Krystal

AAD GEM-3 Phase 3 Data Conference Call

Forward looking statements

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Agenda

1	**Introductory Comments**	Krish Krishnan – Chairman and CEO
2	**DEB Background and GEM-3 Results (AAD Late-Breaking Presentation)**	Dr. Hubert Chen – SVP, Clinical Development
3	**Market Opportunity and Commercial Preparations**	Andy Orth – Chief Commercial Officer
4	**Closing and Q&A**	Krish Krishnan – Chairman and CEO

Krystal Biotech: Bringing Transformative, Redosable Gene Therapies to Underserved Patient Populations

Leader in the science of redosable gene therapies – powered by proprietary HSV-1 vector technology

Initial focus on rare dermatologic diseases established clinical POC and a broad pipeline

Fully integrated, commercial-ready/pivotal gene therapy company

Expanded focus on larger indications, new tissue types and alternative routes of administration

Well funded with cash of $502.5 million[1], providing runway through multiple clinical and commercial milestones

1. Cash position as of December 31, 2021

Lead Program: B-VEC (beremagene geperpavec) for DEB

A Topical Redosable Gene Therapy Designed to Treat Dystrophic EB

Topically applied B-VEC gel designed to induce local COL7 expression and molecular correction

Topline Phase 3 data announced in Nov 2021; Detailed data presented at AAD in March 2022

> 2,500 patients diagnosed across the US, Europe and ROW[1]

Global commercial & medical teams with deep expertise in rare diseases

United States — **BLA filing in 2Q22**

- Orphan Drug Designation
- Rare Pediatric Disease Designation
- Regenerative Medicine Advanced Therapy (RMAT) designation
- Fast Track Designation

Europe — **MAA filing in 2H22**

- Orphan Drug Designation
- PRIority MEdicines (PRIME) Designation

Japan + Other — **Evaluate path forward in other markets**

- Japan in progress
- Known patient populations in rest-of-world (i.e., China)
- Evaluating approaches in these markets

