Krystal

Developing Genetic Medicines for Rare Diseases

June 2023

Forward Looking Statement

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™, including efforts to bring VYJUVEK to market in the United States, Europe, Japan and elsewhere, and the market opportunity for and the potential market acceptance of VYJUVEK; the Company's technology platform; the development and commercialization of the Company's product candidates; conduct and timelines of preclinical and clinical trials; the 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, and efforts to bring the Company's product candidates to market; the market opportunity for and the potential market acceptance of the Company's product candidates; the Company's plans to pursue research and development to expand its product pipeline; 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.

VYJUVEK is a herpes-simplex virus type 1 (HSV-1) vector-based gene therapy indicated for the treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa

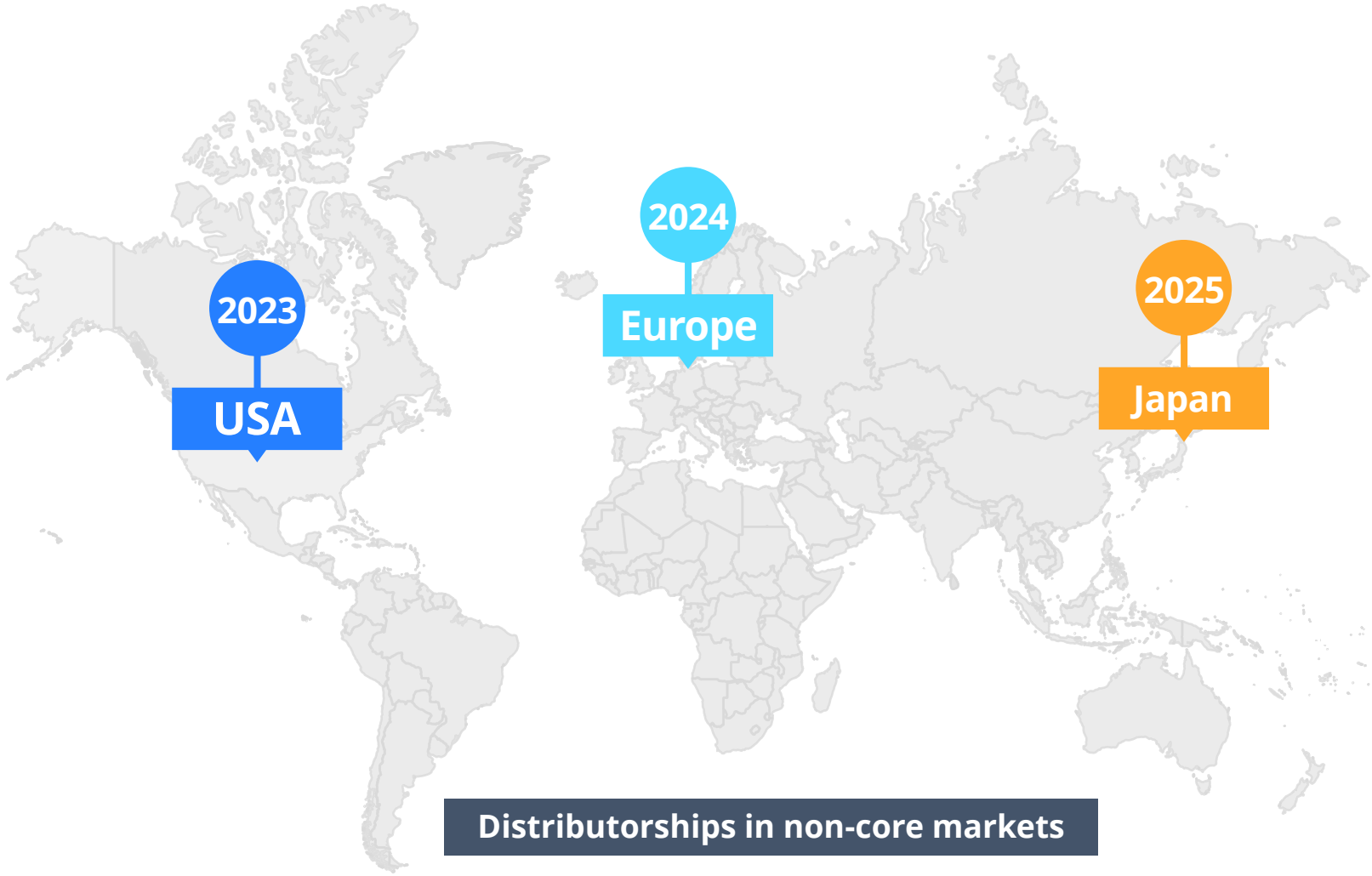
FDA approved on May 19, 2023

Vyjuvek™

beremagene geperpavec-svdt

Commercial Strategy Focused on Major Rare Disease Markets

US launch in 2023 followed by direct expansion to EU and Japan and distributorship agreements in non-core markets



