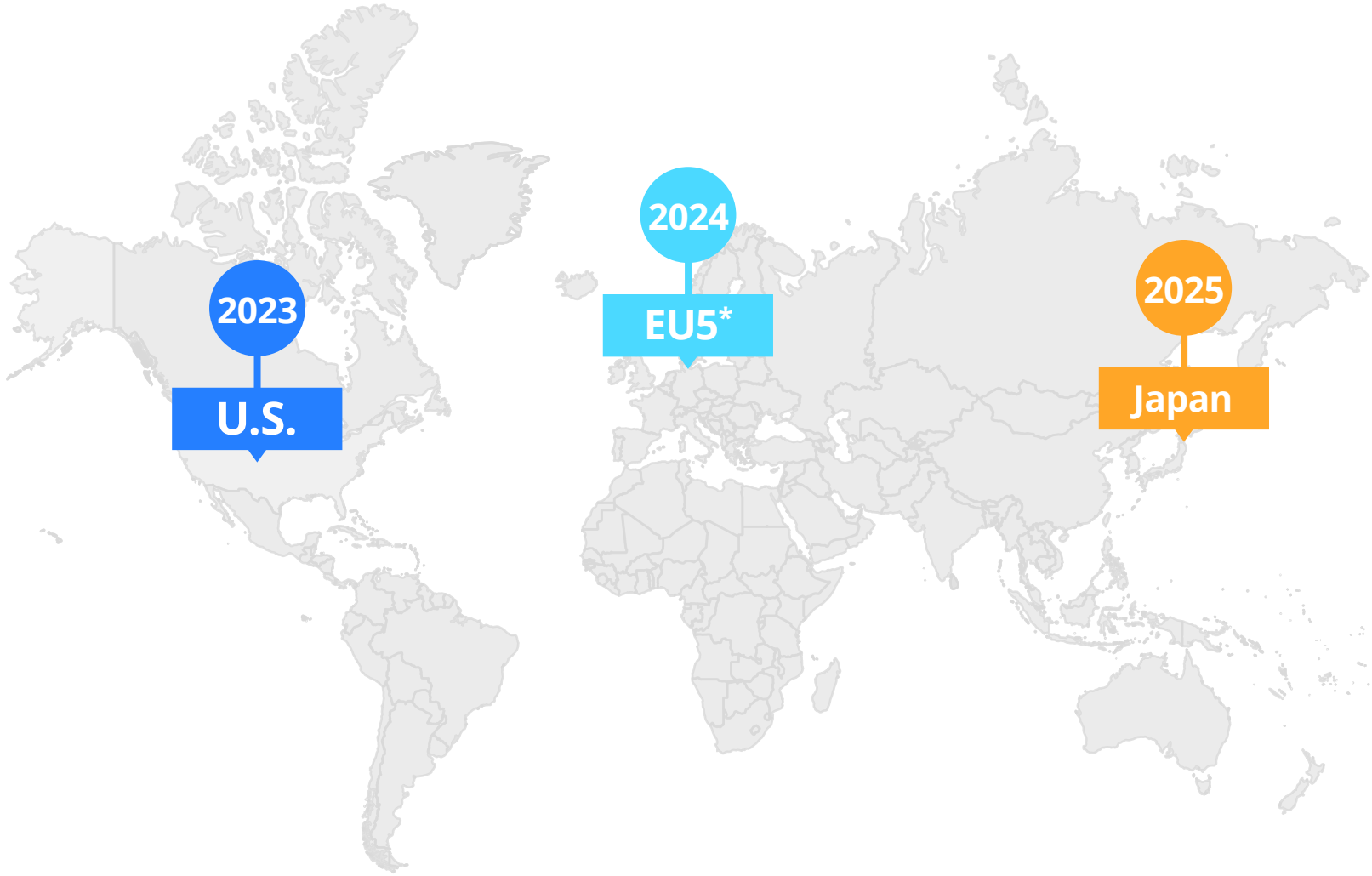
5x10⁹ PFU/mL single-use vial

- ***First* and *Only* FDA-approved treatment for DEB, approved on May 19, 2023**
  - Indicated for the treatment of wounds in patients 6 months of age and older with DEB
  - Approved for recessive and dominant DEB with no restrictions on use by wound type
- **Strong Demand: Rapidly penetrating DEB patient pool and new patients emerging**
  - 284 Patient Start Forms (PSFs) through Q3; over 20% of identified patient pool at launch
  - New PSFs from previously unknown dominant DEB patients organically expanding pool
- **Nearing Full Access: Over 70% of patients eligible for reimbursement**
  - Positive coverage determinations from all major commercial national health plans
  - Over 80% of patients are presently eligible for commercial reimbursement
  - 74% of patients on government insurance are presently eligible for reimbursement
- **Convenience Supporting Utilization: Site of care flexibility enables high compliance**
  - Approved for HCP administration irrespective of care setting, including home or clinic
  - Home dosing by HCP requested by over 88% of patients through Q3
  - 96% compliance with weekly treatment to date

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

VYJUVEK Global Regulatory Approval Timelines and Market Opportunity

U.S. approval and launch in 2023; expect regulatory decisions for EU5 in 2024 and Japan in 2025



Over $750M

Estimated VYJUVEK global market opportunity based on approvals to date

+

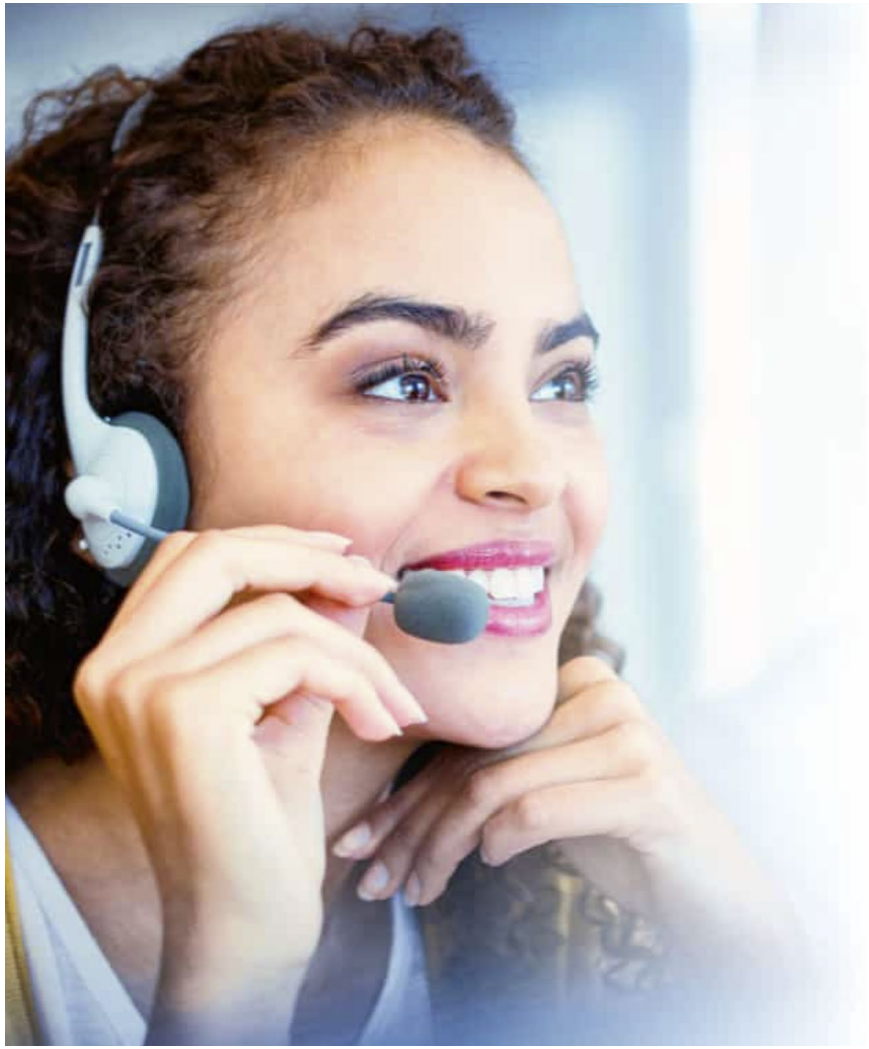
Additional revenue upside from ophthalmic formulation label expansion

*EU5 to include European countries: France, Germany, Italy, Spain and the United Kingdom.

U.S., United States

Supporting the US Patient Journey and Shortening Time to Therapy

Krystal infrastructure in place and supporting patient diagnosis and access



Krystal CONNECT™ Personalized Support Services

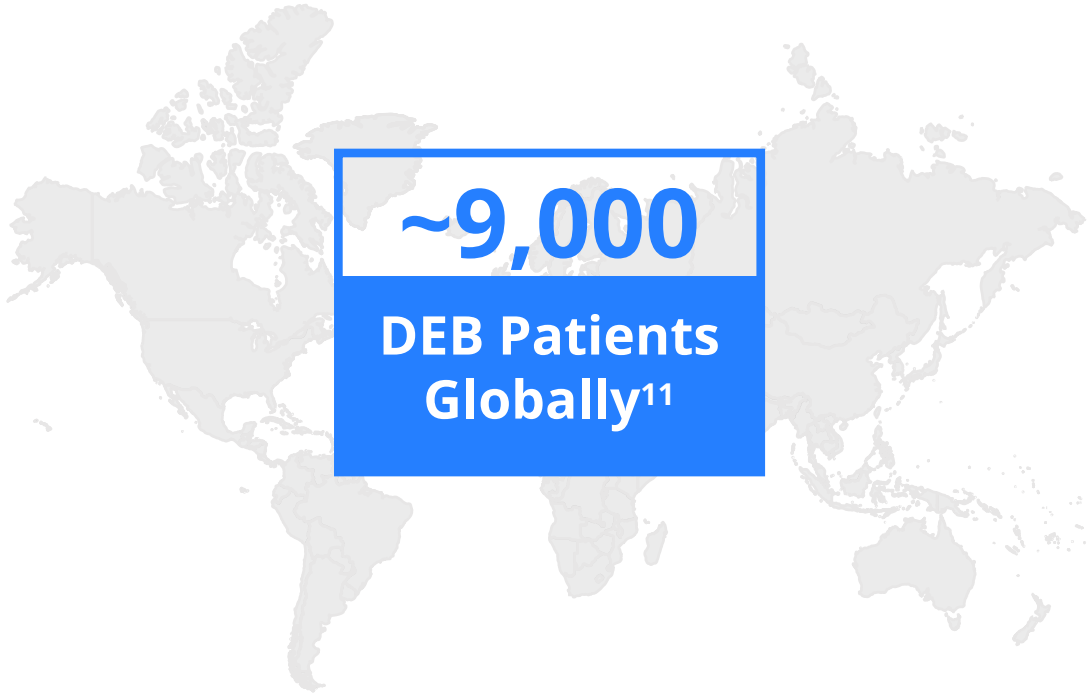
Decode DEB™

Krystal Connect Patient Support Services

- No-cost genetic testing program through Decode DEB™ to provide patient genotyping
- Personalized patient support throughout treatment journey
- Financial assistance for eligible patients
- Disease state and product education
- Reimbursement assistance
- Help with treatment planning and administration

Dystrophic Epidermolysis Bullosa (DEB)

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]

Until Now, Only Supportive Care Available in the U.S.

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

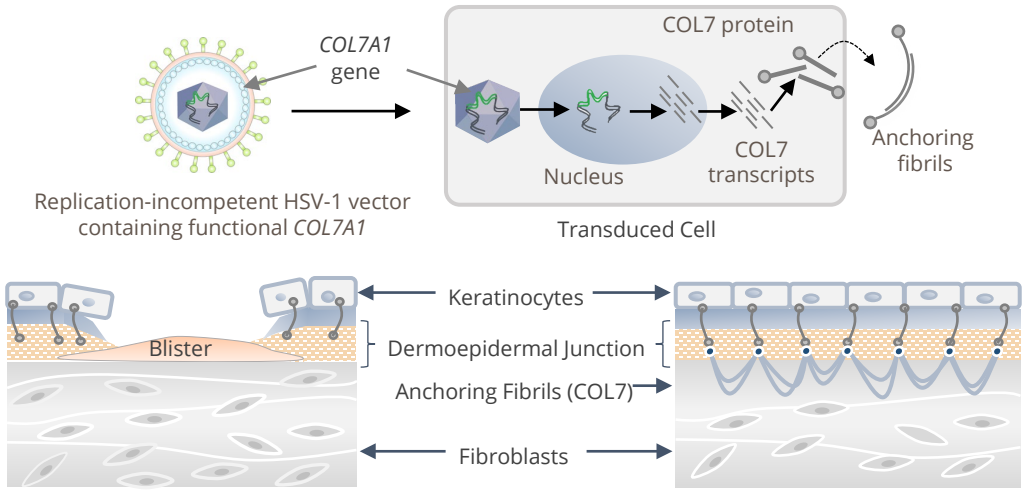
COL7, type VII collagen; COL7A1, collagen type VII alpha 1 chain; DEB, dystrophic epidermolysis bullosa; U.S., United States