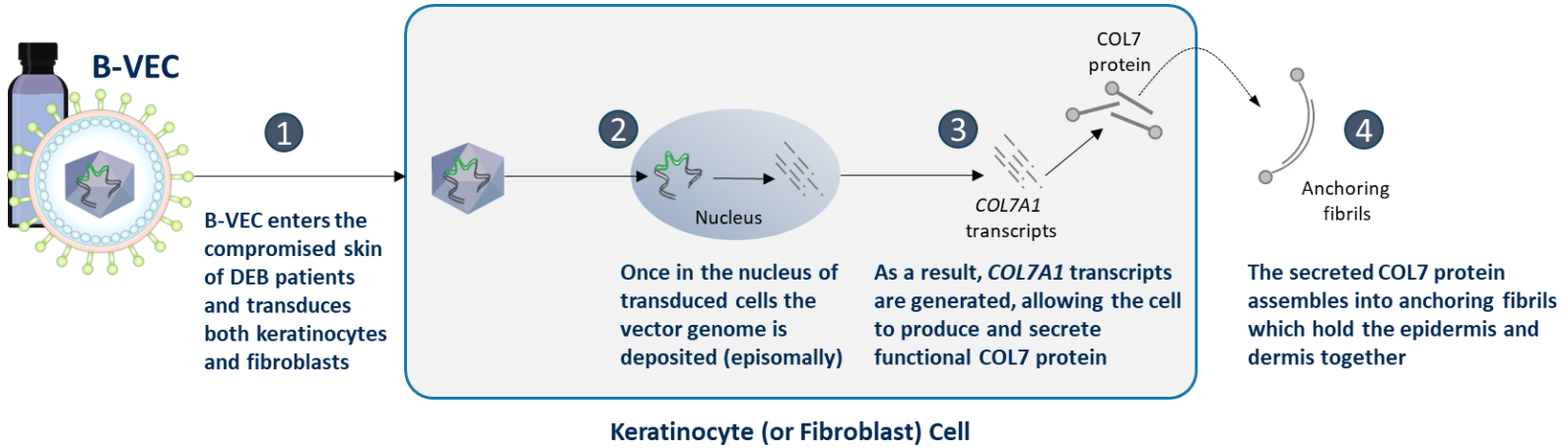
1. Internal data on file

Dr. Hubert Chen

SVP, Clinical Development

Dystrophic Epidermolysis Bullosa and B-VEC

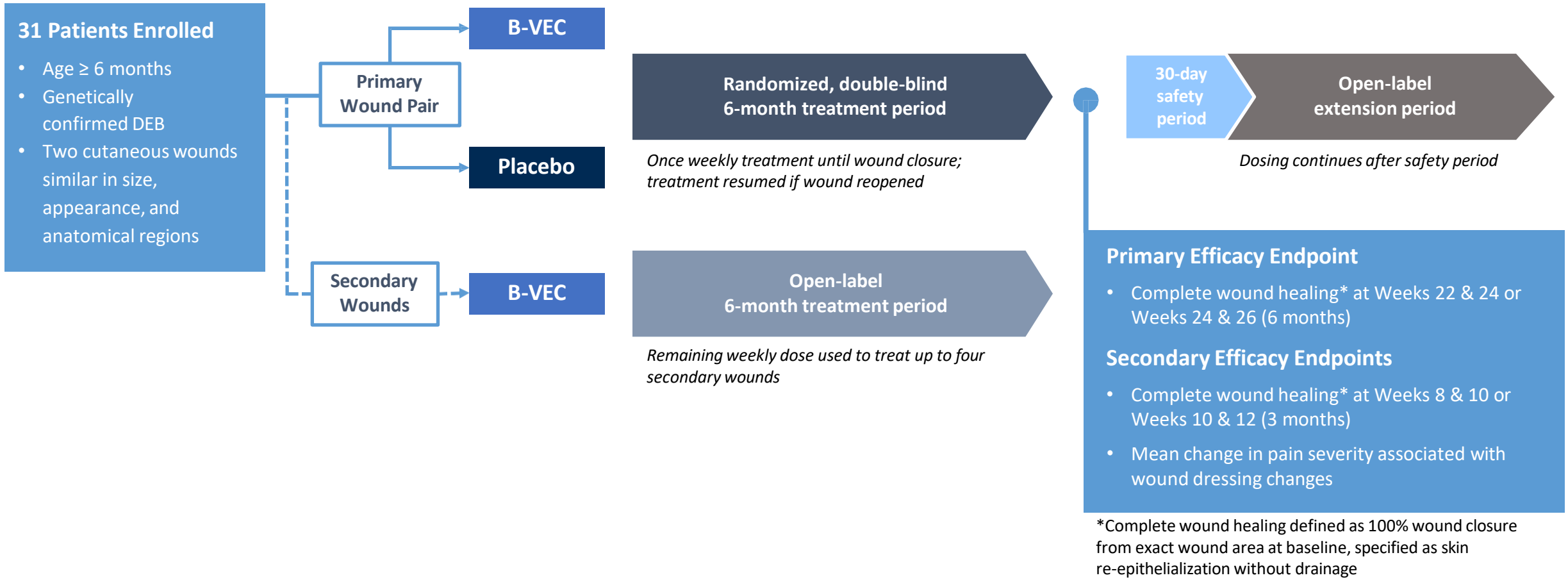
- Dystrophic epidermolysis bullosa (DEB) is a serious, ultra-rare genetic blistering disease caused by mutations in the *COL7A1* gene which lead to skin fragility and wounds[1-3]
  - Patients with DEB are at increased risk for serious complications, including aggressive squamous cell carcinoma[4-6]; management is currently supportive in nature[7,8]
- Beremagene geperpavec (B-VEC) is an investigational HSV-1-based topical, redosable gene therapy designed to restore functional COL7 protein by delivering the *COL7A1* gene
  - B-VEC utilizes a differentiated HSV-1 vector platform that allows for episomal delivery, high payload capacity, tropism for skin cells, and evades the immune system enabling repeat delivery



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. Condorelli A, et al. *Int J Mol Sci*. 2019;20(22):5707; 5. Montaudié H, et al. *Orphanet J Rare Dis*. 2016;11(1):117; 6. Fine J-D, Mellerio JE. *J Am Acad Dermatol*. 2009;61:367-384; 7. Denyer J, et al. Accessed March 16, 2022. https://www.woundsinternational.com/download/resource/5921; 8. Bruckner AL, et al. *Orphanet J Rare Dis*. 2020;15(1):1.
B-VEC, beremagene geperpavec; COL7, type VII collagen; *COL7A1*, collagen type VII alpha 1 chain; DEB, dystrophic epidermolysis bullosa; HSV-1, herpes simplex virus type 1

GEM-3 Study Design

- GEM-3 (NCT04491604) is a Phase 3, multicenter, randomized, double-blind, placebo-controlled intra-patient study evaluating the efficacy and safety of B-VEC in patients with DEB