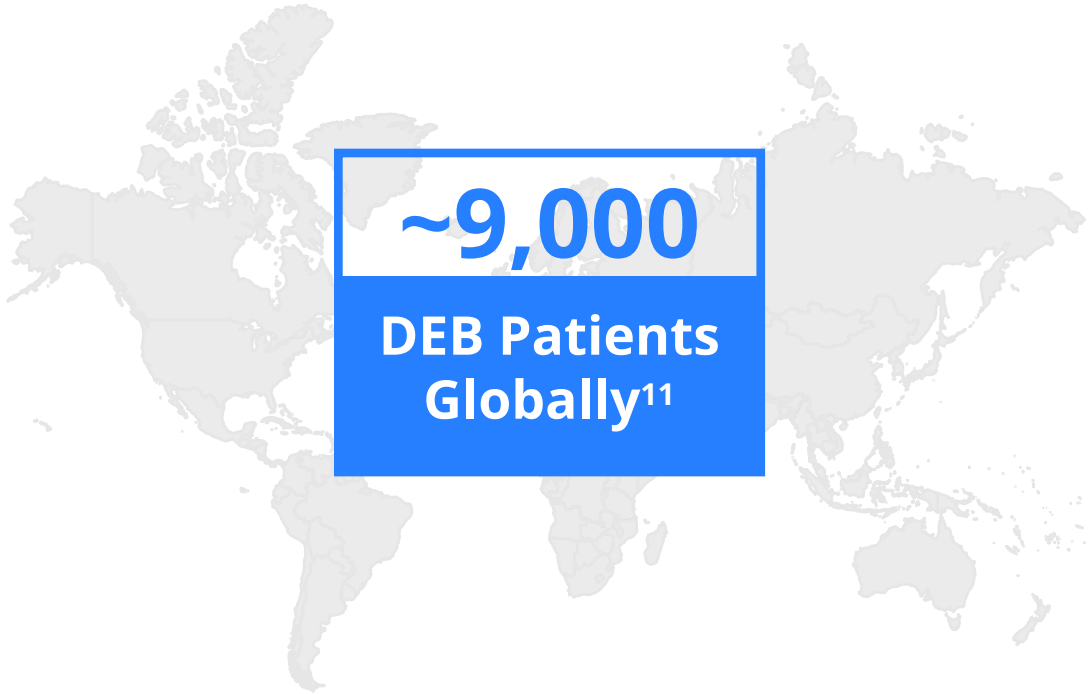
Over $750M

Estimated Global Market Opportunity

Vyjuvek™
beremagene geperpavec-svdt

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 US

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

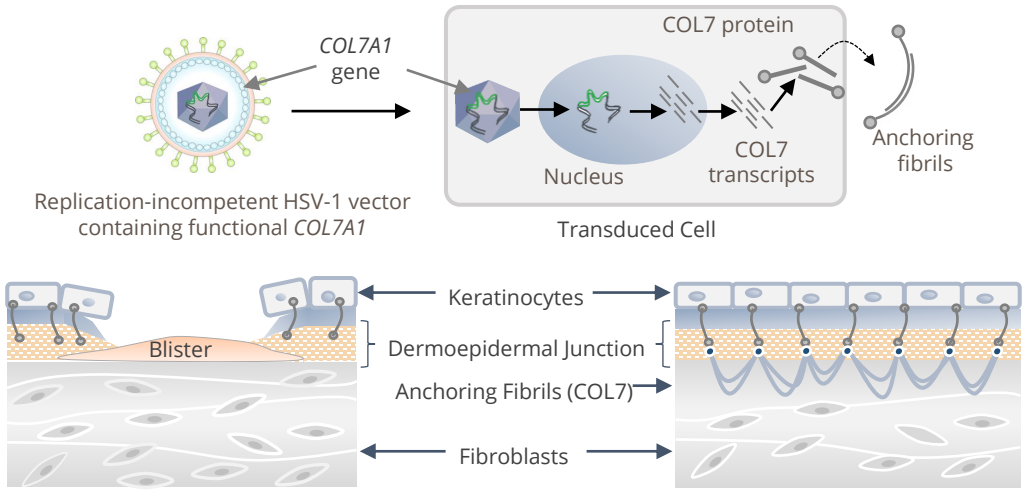
COL7, type VII collagen; DEB, dystrophic epidermolysis bullosa

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

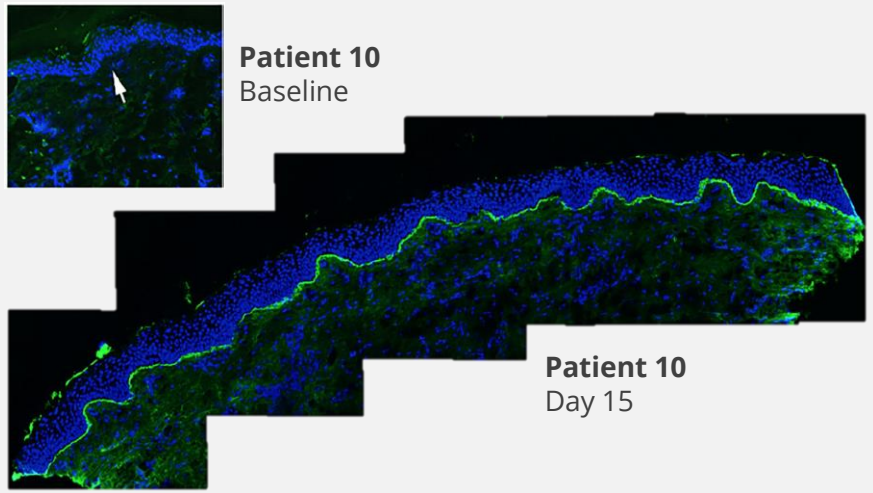
VYJUVEK Mechanism of Action

- 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

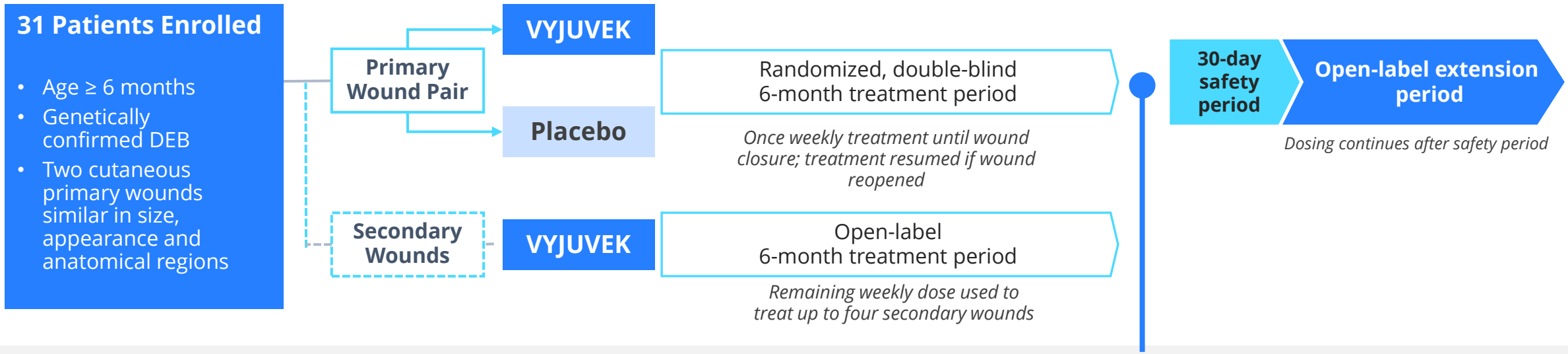
- Representative data from patient in Phase 1/2 study assessing COL7 deposition in the skin by immunofluorescence (in green)[3]
- Strong, properly localized COL7 signal detected in treated skin
- Anchoring fibril formation also detected by electron microscopy



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; 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 intent-to-treat (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

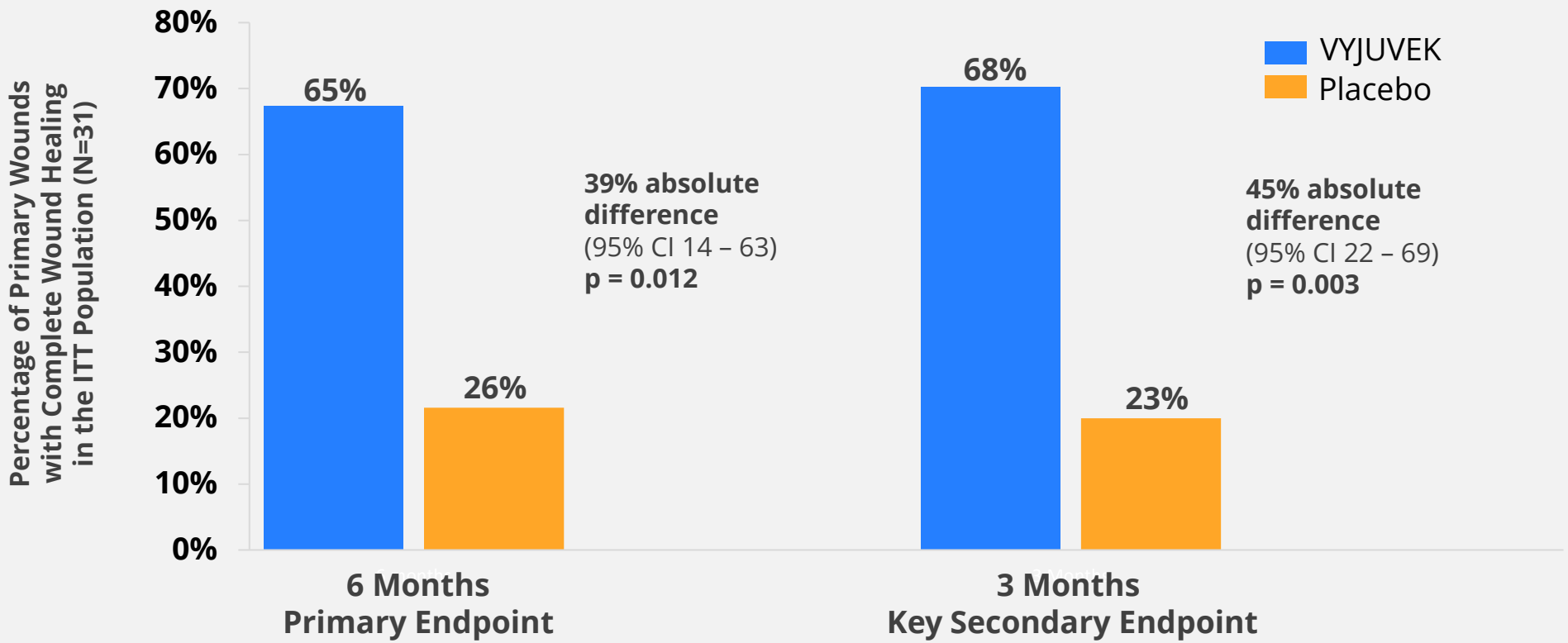
Guide SV, et al. *N Engl J Med.* 2022; 387(24):2211-9