VYJUVEK is the First and Only Corrective Therapy for DEB

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

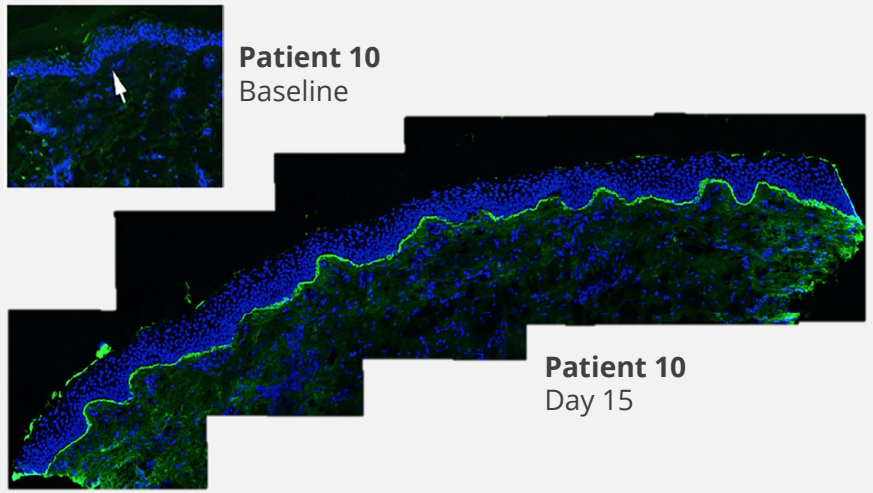
VYJUVEK Mechanism of Action

- When applied topically to the wound, VYJUVEK transduces local keratinocytes and fibroblasts and delivers *COL7A1* to the nucleus[1-3]
- The *COL7A1* payload then persists episomally, enabling the transduced cell to produce and secrete functional COL7 protein without host genomic disruption[1-3]
- Secreted COL7 assembles into anchoring fibrils, holding skin together[1-3]



Clinical Evidence of Molecular Correction in Phase 1/2

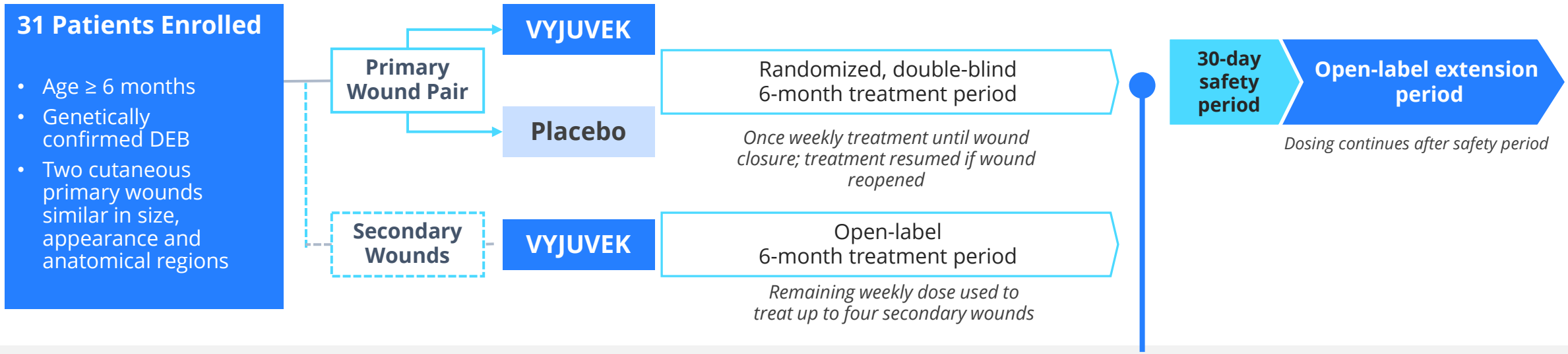
- Representative data from patient in Phase 1/2 study assessing COL7 deposition in the skin by immunofluorescence (in green)[3]
- Strong, properly localized COL7 signal detected in treated skin
- Anchoring fibril formation also detected by electron microscopy



1. Marinkovich MP, et al. Oral presentation at 2022 American Academy of Dermatology (AAD) Annual Meeting; 2. Guide SV, et al. *N Engl J Med.* 2022;387(24):2211-9; 3. 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

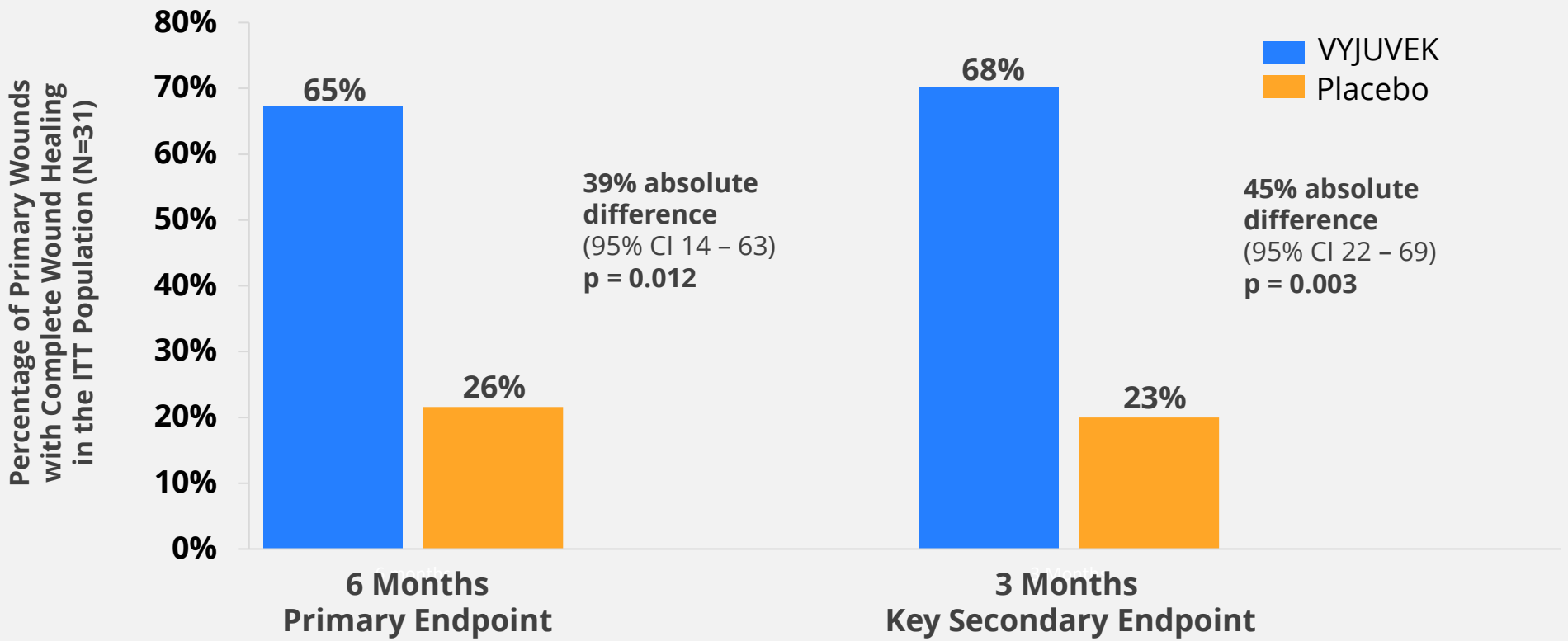
- Complete wound healing† at Week 8 and Week 10, or at Week 10 and Week 12 (3-months)
- Mean change in pain severity (VAS or FLACC-R Scale) associated with wound dressing changes

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; ITT, intent-to-treat

Consistent Evidence of Treatment Response with VYJUVEK

Treatment response was in favor of VYJUVEK regardless of wound size†

Complete Wound Healing at 6 Months by Baseline Wound Size

Baseline primary wound area/size*	VYJUVEK		Placebo	
	N	Complete wound healing at 6 months, n (%)	N	Complete wound healing at 6 months, n (%)
<20 cm^2	23	14 (60.9)	22	5 (22.7)
20 - <40 cm^2	6	4 (66.7)	8	1 (12.5)
40 – 60 cm^2	2	1 (50.0)	1	0 (0)

*In a small number of patients, the pre-defined threshold values for wound area/size category fell in between the size of the two wounds

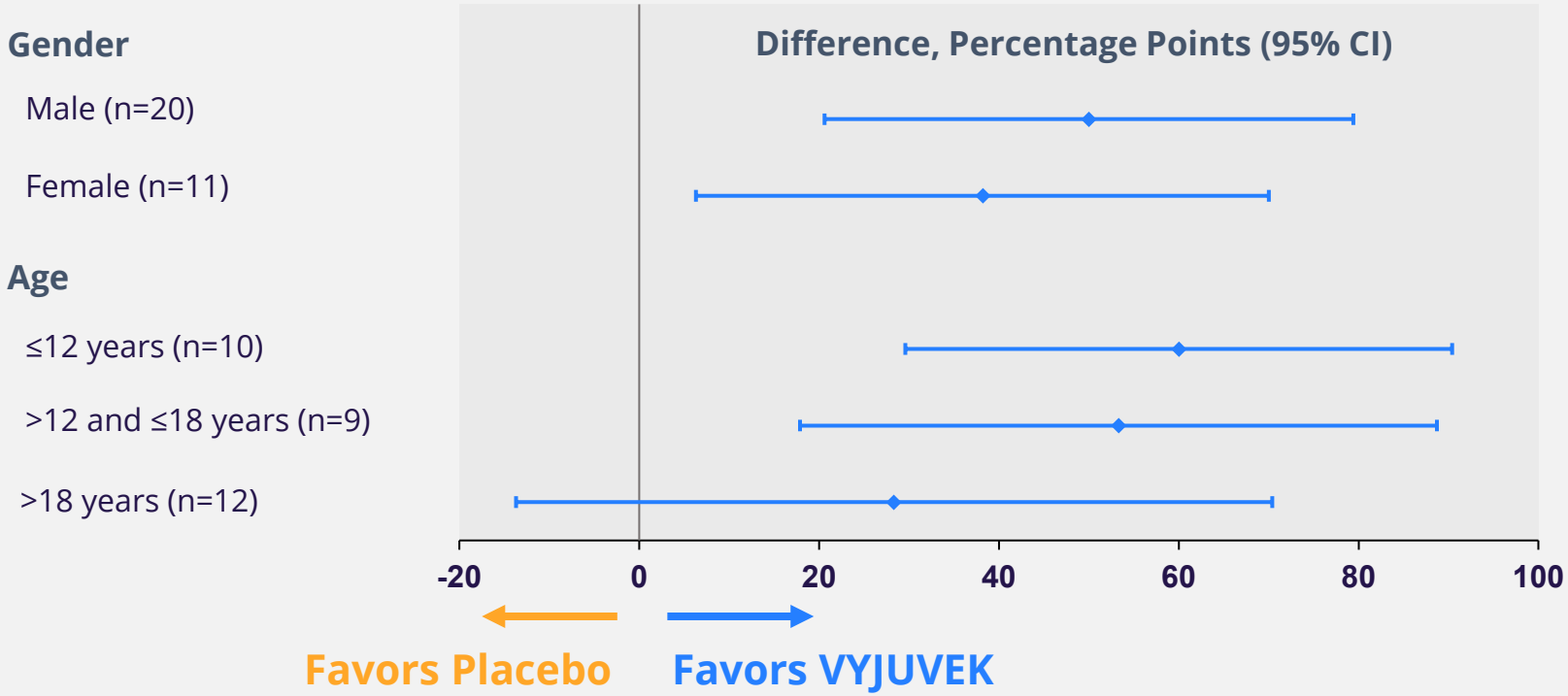
Guide SV, et al. *N Engl J Med.* 2022;387(24):2211-9, Data in figure based on ITT population (imputed); CIs are based on exact McNemar's test

†Individual subgroups were not powered to demonstrate statistical significance

Consistent Evidence of Treatment Response with VYJUVEK

Treatment response was in favor of VYJUVEK regardless of wound size, gender, and age†

Complete Wound Healing at 6 Months by Gender & Age



†Individual subgroups were not powered to demonstrate statistical significance

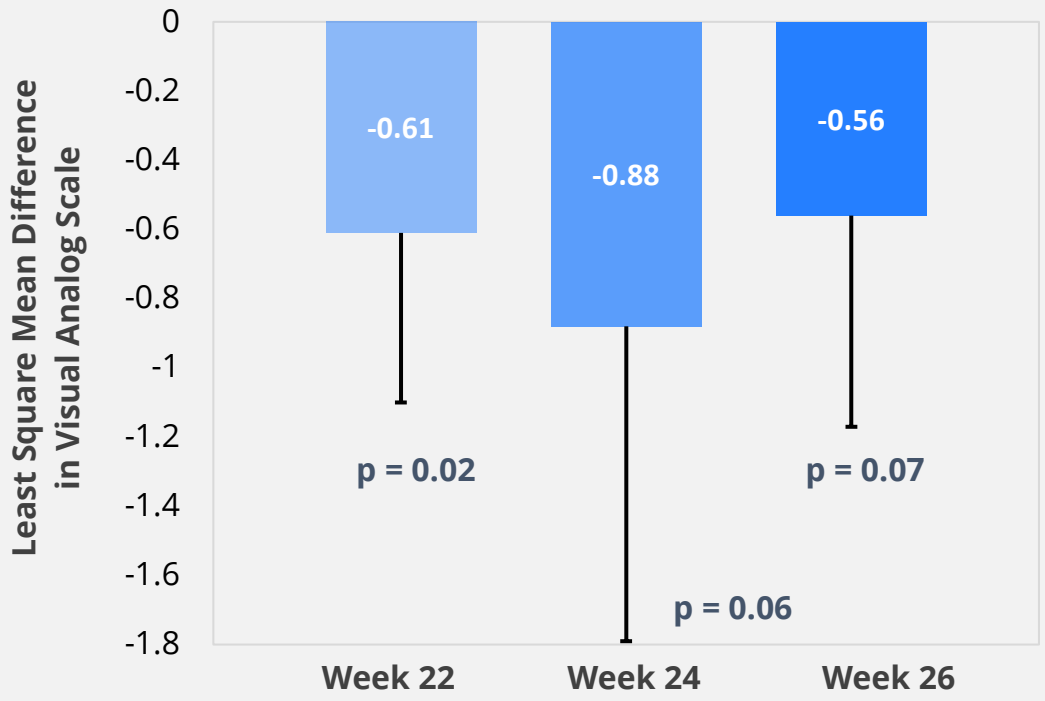
Guide SV, et al. *N Engl J Med.* 2022;387(24):2211-9, Data in figure based on ITT population (imputed); CIs are based on exact McNemar's test

CI, confidence interval

Pain Improvement Consistent with a Wound Healing Response

Trend in favor of VYJUVEK across all time points tested

Change from Baseline in Pain following VYJUVEK Treatment



- Baseline VAS score of enrolled patients were approximately 2 to 3 on average[1]
- A trend towards decreased pain in VYJUVEK treated versus placebo treated wounds was observed across Weeks 22, 24, and 26; improvement in pain was consistent with wound healing[1,2]
- PRO measures (EQ-5D-5L and Skindex-29) assessed before and after treatment with VYJUVEK demonstrated improvement across multiple domains directionally, consistent with a wound healing response[1,2]

Change from baseline in pain severity associated with wound dressing changes, as measured by Visual Analog Scale, at Weeks 22, 24, and 26 for the ITT population, ages 6 and above.