DEB, dystrophic epidermolysis bullosa

†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

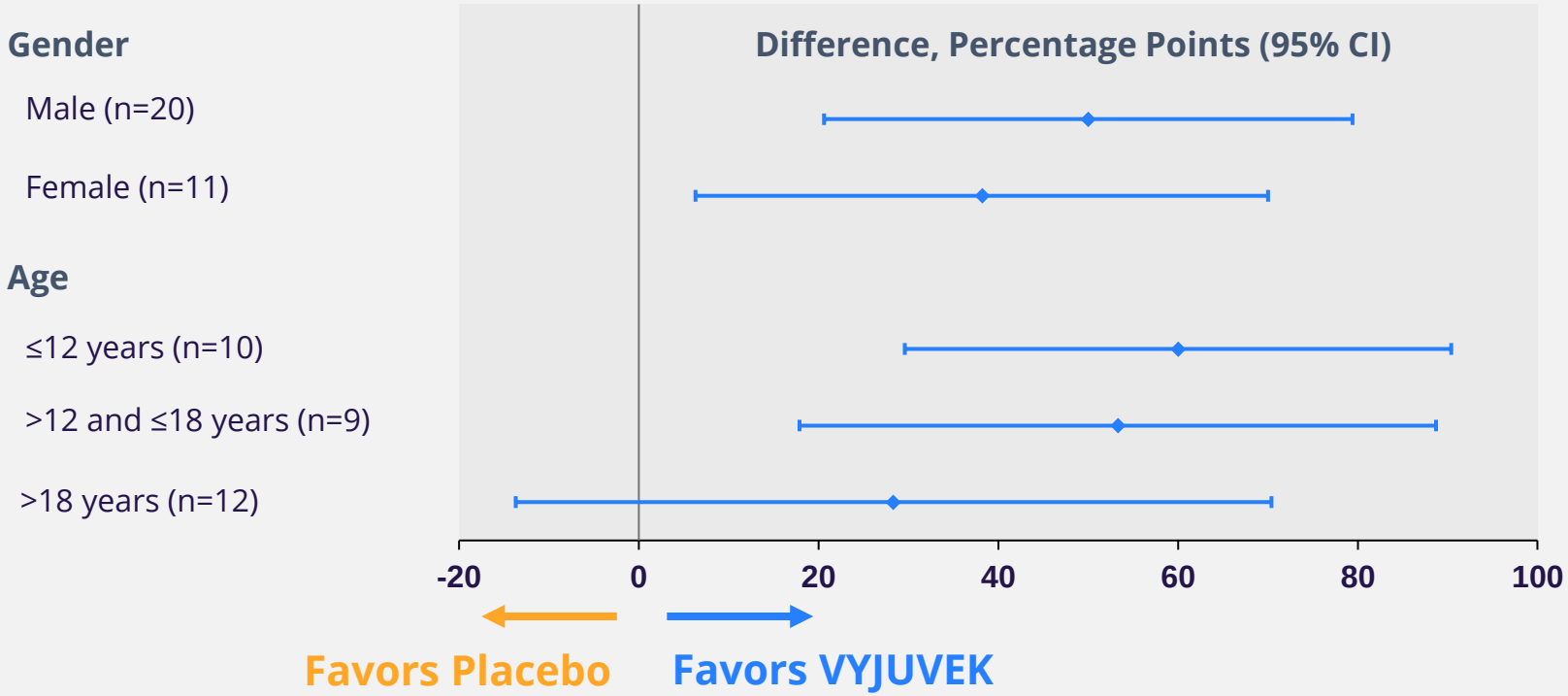
Guide SV, et al. *N Engl J Med.* 2022;387(24):2211-9, Data in figure based on ITT population (imputed); CIs are based on exact McNemar's test

†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

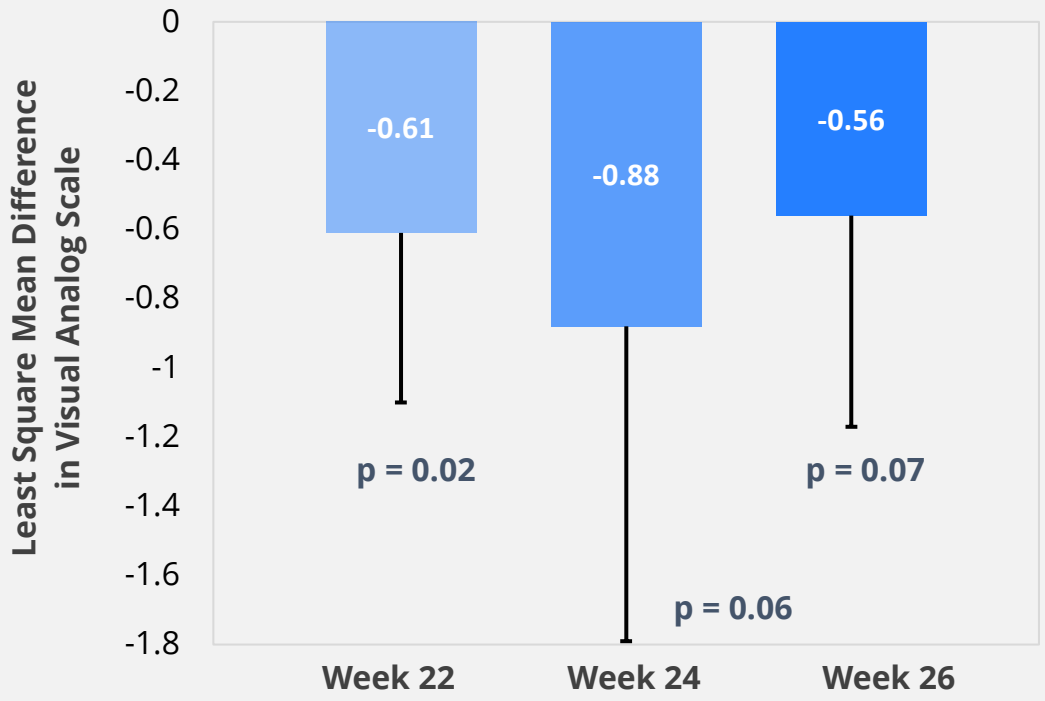
Guide SV, et al. *N Engl J Med.* 2022;387(24):2211-9, Data in figure based on ITT population (imputed); CIs are based on exact McNemar's test

CI, confidence interval; ITT, intent-to-treat

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

Fully Integrated

In-House Manufacturing Capacity and Expertise

Two US GMP facilities with capacity to support global VYJUVEK product needs and future growth