Least square mean difference, 95% CI (shown as error bars), and p values were generated from analysis of covariance linear model with treatment and subject as the fixed effects and the baseline value as the covariate and change from baseline as the dependent variable.

1. Marinkovich MP, et al. Oral presentation at 2022 American Academy of Dermatology (AAD) Annual Meeting; 2. Guide SV, et al. *N Engl J Med.* 2022;387(24):2211-9

PRO, patient-reported outcomes; VAS, Visual Analog Scale

VYJUVEK Well-Tolerated and Demonstrated Strong Safety Profile

Safety profile consistent across all studies to date

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

Label Expansion Opportunity to Address DEB Ocular Complications

A cause of progressive vision loss with no specific therapy available

Ocular Complications of Dystrophic Epidermylosis 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 is 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

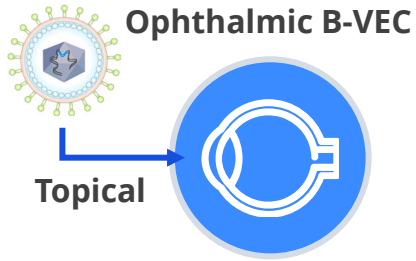
Estimated Patients in U.S.*

2K+

Estimated Patients WW*†

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

† Reimbursable markets only



Ophthalmic formulation of B-VEC 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; RDEB, recessive dystrophic epidermolysis bullosa; U.S., United States; WW, worldwide

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

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

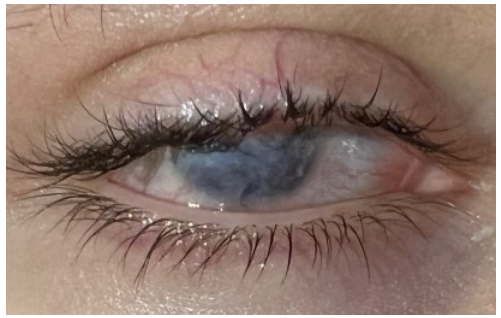
Well-tolerated and associated with full corneal healing and visual acuity improvement to 20/40

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)
- Weekly applications 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

Ophthalmic B-VEC well-tolerated and associated with corneal healing, epithelization, and continuing visual acuity improvement from hand motion to 20/40

Sabater A et al., Poster # 787 - C0388. at the 2023 Association for Research in Vision and Ophthalmology Annual Meeting

B-VEC, beremagene geperpavec; DEB, dystrophic epidermolysis bullosa; HM, hand motion; PFU, plaque-forming unit

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

In-House Manufacturing Capacity and Expertise

Two U.S. GMP facilities with capacity to support global VYJUVEK product needs and future growth

ANCORIS Facility

- ~21,100 sq. ft. GMP facility
- Capabilities: Virus Banks, Cell Banks, Pilot Scale Process Development, Drug Substance, Drug Product GMP Storage, Clinical and Commercial Packaging, Analytical Development, Analytical Testing, Waste Handling, Environmental Monitoring, and Logistics
- Fully equipped AD/QC labs
- Validated methods for titering/release
- Built to support global VYJUVEK launch

ASTRA Facility

- ~155,000 sq. ft. GMP facility
- Capabilities: Virus Banks, Cell Banks, Drug Substance, Drug Product, Packaging, Storage, General Office Space, GMP Storage, Bulk Packaging, Waste Handling, Environmental Monitoring, and Logistics
- Operational in H1 2023
- Able to scale up and scale out

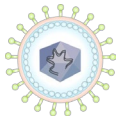
GMP, good manufacturing practice; MVB, master virus bank; U.S., United States

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

Technology Platform

HSV-1: A Differentiated Vector Platform

Unique properties of HSV-1 overcome capacity, immunogenicity, and potential safety issues of other commonly used vectors



Krystal's Engineered Replication Deficient HSV-1 Platform

Large genetic payload capacity well in excess of other viral vectors

HSV-1 has a large genome, theoretical cargo capacity > 30 kb significantly exceeds capacity of AAV (< 5 kb) and lentiviruses (~9 kb); VYJUVEK contains over 19 kb genetic cargo

Efficient transduction of wide range of cell types

HSV-1 employs multiple mechanisms to gain cell entry and majority of cell types are permissive; Krystal vectors shown to transduce keratinocytes, fibroblasts, and various cells of the eye and lung so far

Evades host immunity allowing for repeat dosing and reducing immunotoxicity

The ability of HSV-1 to block innate and adaptive immune responses is retained in Krystal vectors; no evidence of significant or persistent neutralizing immunity in clinical studies to date

DNA payload enables durable expression without integration risk

HSV-1 delivers genome to nucleus where it persists episomally; no reports of integration with wild-type virus or Krystal constructs

Scalable manufacturing of viral gene therapies

Capable of increasing manufacturing in a streamlined manner because of in-house capabilities

AAV, adeno-associated virus; DNA, deoxyribonucleic acid; HSV-1, herpes simplex virus type 1

Pipeline

Near-term focus on three target tissues with recent pipeline expansion under investigation

		Indication	Payload	Preclinical	Phase 1/2	Phase 3
Vyjuvek™ beremagene geperpavec-svdt		Dystrophic epidermolysis bullosa (DEB)	*COL7A1*	**FDA Approved May 2023**		
Dermatology	**KB105**	Autosomal recessive congenital ichthyosis (ARCI)	*TGM1*			
	KB104	Netherton syndrome	*SPINK5*			
	Additional program(s) targeting dermatology indications					
Respiratory	**KB407**	Cystic fibrosis	*CFTR*			
	KB408	Alpha-1 antitrypsin deficiency (AATD)	*SERPINA1*			
	Additional program(s) targeting respiratory indications					
Oncology	**Injectable KB707**	Solid tumors including cutaneous	*IL2 + IL12*			
	Inhaled KB707	Solid tumors of the lung	*IL2 + IL12*			
Ophthalmology	**Ophthalmic B-VEC**	Ocular complications of DEB	*COL7A1*			
	Program(s) targeting ophthalmology indications					

B-VEC, beremagene geperpavec; CFTR, cystic fibrosis transmembrane conductance regulator; COL7A1, collagen type VII alpha 1 chain; DEB, dystrophic epidermolysis bullosa; FDA, US Food and Drug Administration; FPI, first patient in; IND, investigational new drug; MAA, marketing authorization application; SERPINA1, serpin family A member 1; SPINK5, serine protease inhibitor Kazal-type 5; TGM1, transglutaminase-1

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

Milestones

Upcoming Milestones

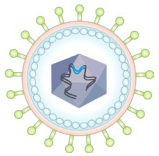
Timing	Event	Program
1H 24	Top line results from Phase 1 Cohort 3	KB301 for Aesthetic Indication(s)
1H 24	Initiate Phase 1 study	KB408 for Alpha-1 Antitrypsin Deficiency
1H 24	Initiate Phase 1 study	Inhaled KB707 for Solid Tumors
2H 24	File New Drug Application in Japan	VYJUVEK for Dystrophic Epidermolysis Bullosa
2H 24	Anticipated Decision on EU Marketing Authorization Application	VYJUVEK for Dystrophic Epidermolysis Bullosa
2H 24	Interim top line results from Phase 1 study	KB407 for Cystic Fibrosis
2H 24	Interim top line results from Phase 1 study	Intratumoral KB707 for Solid Tumors

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

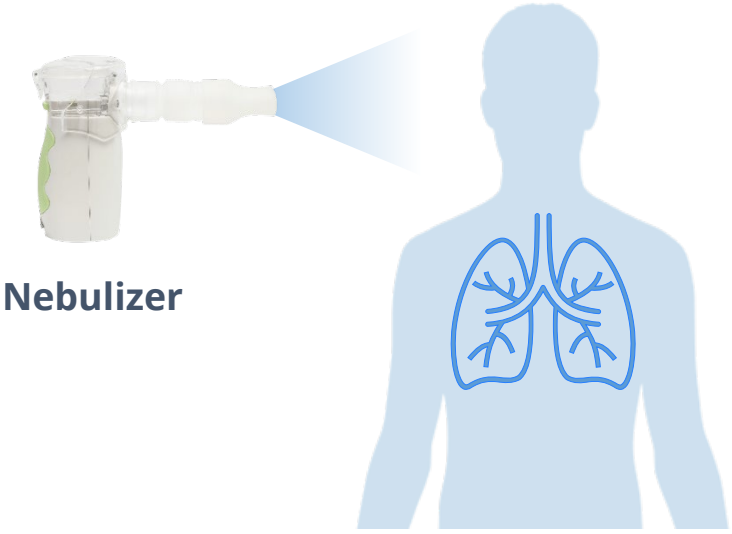
Respiratory Pipeline

Krystal Respiratory Pipeline

Developing redosable, inhaled gene therapies to address monogenic disorders of the lung



KB407
KB408



Nebulizer

Product	Preclinical	Phase 1/2	Phase 3	Upcoming Milestone(s)
KB407				Interim Phase 1 data in 2024
KB408				Begin Phase 1 in H1 2024

Historical Challenges with Inhaled Gene Therapy[1]

- 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 Addresses 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
- Expected nebulization time is under 30-minutes using off-the-shelf nebulizer
- **Robust preclinical data package:** Krystal's inhaled candidates well-tolerated and distribute broadly in lung to drive local payload expression

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

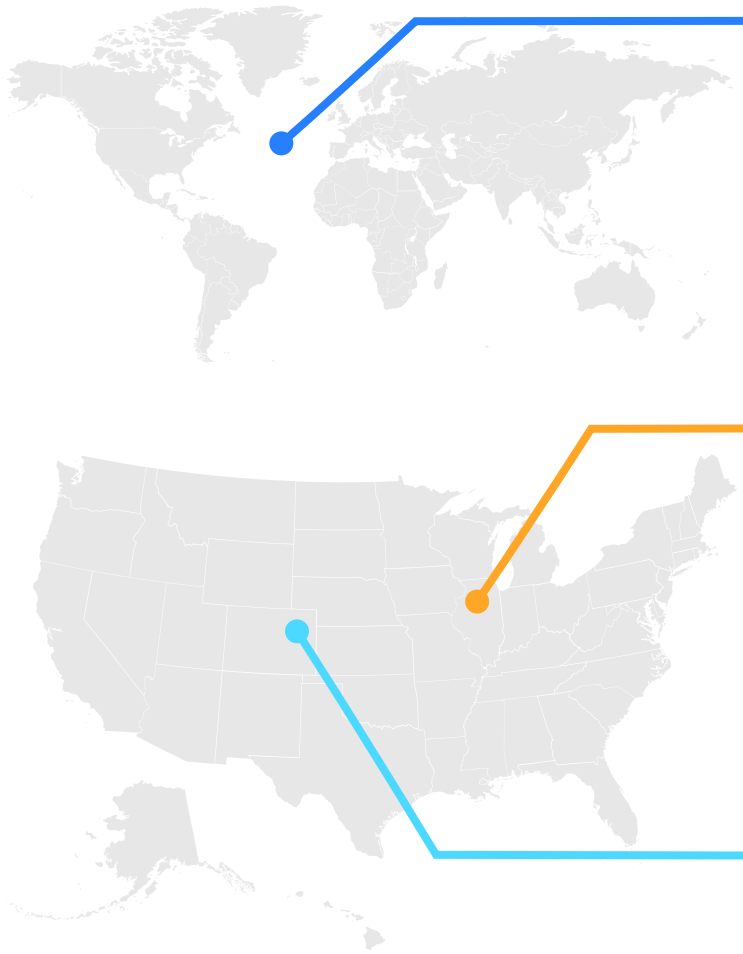
AAV, adeno-associated virus; CFTR, cystic fibrosis transmembrane conductance regulator; DEB, dystrophic epidermolysis bullosa; HSV-1, herpes simplex virus type 1

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

Cystic Fibrosis Disease Overview

A life-span shortening progressive disease of the lung

CF Prevalence & Incidence[1,2]



105,000

CF Patients in 94 Countries

32,000+

CF Patients in U.S. Registry

+1,000

New Cases Annually in U.S.

- Cystic fibrosis (CF) is a life-threatening inherited disease caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR), leading to reduced and/or loss of CFTR function[3,4,5]
- Progressive lung disease is the primary cause of morbidity and mortality with loss of CFTR-mediated ion transport leading to[6]
  - Airway mucus obstruction
  - Recurrent bacterial infection
  - Inflammation
- As of 2017, median survival age for CF patients in North America and Europe was between 44 and 53 years[7]
- CFTR modulators, first approved in 2012 and now used in combination, are emerging as standard of care for eligible patients[8]
- **Limitations of CFTR Modulators:** Not effective for all CFTR mutation types, heterogeneous patient response, GI / liver tolerability, frequent dosing[8]

1. U.S. Cystic Fibrosis Foundation – About Cystic Fibrosis, accessible at: About Cystic Fibrosis | Cystic Fibrosis Foundation (cff.org); 2. U.S. Cystic Fibrosis Foundation – 2022 CFF Patient Registry Highlights; 3. O'Sullivan BP, et al. *Lancet* 2009;373:1891-904; 4. Elborn JS, et al. *Lancet* 2016; 388:2519-31; 5. Sanders DB, et al. *Pediatr Clin North Am.* 2016;63:567-84; 6. Stoltz DA, et al. *N Engl J Med*. 2015, 372 (4): 351-362; 7. Scotet V. *Genes* 2020;11:589;
8. Hapnadak SG, et al. *J Cyst Fibros.* 2020;19(3):344-354

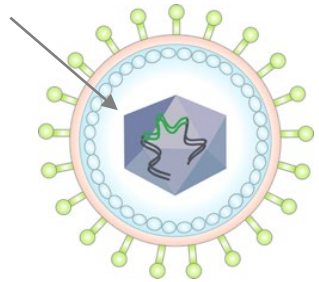
CF, cystic fibrosis; CFTR, cystic fibrosis transmembrane conductance regulator; GI, gastrointestinal; U.S., United States

KB407 Designed To Address Major Unmet Needs in CF

Multiple opportunities for KB407 to improve CF patient outcomes as mutation agnostic, redosable gene therapy

KB407

CFTR gene



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

Target Segments for KB407	Estimated Patients
1 **Patients ineligible for CFTR modulator therapy including CFTR null patients** 10%+ of all CF patients[1]	**10K**
2 **Patients either weakly or non-responsive to TRIKAFTA®, ppFEV$_1$ increase < 5%** 15-25% of patients otherwise eligible for TRIKAFTA[2]	**19K**
3 **Alternate regimen for patients that poorly tolerate TRIKAFTA** 5% of patients otherwise eligible for TRIKAFTA[2]	**5K**
+ **Upside: Combination therapy or direct competition with TRIKAFTA if demonstrating superior dosing, efficacy, and/or safety**	**All 105K**

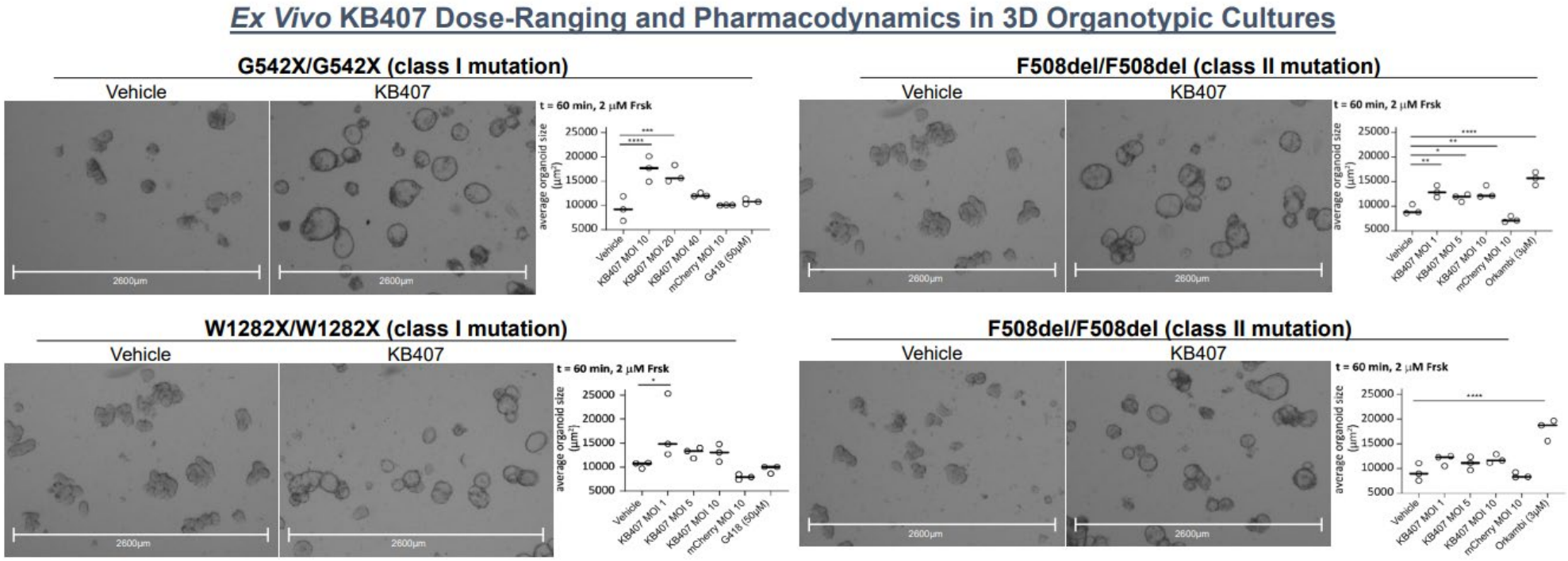
1. Krystal estimates based on CFF Patient Registry 2019, ECFS Patient Registry 2018; 2. Krystal estimates based on Middleton PG, et al. *N Engl J Med*. 2009;381:1809-1819; Heijerman HG, et al. *Lancet* 2019;394:1940-1948; Trikafta® FDA Label, Revised 10/2021

CF, cystic fibrosis; CFTR, cystic fibrosis transmembrane conductance regulator; HSV-1, herpes simplex virus type 1; ppFEV$_1$, percent predicted forced expiratory volume in 1 second

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

KB407 Corrected *CFTR* Defect in 3D Patient-Derived Intestinal Organoids

Restoration of normal cystic organoid morphology occurs irrespective of underlying *CFTR* mutation



- Transduction by KB407 leads to a restoration of normal cystic organoid morphology within 24 hours of infection, irrespective of the underlying *CFTR* mutation
- KB407 also found to transduce primary CF patient derived small airway epithelial cells in a dose-dependent manner; the vector efficiently produces functional, full-length CFTR protein that properly traffics to the cell membrane

Freedman C, et al. Poster at the ASGCT 2020 Annual Meeting. Virtual. May 12-15, 2020; Krystal Biotech. Data on file.

CF, cystic fibrosis; MOI, multiplicity of infection

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

Repeat Dose GLP IND-Enabling Toxicology Study in NHPs

Repeat dose of KB407* well-tolerated and broadly distributed throughout lung tissue in NHPs

Study Design

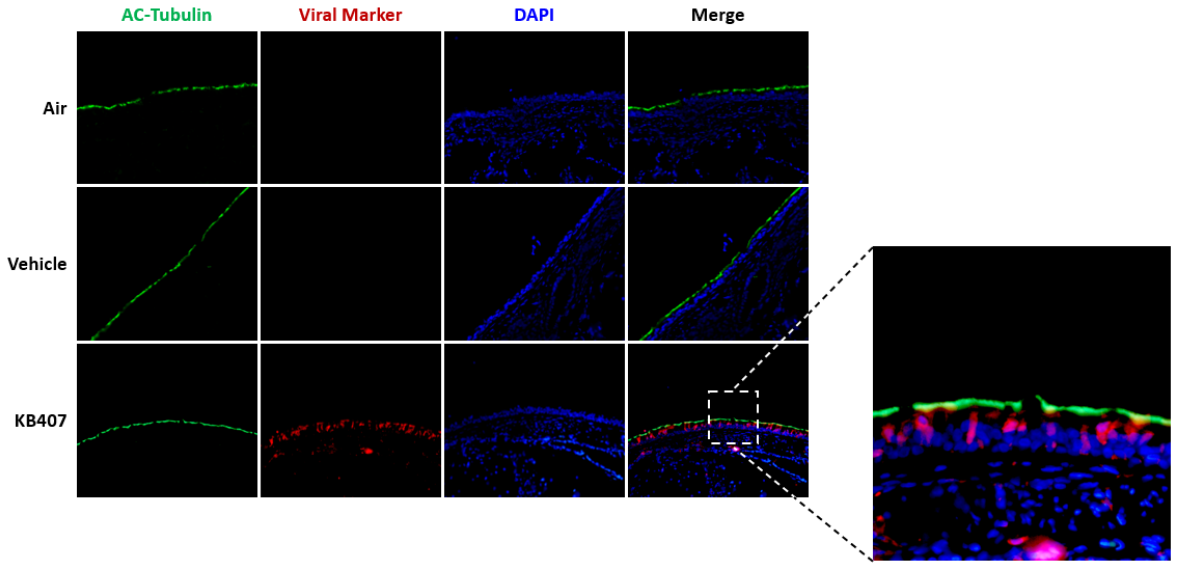
Group	n	Avg. Dose Deposited in Lungs (PFU / administration)	Dosing Days	Necropsy Days
Air	6	-	1, 8, 15	16
Vehicle	10	-	1, 8, 15	16, 43
Low Dose KB407	10	1.81×10^8 (male) 2.33×10^8 (female)	1, 8, 15	16, 43
High Dose KB407	10	1.43×10^9 (male) 2.11×10^9 (female)	1, 8, 15	16, 43

Toxicology: NOAEL determined to be high dose

- No toxicity based on mortality, cage side/clinical observations, body weights, pulmonary function, and pathology
- Effects considered non-adverse due to the mild severity, lack of impact on health, and reversible on recovery

Biodistribution: Broad distribution and sustained expression in NHP lungs

- A significant percentage of airway epithelial cells KB407+ positive by microscopy; quantification based on 10 fields of view, high dose group, lungs collected on Day 16, one day after last dose
  - **59.6%** (n = 298/500) of ciliated cells (AC-Tubulin+) were KB407+ ***representative image below***
  - **17.4%** (n = 38/218) of club cells (SCGB1A1+) were KB407+
  - **8.0%** (n = 8/100) of goblet cells (MUC5AC+) were KB407+
  - Only 20.6% of KB407+ cells were also CD163+ suggestive of limited macrophage uptake
- Human *CFTR* expression also detected in lungs harvested on Day 43, 28 days after last dose



*KB407 IND cleared

Parry T, et al. Poster #541 at the 2021 North American Cystic Fibrosis Conference (NACFC). Virtual. November 1-5, 2021; Krystal Biotech. Data on file.

GLP, good laboratory practice; IND, Investigational New Drug; NHPs, nonhuman primates; NOAEL, no observed adverse effect level; PFU, plaque forming unit

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

Alpha-1 Antitrypsin Deficiency (AATD)

Monogenic disorder that leads to progressive lung disease

AATD[4]

- Alpha-1 Antitrypsin (AAT) is the most abundant serine protease inhibitor in human plasma and regulator of protease activity, in particular neutrophil elastase in lungs
- AATD is an autosomal co-dominant inherited genetic disorder resulting from mutations in *SERPINA1* gene encoding AAT; with misfolding mutations Pi*ZZ and Pi*SZ as the most common
- Genetic deficiency of AAT can result in unopposed neutrophil elastase activity, excessive degradation of elastin, collagen, and fibronectin and progressive pulmonary impairment

Unproven and Limited Treatment Options[4,5]

- There is no cure available for patients with AATD
- Standard of care is augmentation therapy, consisting of weekly IV infusions of AAT
- Multiple limitations with current treatment options: burdensome on patients and clinical benefit of augmentation therapy on lung function is not well defined

Severe AATD Prevalence[1-3*]

*Over **60,000** patients in the U.S.*

*Over **250,000** patients globally*

KB408 in Development as Redosable, Non-Invasive, Inhaled Gene Therapy to Enable Local AAT Expression in Lung