ANCORIS Facility

- ~21,100 sq. ft. GMP facility
- Capabilities: Drug Substance, Drug Product, GMP Storage, Bulk Packaging, Waste Handling, Environmental Monitoring, and Logistics
- Fully equipped AD/DC labs
- Validated methods for tittering/release
- Built to support global VYJUVEK launch

ASTRA Facility

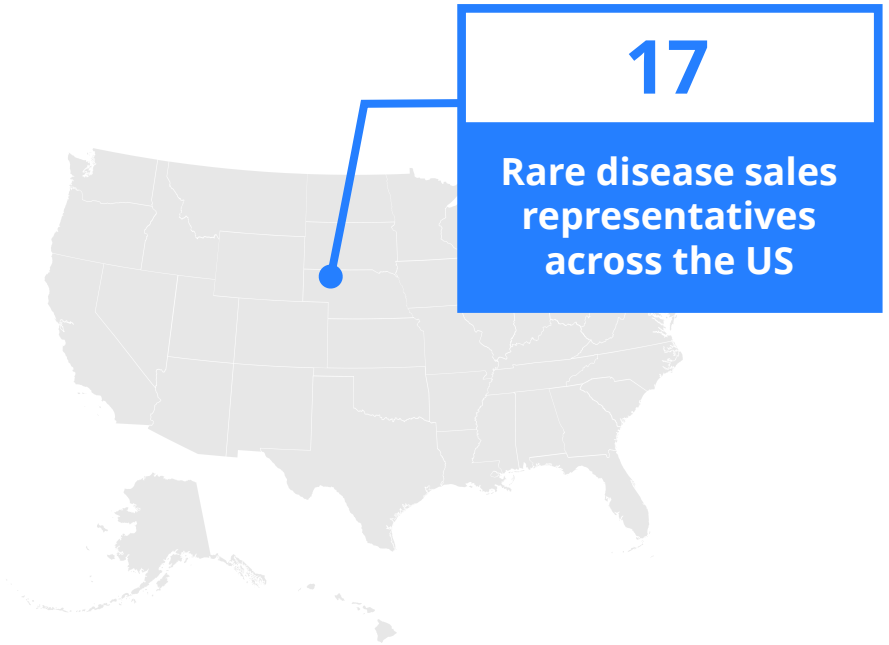
- ~155,000 sq. ft. GMP facility
- Capabilities: Process Development, MVB, Drug Substance, Drug Product, Packaging, Analytical Testing, Storage, General Office Space, GMP Storage, Bulk Packaging, Waste Handling, Environmental Monitoring, and Logistics
- Operational in H1 2023
- Able to scale up and scale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

GMP, good manufacturing practice; MVB, master virus bank

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

Commercial Readiness

US commercial infrastructure established and operational



Field team is supported by 10+ patient access, community education, and regional medical directors with extensive rare disease, gene therapy and managed care/payer expertise

Patient Support and Genetic Testing Programs

Decode DEB™

Krystal CONNECT™
Personalized Support Services

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 is relatively complex virus with 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 preclinical or 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 live 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

Krystal Pipeline

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

	Indication	Payload	Preclinical	Phase 1/2	Phase 3	Upcoming Milestone(s)
Vyjuvek™ beremagene geperpavec-svdt	Dystrophic epidermolysis bullosa (DEB)	*COL7A1*	**FDA Approved May 2023**			File MAA in H2 2023

Therapeutic Area	Product	Indication	Payload	Preclinical	Phase 1/2	Phase 3	Upcoming Milestone(s)
Dermatology	**KB105**	Autosomal recessive congenital ichthyosis (ARCI)	*TGM1*				Initiate Phase 2 mid 2023
	KB104	Netherton syndrome	*SPINK5*				File IND in H2 2023
	Additional program(s) targeting dermatology indications						
Respiratory	**KB407**	Cystic fibrosis	*CFTR*				Phase 1 FPI in H1 2023
	KB408	Alpha-1 antitrypsin deficiency (AATD)	*SERPINA1*				File IND in H2 2023
	Additional program(s) targeting respiratory indications						
Ophthalmology	**Ophthalmic B-VEC**	Ocular complications of DEB	*COL7A1*				Meet with FDA
	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

Opportunity and Milestones

VYJUVEK Approval is Springboard for Growth

First approval to drive near-term revenue growth and validates differentiated, wholly-owned platform

Vyjuvek™ beremagene geperpavec-svdt

First Commercial Product VYJUVEK Approved by FDA for DEB

- ✓ First FDA approved redosable gene therapy
- ✓ Addresses genetic cause of DEB with clear evidence of molecular correction
- ✓ Robust clinical benefit established in Phase 3 double-blind RCT
  - **Durable Efficacy:** Significant improvements in wound closure at 3 and 6 months
  - **Well-Tolerated:** Minimal related AEs, no drug related SAE or discontinuations
- ✓ Available in US for patients 6 months or older for any wound size

Over $750M

Estimated Global Market Opportunity for VYJUVEK

Upcoming VYJUVEK Milestones

H2 2023
File MAA for EU

H2 2023
Initiate Japan Clinical Trial

Krystal

Fully Integrated Genetic Medicines Biotech

- Over 175K sq. ft. GMP manufacturing in US
- Fully integrated R&D, commercial, and manufacturing teams in place
- Strong balance sheet with over $355.5M in cash[1], PRV, and no debt

Future Growth Drivers

- Wholly owned, proprietary, redosable HSV-1 based gene delivery platform
- Multiple clinical stage assets in respiratory, dermatology, and aesthetics by end of 2023
- Expanding pipeline into ophthalmology

AE, adverse event; DEB, dystrophic epidermolysis bullosa; EU, European Union; FDA, US Food and Drug Administration; GMP, good manufacturing practice, PRV, priority review voucher, RCT, randomized controlled trial; SAE, serious adverse event; US, United Stated

1. Cash, cash equivalents and investments position as of Q1 2023

2023 Milestones

Timing	Program	Event
H1 23	KB105 for Autosomal Recessive Congenital Ichthyoses	Initiate Phase 2 Study in adults and pediatric populations
H1 23	KB407 for Cystic Fibrosis	Initiate dosing in Phase 1 clinical study
H2 23	KB408 for Alpha-1 Antitrypsin Deficiency	Initiate Phase 1 clinical safety and efficacy study
H2 23	VYJUVEK for Dystrophic Epidermolysis Bullosa	File Marketing Authorization Application in EU
H2 23	VYJUVEK for Dystrophic Epidermolysis Bullosa	Initiate clinical study in Japan on small subset of Japanese patients
H2 23	KB104 for Netherton Syndrome	File IND
H2 23	KB301 for treatment of Lateral Canthal lines	Initiate Phase 2 clinical study

IND, Investigational New Drug

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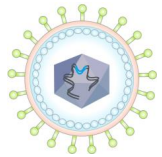
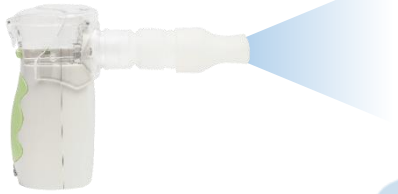
Respiratory Pipeline

Krystal Respiratory Pipeline

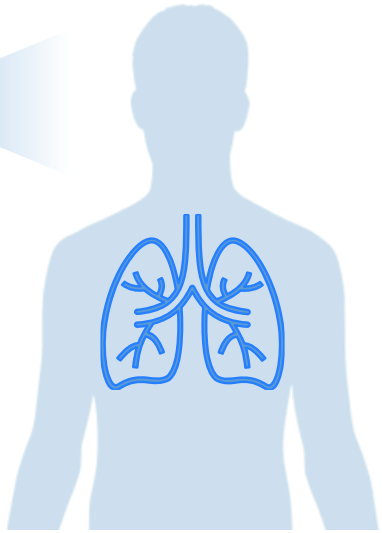
Developing redosable, inhaled gene therapies to address monogenic disorders of the lung