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

*Severe AATD defined as patients with Pi*ZZ genotype

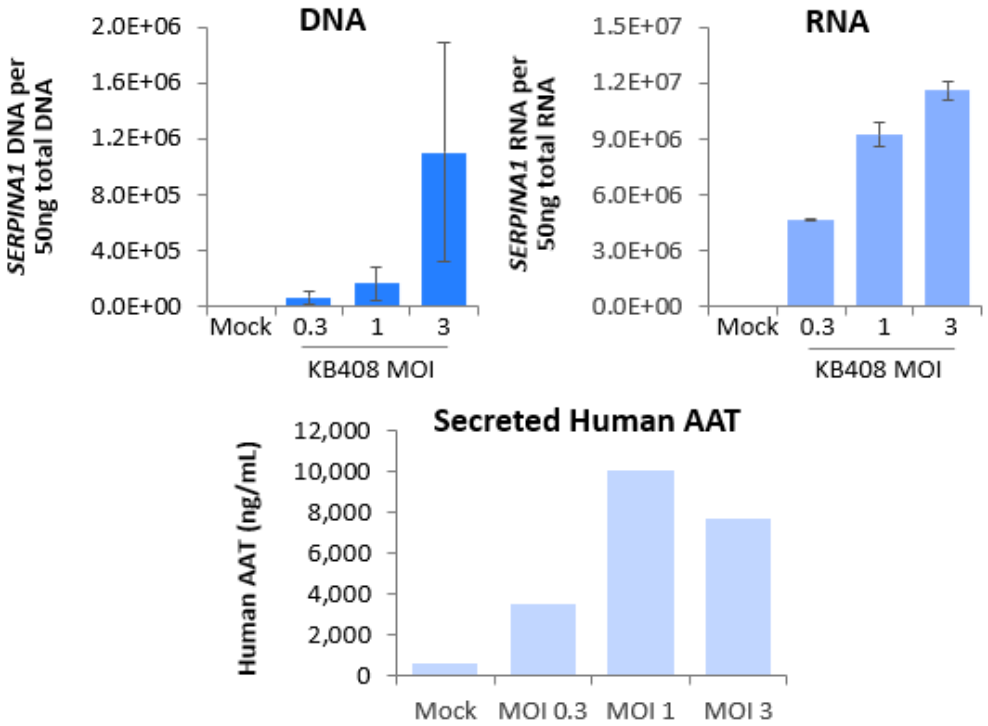
AAT, Alpha-1 Antitrypsin; AATD, Alpha-1 Antitrypsin Deficiency; IV, intravenous; U.S., United States

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

KB408 for AATD

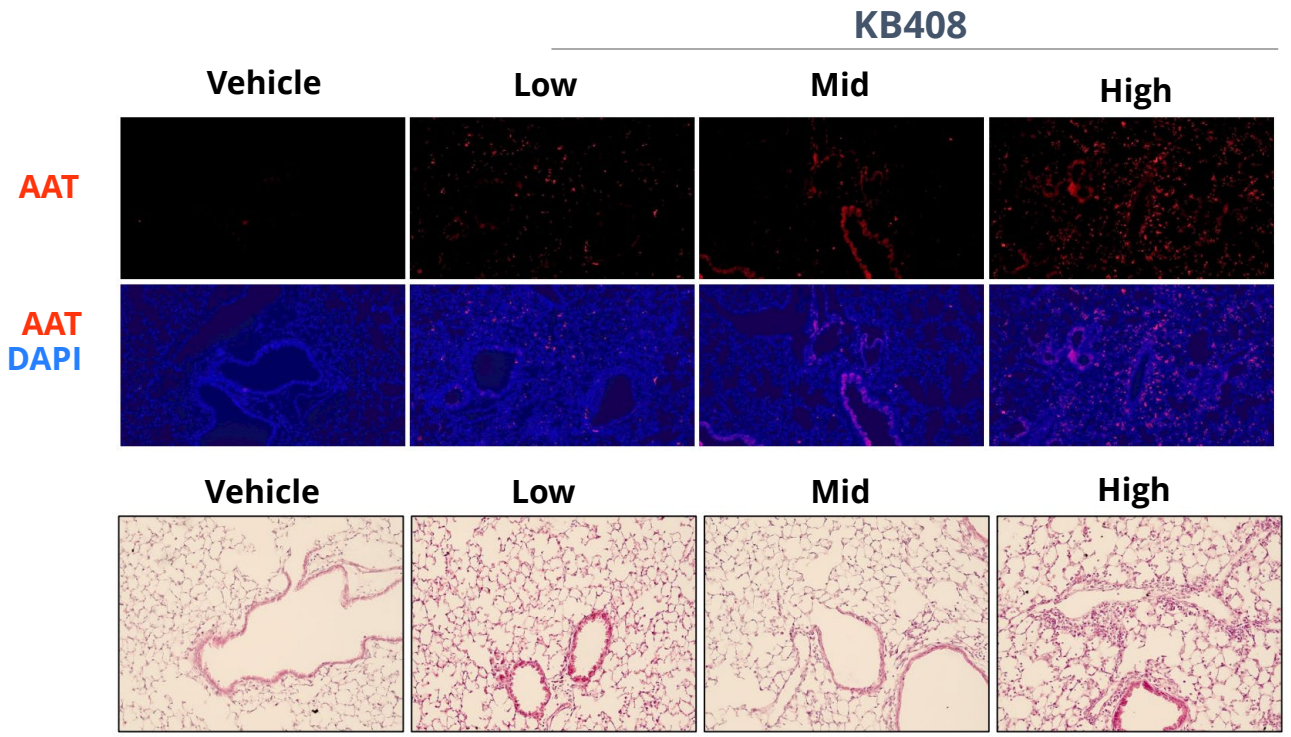
Dose-dependent expression of human AAT in clinically relevant cells and mouse lungs

Dose-dependent expression of AAT in primary human small airway epithelial cells



Widespread human AAT expression in mouse lungs without visible toxicity

- Mice received vehicle or KB408 intratracheally on Day 1 and Day 3, three dose levels
- Lungs collected on Day 4 for histology and AAT expression analysis by immunofluorescence
- Similar findings in *SERPINA1* deficient (*Serpina1*^{em3Chmu}) mice



Artusi S et al., Poster # 40. at the 2021 European Society of Gene and Cell Therapy

AAT, alpha-1 antitrypsin; AATD, DAPI, Alpha-1 Antitrypsin Deficiency; 4',6-diamidino-2-phenylindole; MOI, multiplicity of infection

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

Next Steps for Respiratory Pipeline

Ramping up clinical activity to evaluate first redosable inhaled gene therapies

KB407 for Cystic Fibrosis

- Conducting Phase 1 study in the U.S. to explore dose range and frequency

Phase 1/CORAL-1 Study

- Open-label dose-finding study to enroll up to 12 adults in three cohorts, receiving either single dose, or two or four daily doses
- Primary endpoint will be safety and tolerability, also assessing changes in lung function and *CFTR* expression by bronchoscopy
- Cohort 1 of the Phase 1 complete and working to initiate Cohort 2 shortly

KB408 for Alpha-1 Antitrypsin Deficiency

- IND cleared by the U.S. FDA and expect to initiate Phase 1 trial in 1H 2024

CFTR, cystic fibrosis transmembrane conductance regulator; IND, investigational new drug

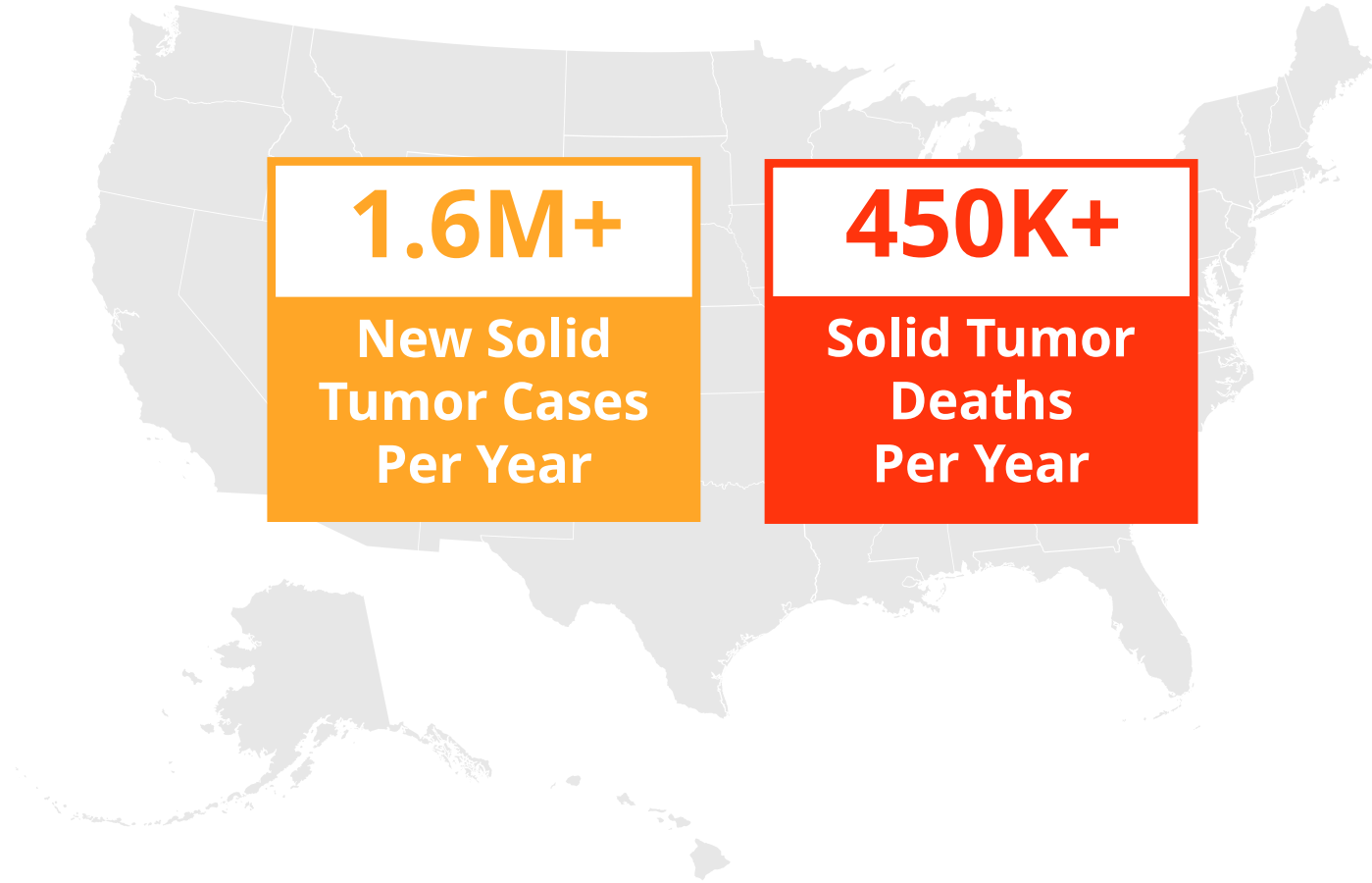
Other than VYJUVEK, all products described in this presentation are investigational therapies

Oncology Pipeline

Major Unmet Needs in Checkpoint Inhibitor (CPI) Refractory Solid Tumors

Solid Tumor Incidence and Mortality in U.S.

2023 SEER Estimates[1]



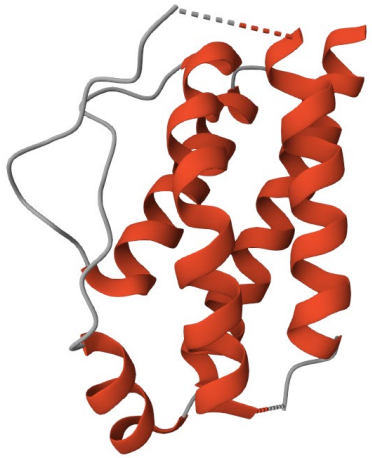
1. NCI SEER. 2023; https://seer.cancer.gov/statfacts/html/common.html [accessed July 20, 2023], combined estimates for incident cases and deaths from cancers of the anus, bladder, bone and joint, brain and nervous system, breast, cervix uteri, colon and rectum, esophagus, kidney and renal pelvis, larynx, liver and intrahepatic bile duct, lung and bronchus, melanoma, oral cavity and pharynx, ovary, pancreas, prostate, small intestine, stomach, testis, thyroid, uterus, and vulva

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

HSV-1 Based Vector Coded for the Local Delivery of Both IL-2 and IL-12

Cytokines with synergistic functions and therapeutic potential

IL-2

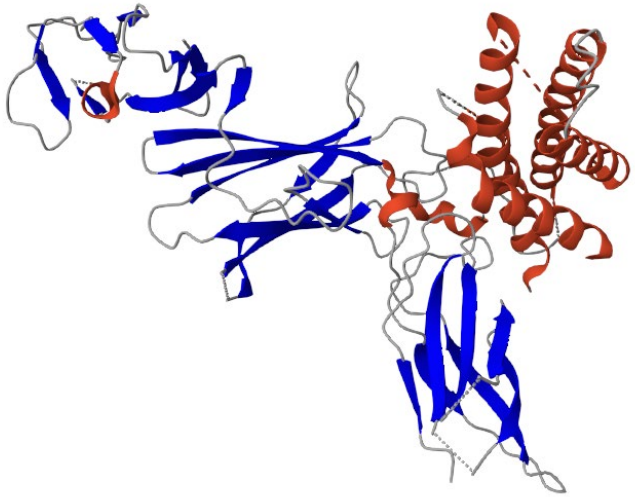


Expand and Activate Lymphocyte Population[1-3]

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

+

IL-12



Reinforce Cytotoxic Effector Functions[4,5]

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

1. IL-2 image from the RCSB PDB (RCSB.org) of PDB ID 1M47 [image generated July 20 2023]; 2. Jiang T, et al. *OncoImmnuology.* 2016; 5(6):e1163462; 3. Morgan DA, et al. *Science*. 1976; 193(4257):1007-1008; 4. IL-12 image from the RCSB PDB (RCSB.org) of PDB ID 1F45 [image generated July 20 2023]; 5. Lasek W, et al. *Cancer Immunol Immunother*. 2014; 63:419-35

IL-12, interleukin-12; IL-2, interleukin-2; NK, natural killer

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

Advantages of Replication-Defective HSV-1 Based Cytokine Delivery

Platform well suited to accomplish dual goals of targeted but sustained delivery of IL-2 and IL-12 to the tumor

Optimal vector platform to maximize cytokine expression and immune activation

- ✓ Efficiently transduces a wide variety of cell types maximizing reach within tumor
- ✓ DNA payload persists in transduced cells extending the window of cytokine expression
- ✓ Lack of replication avoids premature lytic cell death or host cell shutdown
- ✓ Redosability to further boost local cytokine expression
- ✓ Safety profile suitable for both **inhaled** or **intratumoral** administration

Krystal Biotech, Data on File.