KB407
KB408



Nebulizer



Product	Preclinical	Phase 1/2	Phase 3	Upcoming Milestone(s)
KB407				Phase 1 FPI in H1 2023
KB408				File IND in H2 2023

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; FPI, first patient in, HSV-1, herpes simplex virus type 1; IND, investigational new drug

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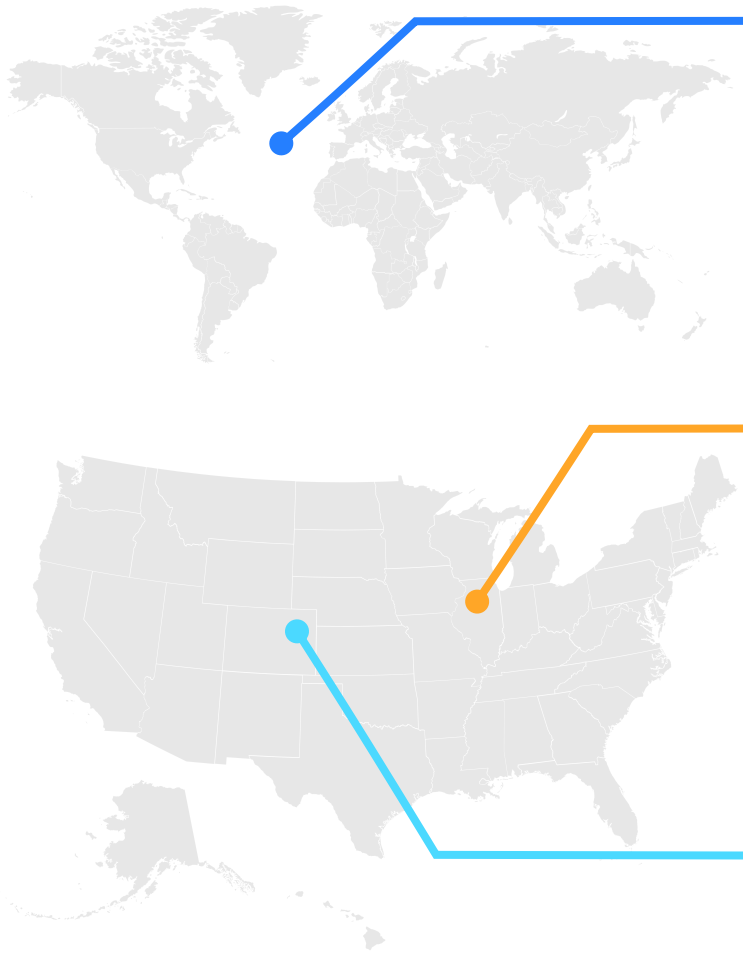
Cystic Fibrosis Disease Overview

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 US Registry

+1,000

New Cases Annually in US

- 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. US Cystic Fibrosis Foundation – About Cystic Fibrosis, accessible at: About Cystic Fibrosis | Cystic Fibrosis Foundation (cff.org); 2. US 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 Cys Fibros.* 2020;19(3):344-354

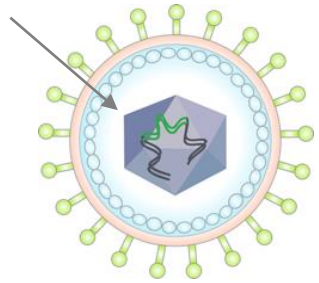
CF, cystic fibrosis; CFTR, cystic fibrosis transmembrane conductance regulator; US, United States

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**

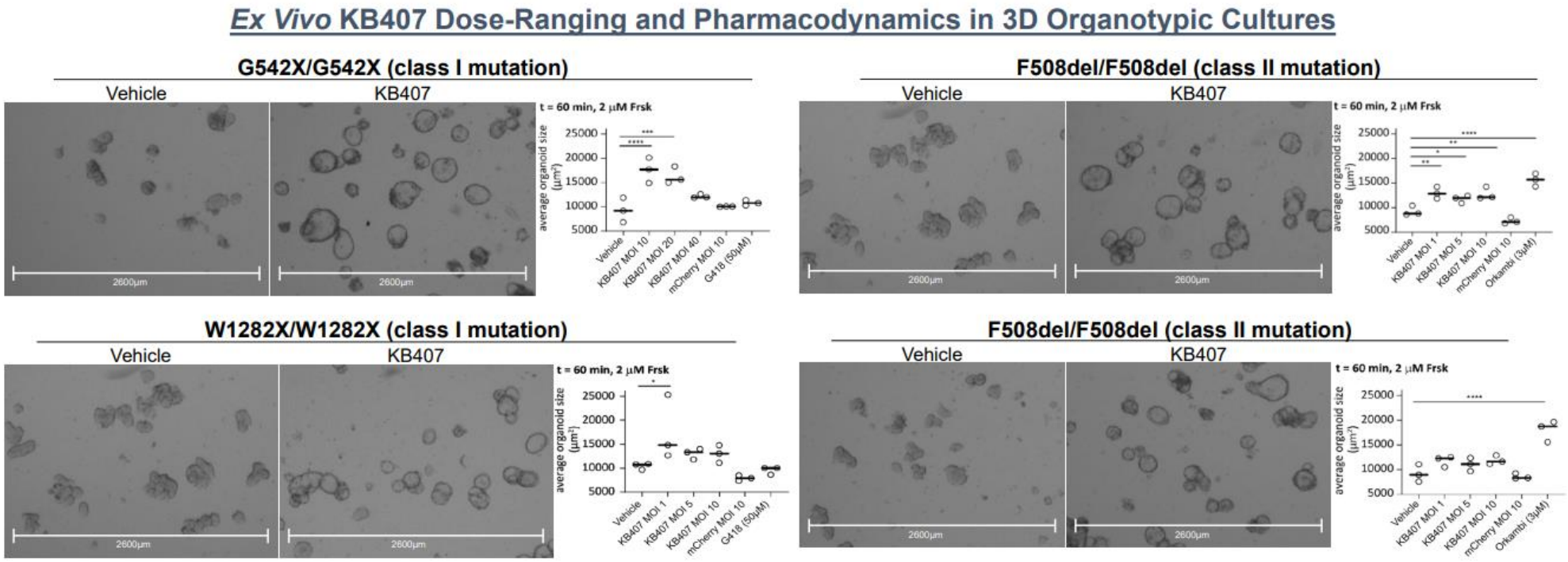
1. Krystal estimates based on CFF Patient Registry 2019, ECFS Patient Registry 2018; 2. Krystal estimates based on Middleton PG, et al. *N Engl J Med*. 2009;381:1809-1819; Heijerman HG, et al. *Lancet* 2019;394:1940-1948; Trikafta® FDA Label, Revised 10/2021

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

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

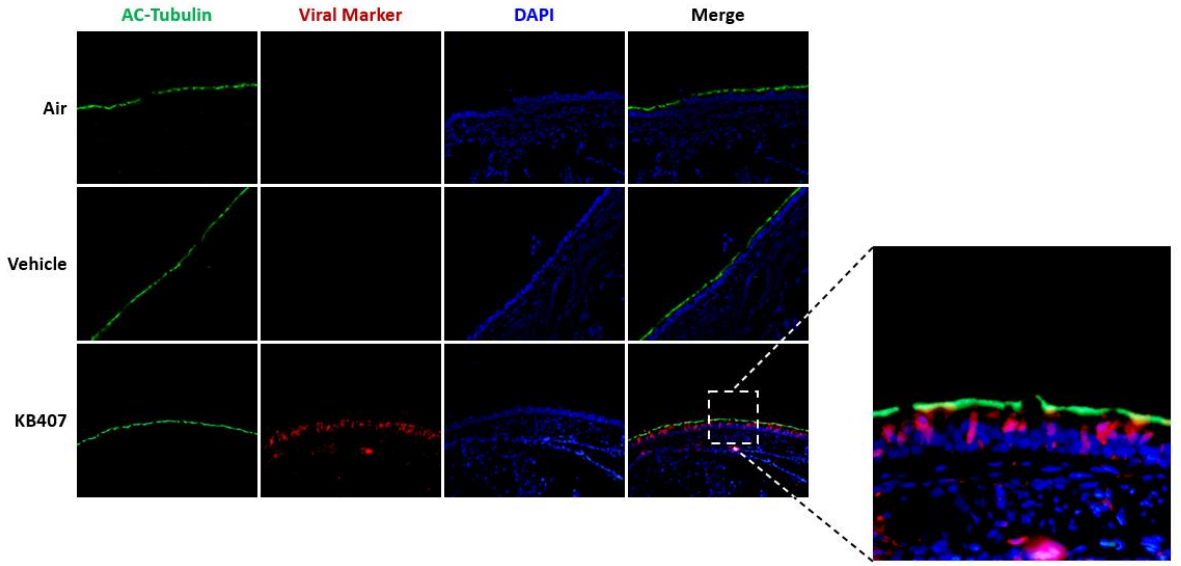
Group	n	Avg. Dose Deposited in Lungs (PFU / administration)	Dosing Days	Necropsy Days
Air	6	-	1, 8, 15	16
Vehicle	10	-	1, 8, 15	16, 43
Low Dose KB407	10	1.81×10^8 (male) 2.33×10^8 (female)	1, 8, 15	16, 43
High Dose KB407	10	1.43×10^9 (male) 2.11×10^9 (female)	1, 8, 15	16, 43

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 US*

*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

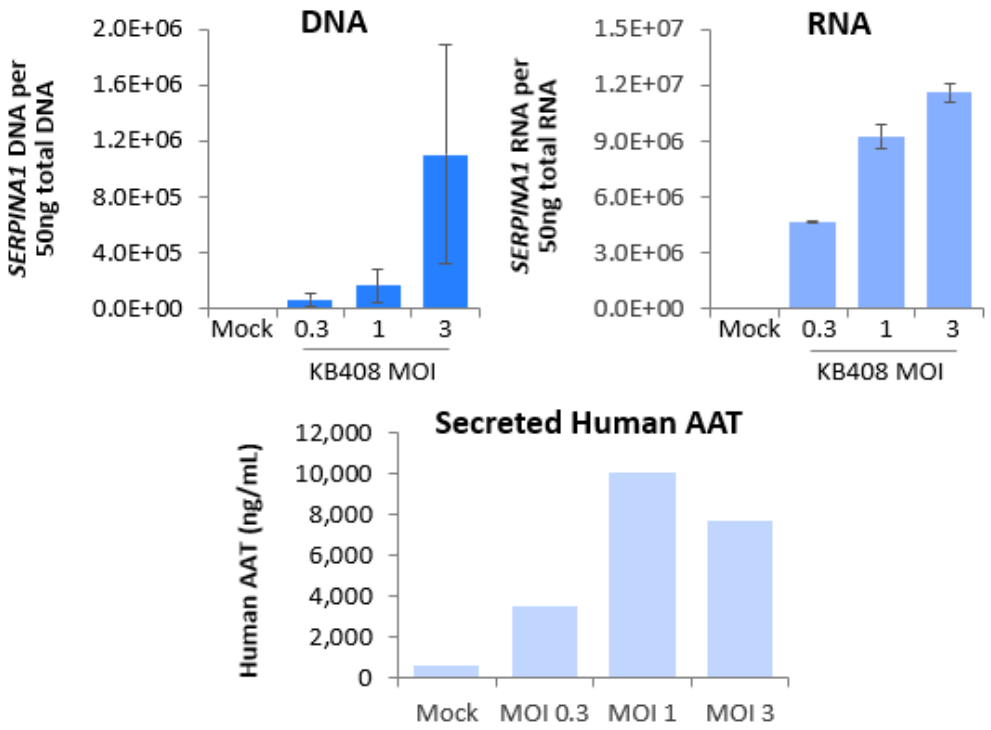
AAT, Alpha-1 Antitrypsin; AATD, Alpha-1 Antitrypsin Deficiency; IV, intravenous

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

KB408 for AATD

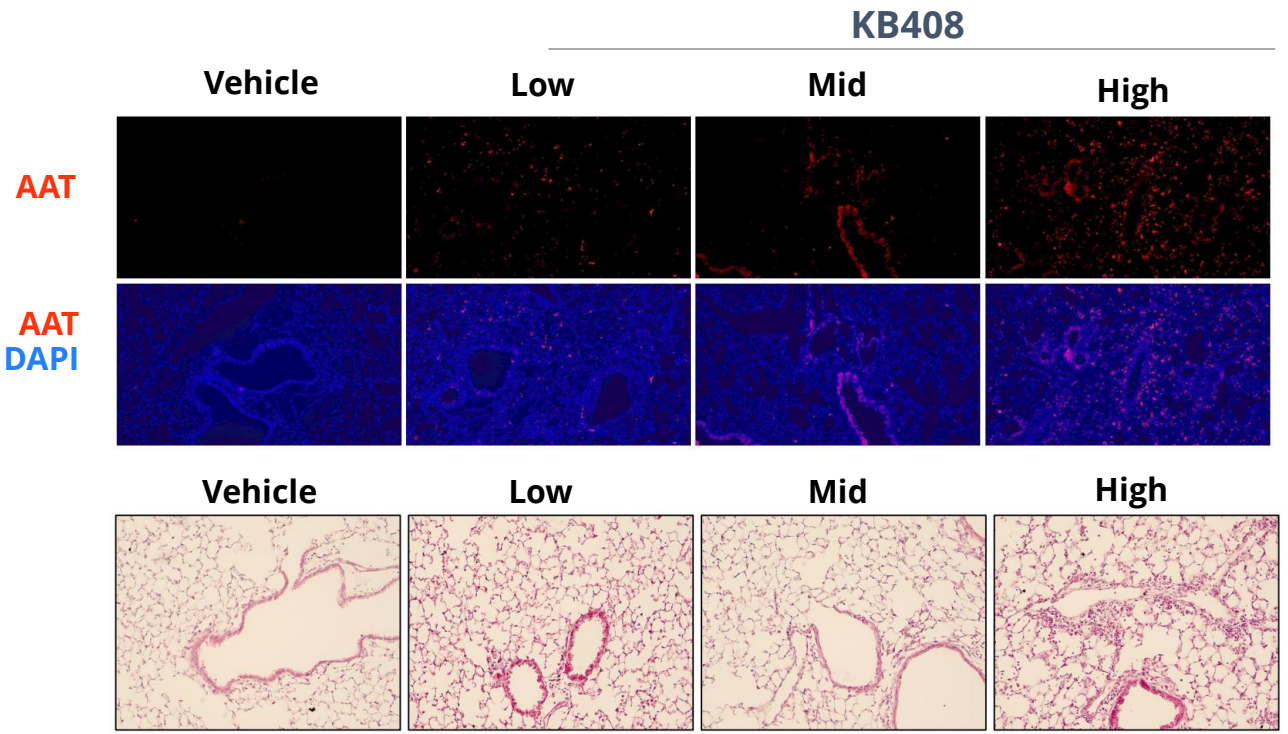
Dose-dependent expression of human AAT in clinically relevant cells and mouse lungs