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

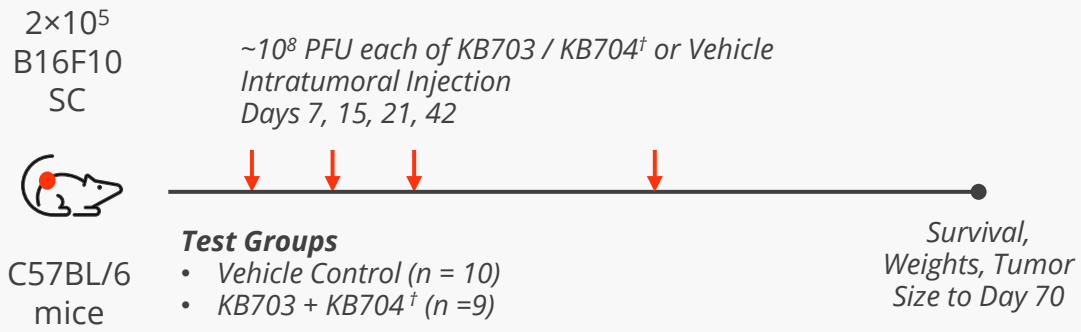
Intratumoral IL-12 and IL-2 Effective in Cold Syngeneic Mouse Tumor Model

Clear antitumor effect and survival benefit in checkpoint inhibitor refractory B16F10 tumor model

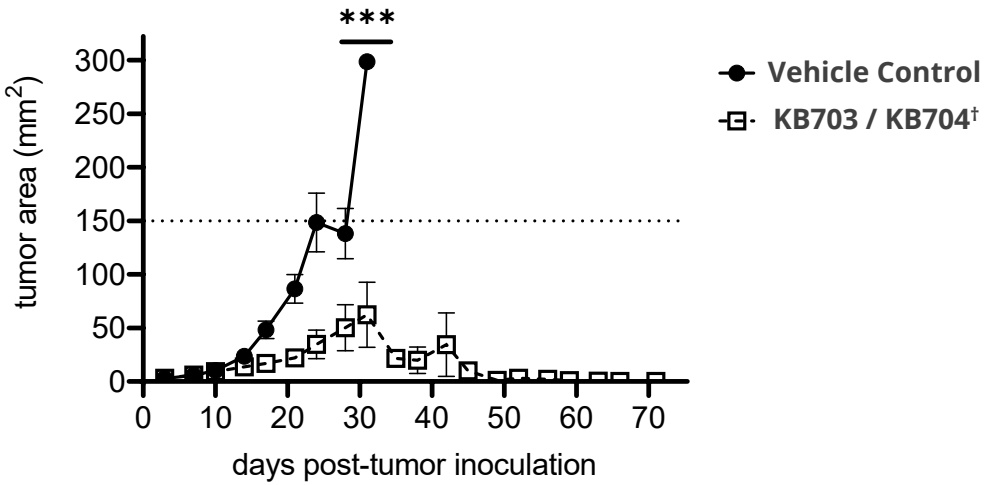
Single Flank B16F10 Melanoma Model

- B16F10 is a subclone of the B16 cancer cell line originally derived from the skin of a C57BL/6 mouse with melanoma
- B16F10 tumors are highly aggressive and minimally responsive to immunotherapy, including refractory to PD-1 targeting CPI
- Among the most stringent melanoma cell lines for the evaluation of candidate immunotherapeutics

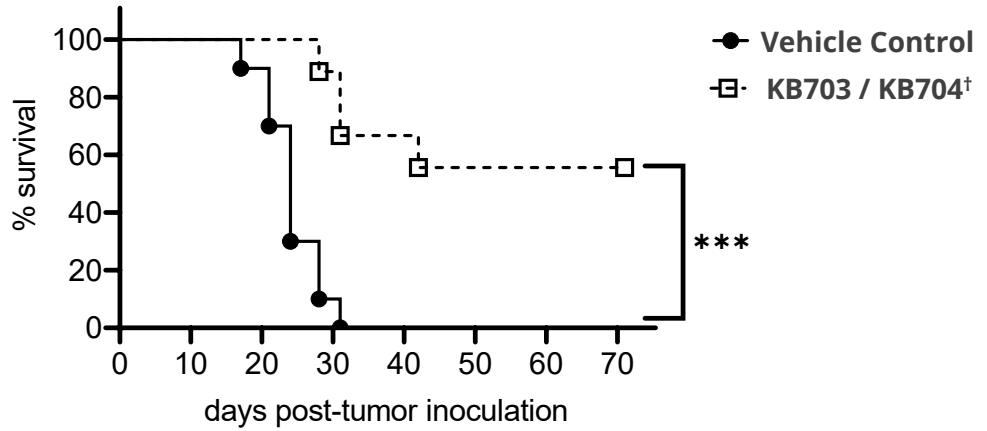
Study Design



Injected Tumor Size



Survival



Krystal Biotech, Data on File.

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

IL-12, interleukin-12; IL-2, interleukin-2; PFU, plaque forming unit; SC, subcutaneous

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

***p<0.001

Evidence of Systemic Immune Response with Intratumoral IL-12 and IL-2

Antitumor effect and survival benefit in dual flank B16F10 tumor model

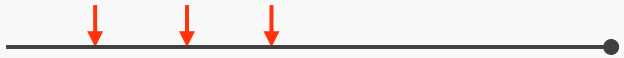
Dual Flank B16F10 Melanoma Model

- Dual flank model mimics metastatic, checkpoint refractory melanoma seen in late line clinical treatment setting
- Only tumor in first flank is injected to evaluate impact of systemic response on secondary tumor outgrowth

Study Design

Day 0
2×10^5 B16F10
First Flank SC

~10^8 PFU each of KB703 / KB704† or Vehicle
Intratumoral Injection First Flank Only
Days 7, 15, 21



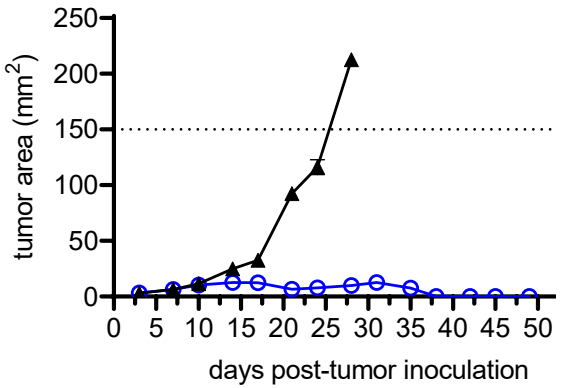
Survival, Weights, Tumor Size to Day 49

Day 4
1×10^5 B16F10
Second Flank SC

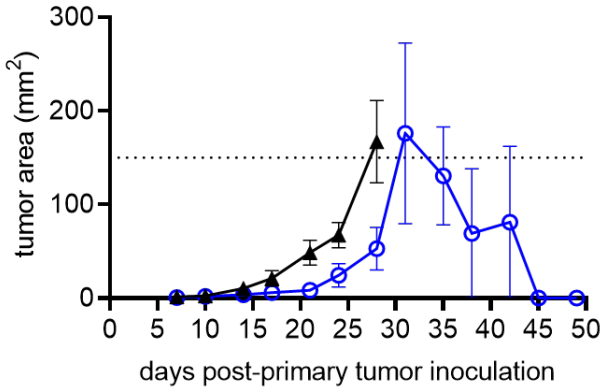
C57BL/6 Mice

Test Groups
- *Vehicle Control (n = 5)*
- *KB703 + KB704† (n =5)*

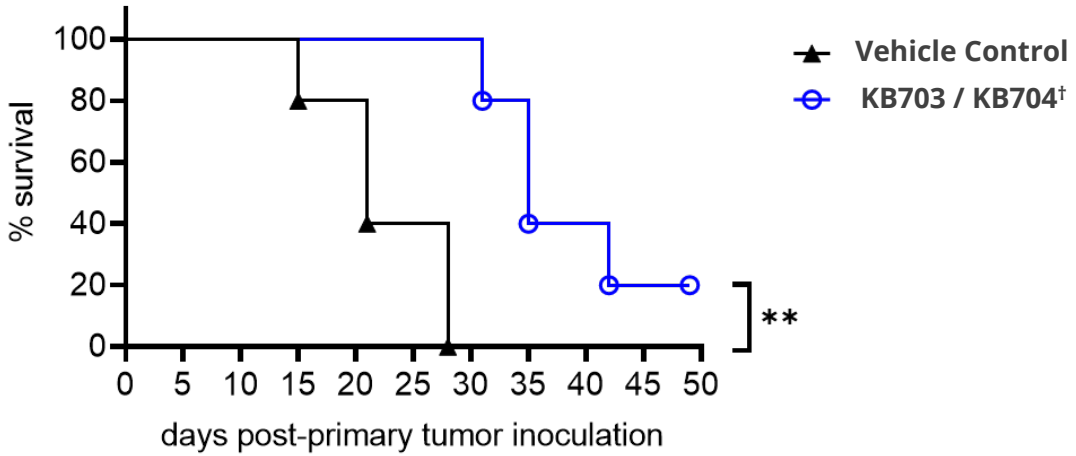
Injected Tumor Size



Secondary Tumor Size



Survival



Krystal Biotech, Data on File.

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

IL-12, interleukin-12; IL-2, interleukin-2; PFU, plaque forming unit; SC, subcutaneous

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

**p<0.01

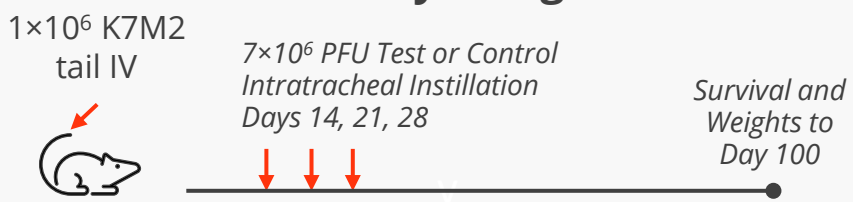
Lung Delivery Effective in Metastatic Osteosarcoma Model

Local delivery of IL-12 and IL-2 confers clear survival benefit in otherwise lethal, metastatic osteosarcoma

Metastatic K7M2 Osteosarcoma Model

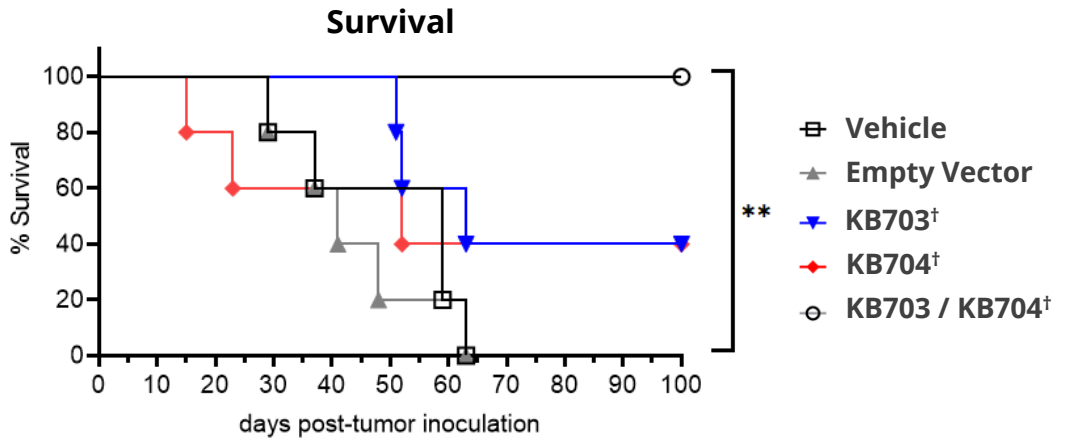
- K7M2 is an osteoblast cell line derived from bone of mouse with spontaneous osteosarcoma[1]
- Considered highly aggressive with pulmonary metastatic rate of over 90% in mice[1]
- Previously shown to be non-responsive to PD-1/PD-L1 targeting therapies, partial benefit from combo therapies[2]

Study Design

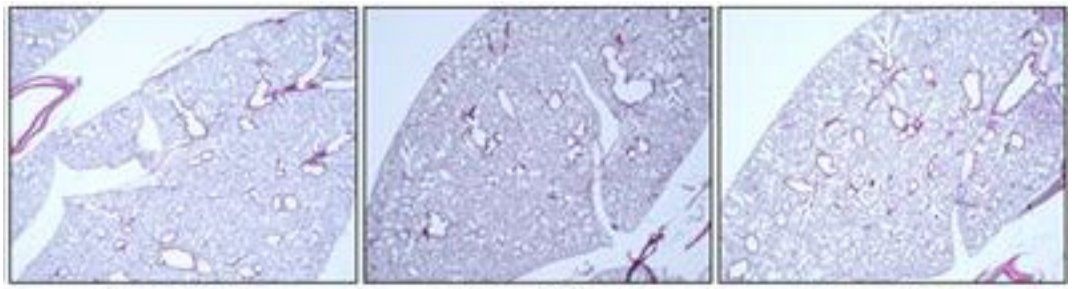


Test Groups

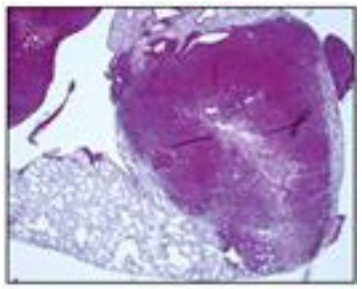
- *KB703 Alone† (n = 5)*
- *KB704 Alone† (n = 5)*
- *KB703 + KB704† (n = 5)*
- *Vehicle Control (n = 5)*
- *Naïve Control (n = 5)*



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.