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 two Phase 1 studies (US / Australia) to explore dose range and frequency; IND cleared in US and recruiting in Australia

Australia Phase 1

- Open-label study to enroll up to 13 adults in three cohorts, receiving either single dose, two doses biweekly, or four weekly doses
- Primary endpoint will be safety and tolerability, also assessing changes in lung function and *CFTR* expression by buccal swab

US Phase 1

- Open-label dose-finding study to enroll up to 20 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

- Expect to dose first patient in **H1 2023**

KB408 for Alpha-1 Antitrypsin Deficiency

- IND-enabling toxicology and manufacturing activities underway to enable IND submission and Phase 1 study start **by end of H2 2023**

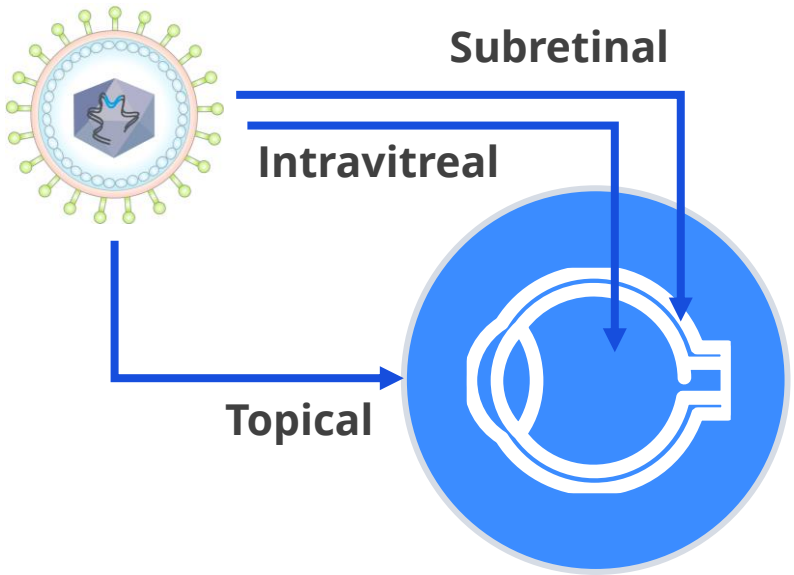
CFTR, cystic fibrosis transmembrane conductance regulator; IND, investigational new drug

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

DEB Ocular Complications Overview

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 ectropions, 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]

700+

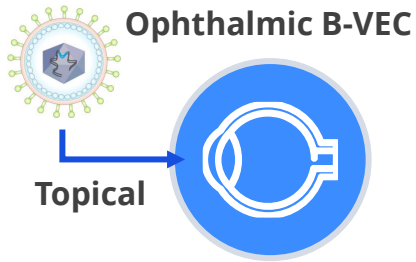
Estimated Patients in US*

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; DEB, dystrophic epidermolysis bullosa; RDEB, recessive dystrophic epidermolysis bullosa; US, 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

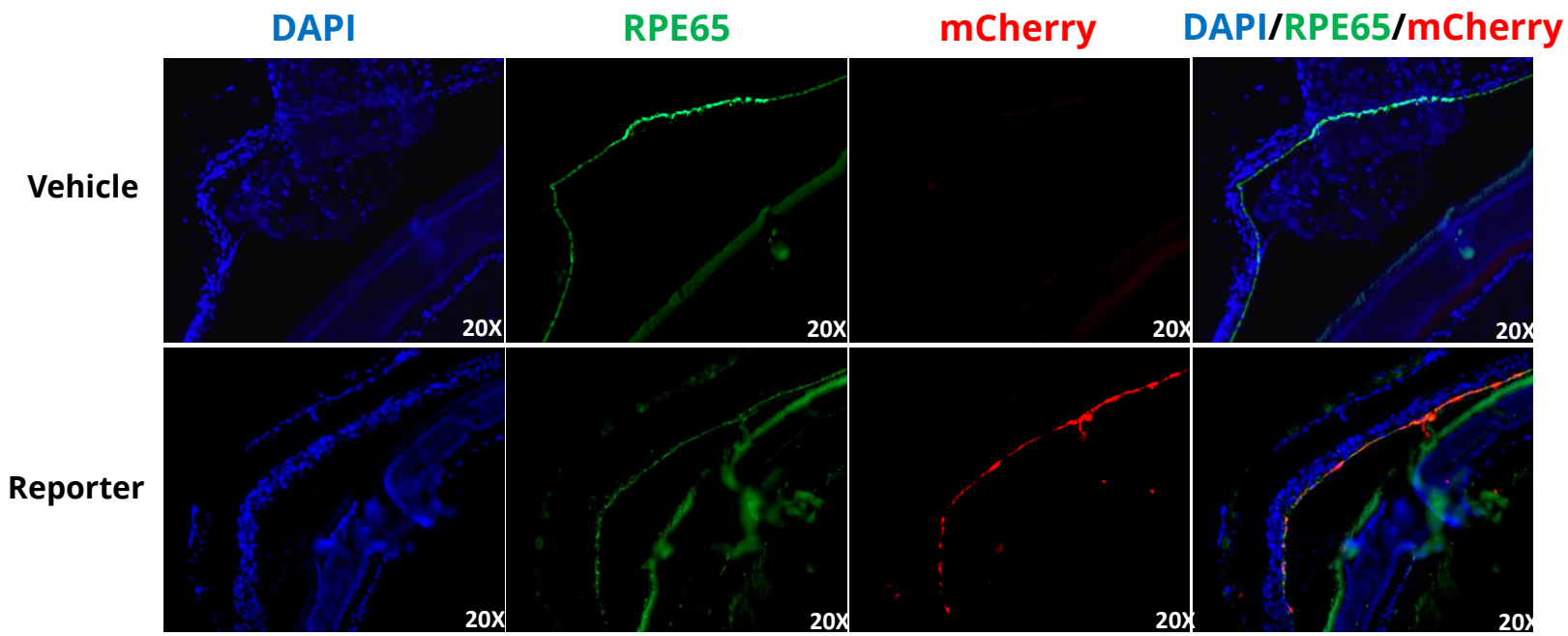
Other than VYJUVEK, all products described in this presentation are investigational therapies

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 US*

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 US 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, US Food and Drug Administration;

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

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]

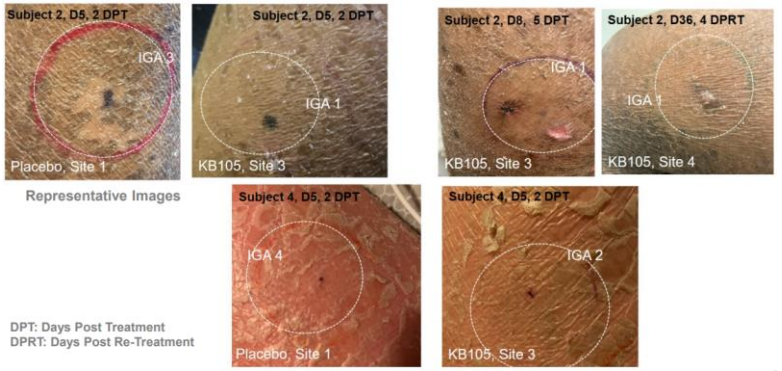
- The most common form of ARCI is caused by a mutation in the *TGM1* gene encoding a protein that is essential for the proper formation of the skin barrier
- The condition is characterized by thick, dry, scaly skin, increased trans-epidermal water loss, risk for dehydration, sepsis, and skin malignancies
- 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 US 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 mid 2023