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

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

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

**p<0.01

KB707-01 Intratumoral Phase 1 Study

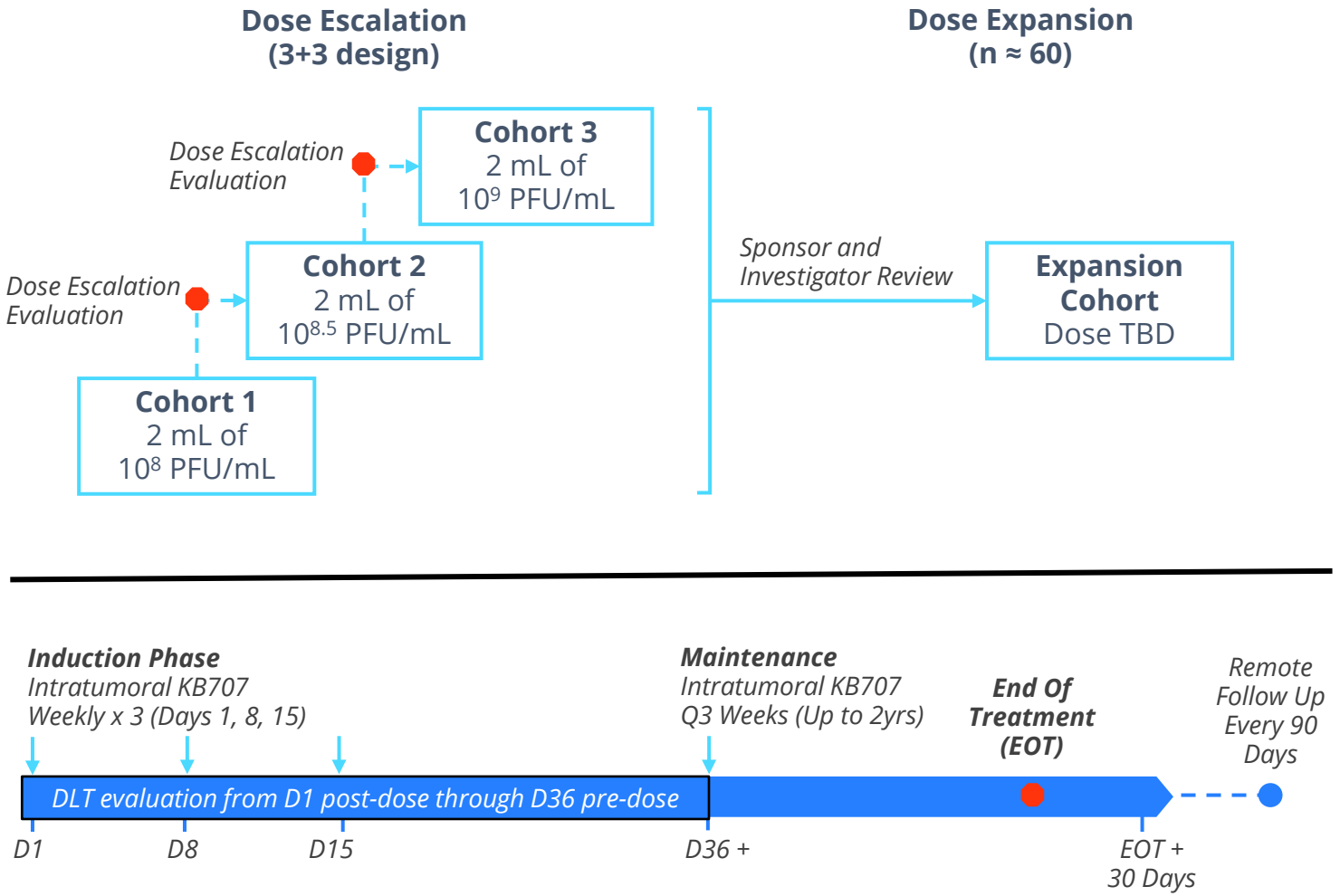
Open-label study to assess safety, tolerability, and preliminary efficacy

Study Objectives

- Evaluate the safety and tolerability
- Evaluate for maximum tolerated dose (MTD)
- Evaluate preliminary efficacy as assessed by multiple measures including
  - Objective response rate (ORR)
  - Progression free survival (PFS)
  - Overall survival (OS)
- Assess immunological effect of KB707 in blood and tumor

Key Enrollment Criteria

- Age ≥ 18 years with histologically confirmed locally advanced or metastatic solid tumor who has relapsed on or are refractory to standard of care.
- At least one measurable and injectable tumor accessible by transcutaneous route, including but not limited to
  - Melanoma
  - Cutaneous Squamous Cell Carcinoma
  - Basal Cell Carcinoma



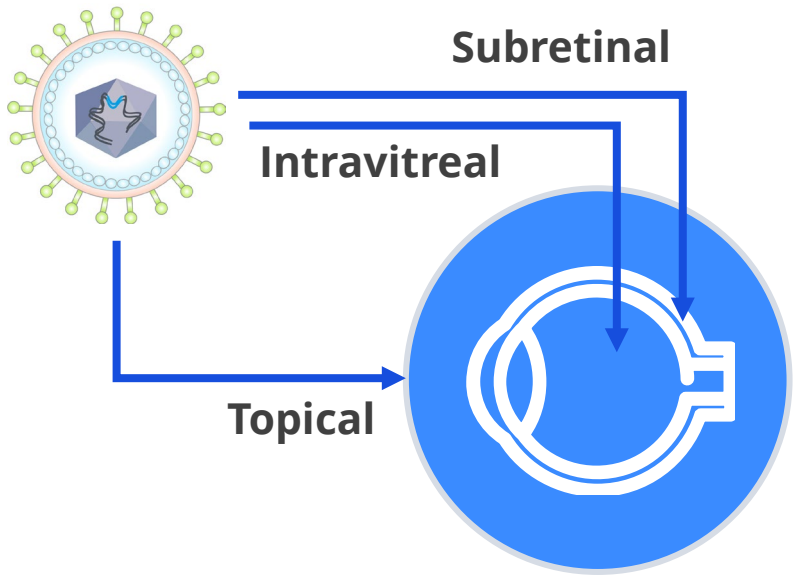
DLT, dose limiting toxicity; EOT, end of treatment; MTD, maximum tolerated dose; ORR, objective response rate; OS, overall survival; PFS, progression free survival; PFU, plaque forming unit; TBD, to be determined

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

Ophthalmology Pipeline

Potential for Pipeline Expansion in Ophthalmology

Pursuing opportunities to leverage unique attributes of HSV-1 platform including large cargo capacity



Current Gene Therapy Pipeline Dominated by Single Vector

- AAVs have had success delivering small genes to back of the eye but many challenges remain
- Small cargo capacity is biggest limitation of AAVs; unable to address many large gene inherited retinal disorders (IRDs) and limits potential to deliver more complex gene editing machinery or regulatory elements
- Clinical applications of AAV have also been primarily focused on the retina; new vectors needed to target all clinically relevant cells of the eye
- Immunotoxicity a persistent concern with AAVs

HSV-1 is a Highly Differentiated, Large Cargo Alternative

- HSV-1 exhibits natural tropism for epithelial and neuronal cells of the eye
- Cargo capacity to address the most common large gene IRDs
- Currently exploring both front and back of the eye delivery, repeat dosing
- Topical, repeat application to the front of eye both safe and effective in clinic under compassionate use

Near-term opportunity to expand utility for ophthalmic B-VEC in DEB followed by potential pipeline expansion to target unmet needs in front and back of eye

Ghobara HH, et al. *Clin Ophthalmol.* 2022;16:1753–1771

AAV, adeno-associated virus; B-VEC, beremagene geperpavec; DEB, dystrophic epidermolysis bullosa; HSV-1, herpes simplex virus type 1; IRD, inherited retinal disorder

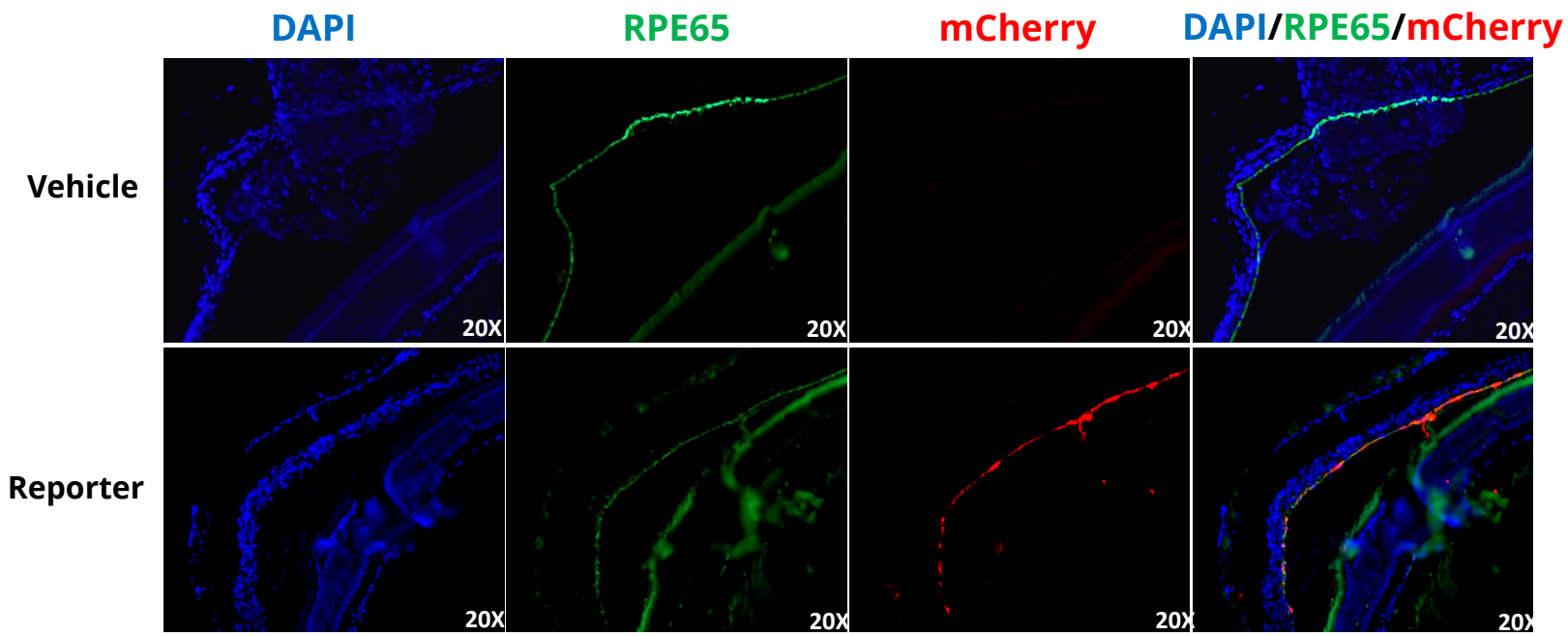
Other than VYJUVEK, all products described in this presentation are investigational therapies

Retinal Pigment Epithelial Cells Transduced via Subretinal Route

Pilot low dose study suggests potential to target IRDs caused by defects in large genes

Pilot Subretinal Delivery Study

- Single subretinal injection study in rats
- Rats received single subretinal injection of Krystal mCherry reporter virus or vehicle (n = 3 per group)
- Eyes collected 24 hours after virus or vehicle injection for histology and immunofluorescence assessments



Reporter virus signal colocalized to RPE65+ cells after subretinal delivery

Further exploration of intravitreal and subretinal routes underway

Krystal Biotech. Data on file

IRD, inherited retinal disorder

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

Next Steps in Ophthalmology

Expedite clinical development of ophthalmic B-VEC while building data to support pipeline expansion

B-VEC for Ocular Complications of DEB

- Plan on meeting with FDA to align on development path for ophthalmic formulation

Pipeline Expansion

- Additional preclinical studies underway to evaluate platform compatibility with various routes of administration

Sample Indication: Stargardt Disease[1-4]

- Inherited retinal disorder primarily caused by mutations in *ABCA4*
- Leads to progressive vision loss and blindness, no FDA approved therapy
- *ABCA4* is a large gene that does not fit in currently used AAV vectors

26K
Estimated Patients in U.S.*

37K
Estimated Patients in EU Major Markets**

1. Cicinelli MV, et al. *Clin Optom (Auckl).* 2019;11:151-165; 2. Runhart EH, et al. *Acta Ophthalmol.* 2022;100:395-402; 3. Bauwens M, et al. *Genet Med.* 2019;21:1761-1771; 4. Schulz H, et al. *Investig Ophthalmol Vis Sci.* 2017;58:394-403