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

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

Aesthetics Pipeline

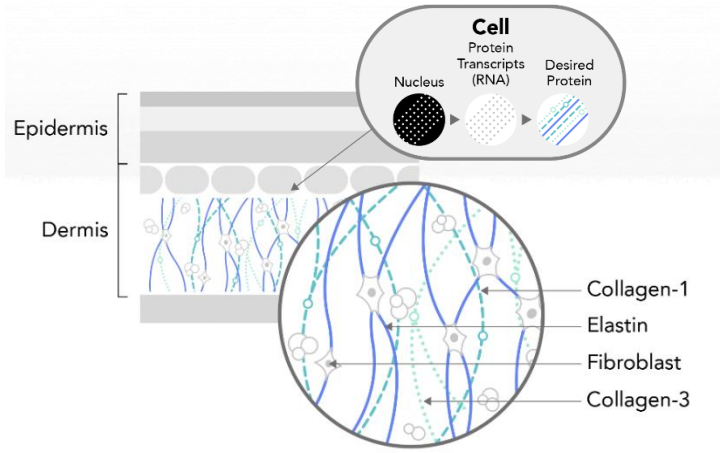
JEUNE

A wholly owned subsidiary of Krystal Biotech, Inc.

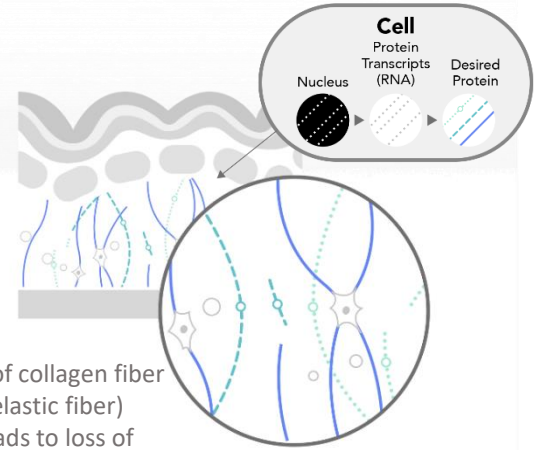
Characteristic Look of Aging Caused by Declining Levels of Key Proteins in Skin's Extracellular Matrix

- 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

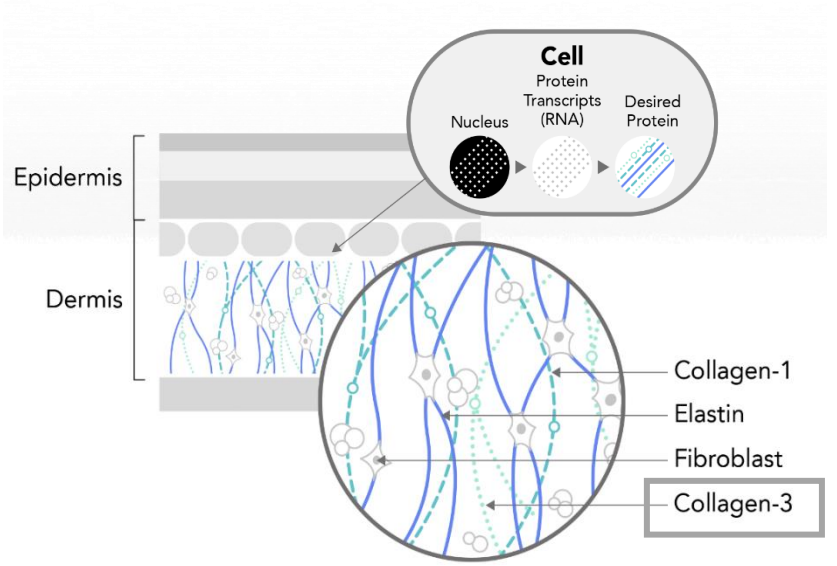
Jeune Pipeline and Lead Program KB301 Aim to Restore Key Skin Proteins

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



Initial Target

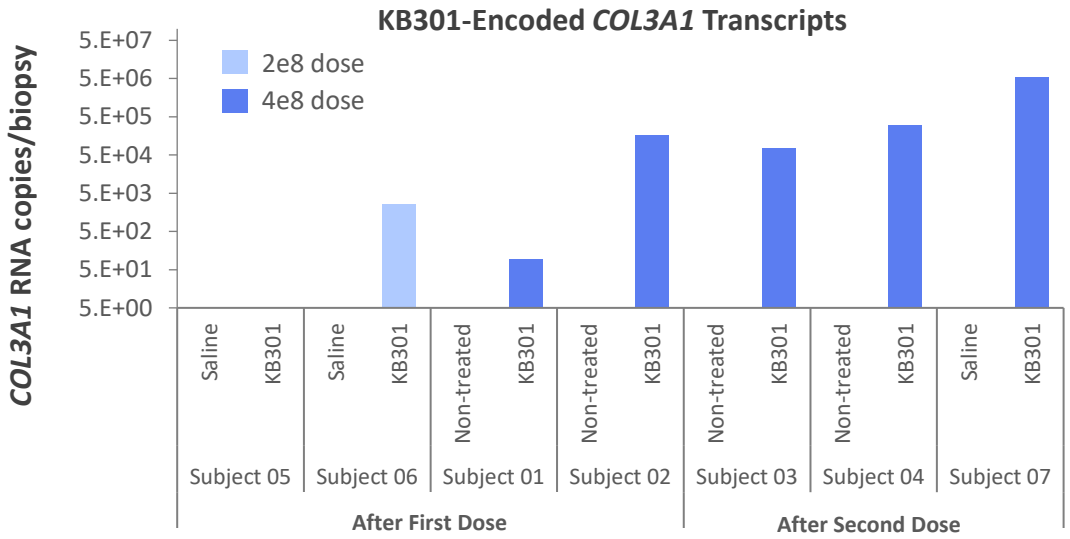
Other than VYJUVEK, all products described in this presentation are investigational therapies

KB301 Phase 1 Cohorts 1 and 2

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

Phase 1 Cohort 1[1]

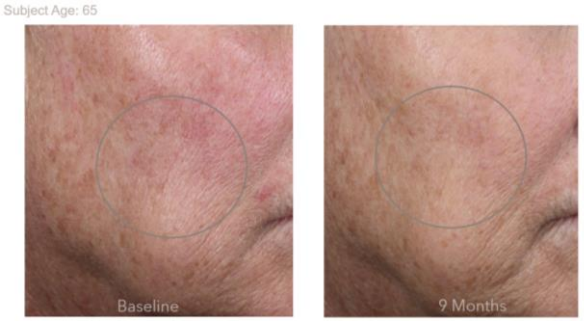
- Open label, dose ranging study designed to evaluate safety and gene delivery after repeat (Day 0, Day 30) intradermal injections to buttocks (1e8, 2e8, 4e8 PFU)
- **Safety:** Repeated intradermal injections of KB301 were well-tolerated; adverse events were transient, mild to moderate injection site 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

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

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 H2 2023

FDA, US Food and Drug Administration; LCL, lateral canthal lines

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

Krystal

Developing Genetic Medicines for Rare Diseases