*Assumed U.S. population of 330M, 1:10K prevalence, 80% *ABCA4;* ** Assumed EU population of 457M focused on major markets only (includes EU-4 + UK, Nordics, Benelux, Ireland, Portugal, Switzerland, Poland, Austria), 1:10K prevalence, 80% *ABCA4*

ABCA4, ATP-binding cassette, sub-family A, member 4; B-VEC, beremagene geperpavec; DEB, dystrophic epidermolysis bullosa; EU, European Union; FDA, U.S. Food and Drug Administration;

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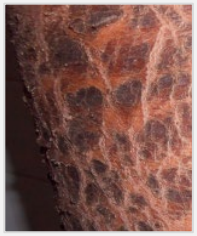
Dermatology Pipeline

KB105, Krystal's Next Clinical Stage Asset in Dermatology

Complementary product for rare disease of the skin significantly derisked by VYJUVEK clinical success

Autosomal Recessive Congenital Ichthyosis Associated with TGM1 Mutations (TGM1-ARCI)[1-8]

- The most common form of ARCI is caused by a mutation in the *TGM1* gene encoding a protein that is essential for the proper formation of the skin barrier
- The condition is characterized by thick, dry, scaly skin, increased trans-epidermal water loss, risk for dehydration, sepsis, and skin malignancies
- There are **no** approved treatments for TGM1-ARCI
- Topical and systemic retinoids and time-consuming supportive treatments are the most commonly used treatments of care

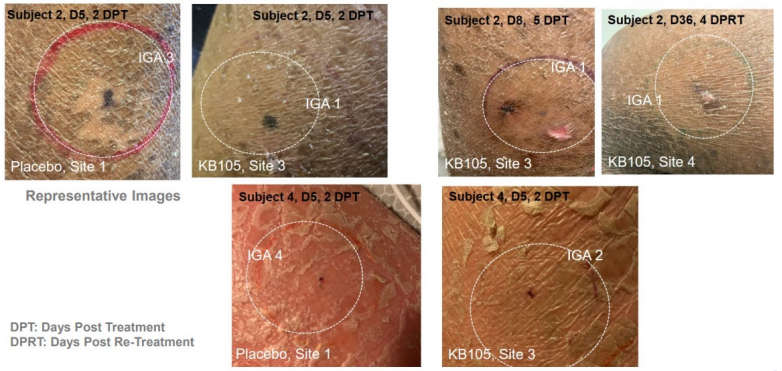


2K-6K

Estimated TGM1-ARCI Patients in U.S. and Europe

KB105: Clinical Stage Asset in Phase 1/2 for TGM1-ARCI[9,10]

- In Phase 1 study, KB105 treatment restored functional TGM1 protein expression and activity in all treated sites
- Phenotypic evaluation limited by small treatment areas, but KB105 treated areas showed reduced reversion to scaling phenotype
- No drug-related AEs noted and no HSV-1 or TGM1 antibodies



Next Step: Initiate Phase 2 cohort in 2024

1. Rodriguez-Pazos L, et al. *Actas Dermosifiliogr.* 2013;104(4):270–84; 2. Dreyfus I, et al. *Orphanet J Rare Dis.* 2014;9:1; 3. Hernandez-Martin A, et al. *J Am Acad Dermatol.* 2012;67(2):240–4; 4. Pigg M, et al. *Eur J Hum Genet.* 1998;6(6):589–96; 5. Pigg M, et al. *Acta Dermato-Venereologica.* 2016;96(7):932–37; 6. Foundation for Ichthyosis & Related Skin Types (FIRST); 7. National Organization for Rare Disorders (NORD); 8. Richard G. Autosomal Recessive Congenital Ichthyosis. In: Adam MP, et al. *GeneReviews® [Internet].* Updated 2017 May 18; 9. Milstone LM, et al. *Arch Dermatol.* 2012;148(9):1080-1; 10. Paller A, et al. Oral presentation at Society for Investigative Dermatology (SID) 2020 Annual Meeting. Virtual. May 13-16, 2020.

ARCI, autosomal recessive congenital ichthyosis; TGM1, transglutaminase 1; U.S., United States

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Aesthetics Pipeline

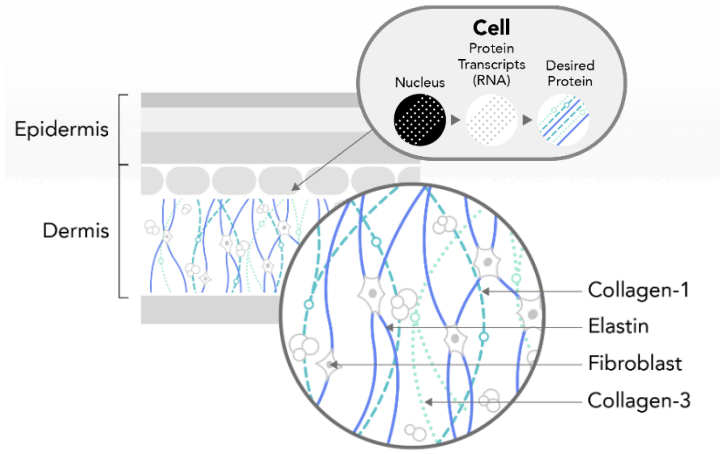
JEUNE

A wholly owned subsidiary of Krystal Biotech, Inc.

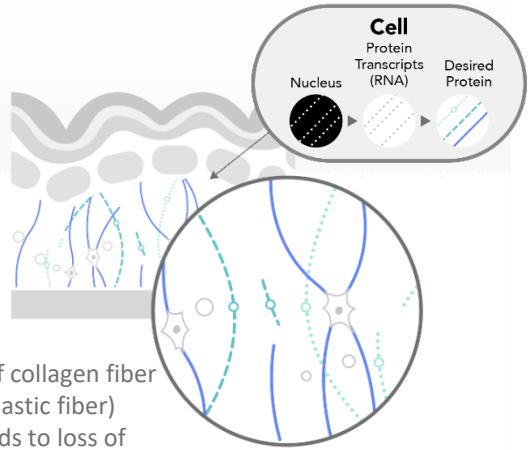
Characteristic Look of Aging Caused by Declining Levels of Key Proteins in Skin's Extracellular Matrix

- 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

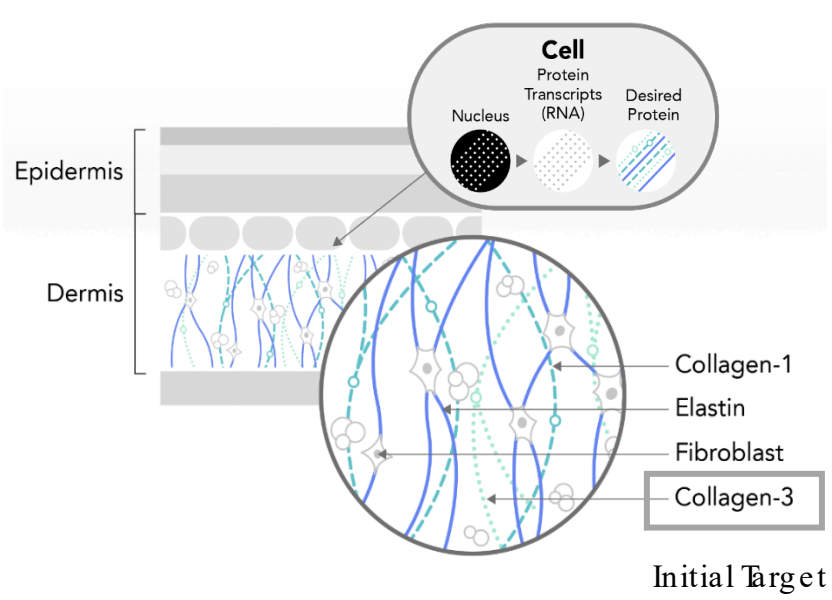
Jeune Pipeline and Lead Program KB301 Aim to Restore Key Skin Proteins

Pipeline

Aesthetics

Product	Gene	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Commercial
KB301	Type III collagen	Lateral Canthal Lines at Rest						
KB302	Type I collagen	TBD						
KB303	Elastin	TBD						
KB304	Type III collagen & Elastin	TBD						
KB305	Type IV collagen	TBD						

Lead Program KB301



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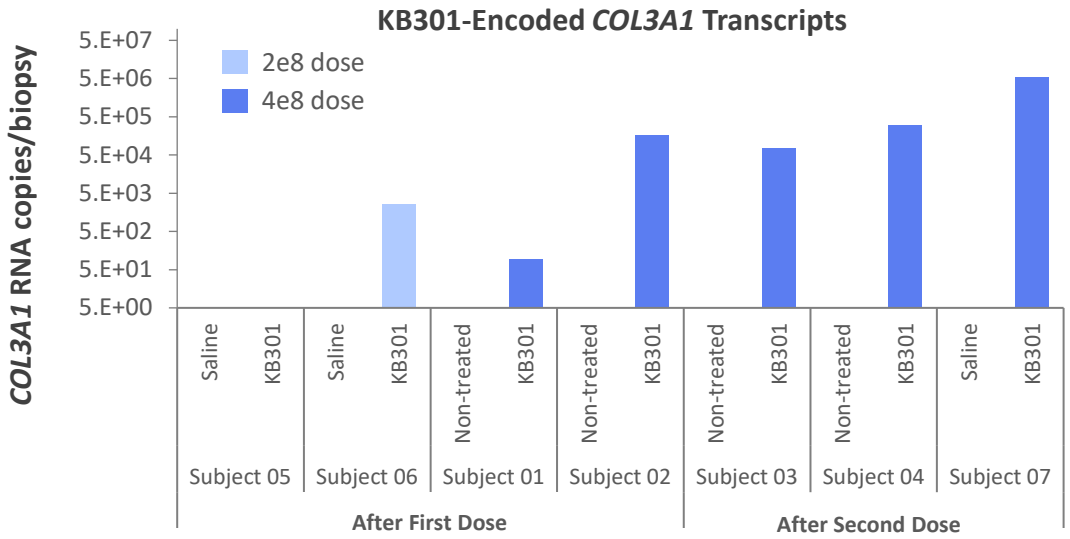
KB301 Phase 1 Cohorts 1 and 2

Safety, Gene Delivery, and Early Signs of Efficacy and Durability All Established

Phase 1 Cohort 1[1]

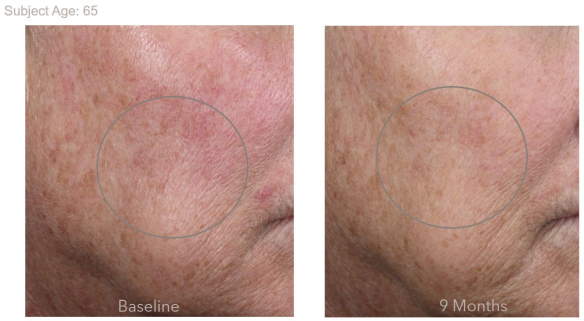
- Open label, dose ranging study designed to evaluate safety and gene delivery after repeat (Day 0, Day 30) intradermal injections to buttocks (1e8, 2e8, 4e8 PFU)
- **Safety:** Repeated intradermal injections of KB301 were well-tolerated; adverse events were transient, mild to moderate injection site or biopsy site reactions
- **Delivery:** KB301-encoded *COL3A1* expression measurable at the mid and high dose; expression was evident by day 2 following the first dose



Phase 1 Cohort 2[2,3]

- Evaluated safety and preliminary efficacy of low and high dose KB301 injections to upper / lower cheeks and knees, injection sites (n = 54) randomized 2:1
- **Safety:** Repeat administration of KB301 well-tolerated across subjects with minimal injection site reactions, all of which resolved within 3-5 days
- **Efficacy:** Treatment with KB301 associated with improved subject satisfaction scores across all three areas compared to placebo
- **Durability:** Subset of lower cheek injection sites (n = 13) followed up out to 9 months; both subject satisfaction and investigator assessments show benefit sustained up to 9 months after last dose

Representative Durability Result



1. Krishnan S et al., Society for Investigative Dermatology Annual Meeting 2021; 2. Guide S. American Academy of Dermatology Annual Meeting 2022; 3. Krystal Biotech. Data on file

COL3A1, collagen type III alpha 1 chain; PFU, plaque forming unit

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Ongoing KB301 Phase 1 Cohort 3

First evaluation of efficacy in target indication of lateral canthal lines at rest

Target Indication: Lateral Canthal Lines (LCL) at Rest

- Improvement of LCL at rest is overwhelmingly sought by subjects and physicians
- There are currently **no** FDA-approved injectable aesthetic drugs for LCL at rest
- Commercially available injectables are not well suited to address the demand for aesthetic treatments of LCL at rest
  - **Neurotoxins:** Indicated for treatment of dynamic but not static LCL
  - **Fillers:** Not well suited for fine, delicate skin around the eye
- Based on KB301 mechanism of action, clinical data generated to date, and current treatment landscape, LCL at rest selected as target indication of KB301
- Phase 1 Cohort 3 underway to evaluate safety and preliminary efficacy of KB301 in LCL at rest and inform Phase 2 design

Phase 1 Cohort 3 Design

- Open-label, single center study enrolling up to 20 subjects
- Subjects will receive either low or high dose KB301, administered bilaterally to the lateral canthal regions, on Days 0, 7, and 14
- Subjects will return for monthly follow up for three months
- Primary endpoint will be safety and tolerability, and both investigator and subject will assess aesthetic improvement

Phase 1 Cohort 3 readout expected in 1H 2024

FDA, U.S. Food and Drug Administration; LCL, lateral canthal lines

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Developing Genetic Medicines for Rare Diseases