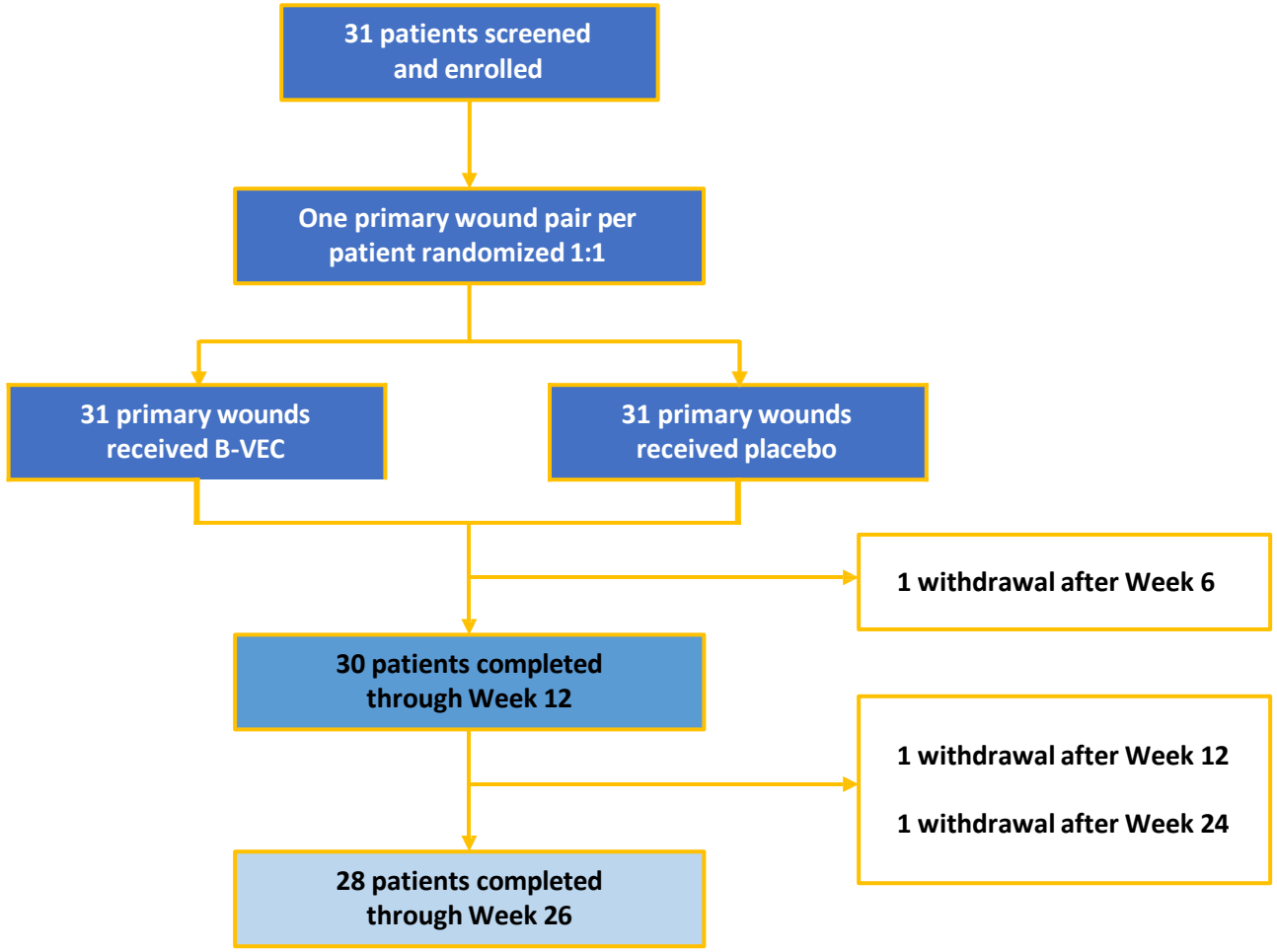


*Complete wound healing defined as 100% wound closure from exact wound area at baseline, specified as skin re-epithelialization without drainage

B-VEC, beremagene geperpavec; DEB, dystrophic epidermolysis bullosa

Patient Disposition

- 31 patients were randomized and made up the intent-to-treat (ITT) population used for all primary and secondary efficacy analyses
- The safety population was the same as the ITT population and used for all safety analyses
- Three patients withdrew from the study for nondrug-related reasons



B-VEC, beremagene geperpavec; ITT, intent-to-treat

Baseline Demographics and Clinical Characteristics

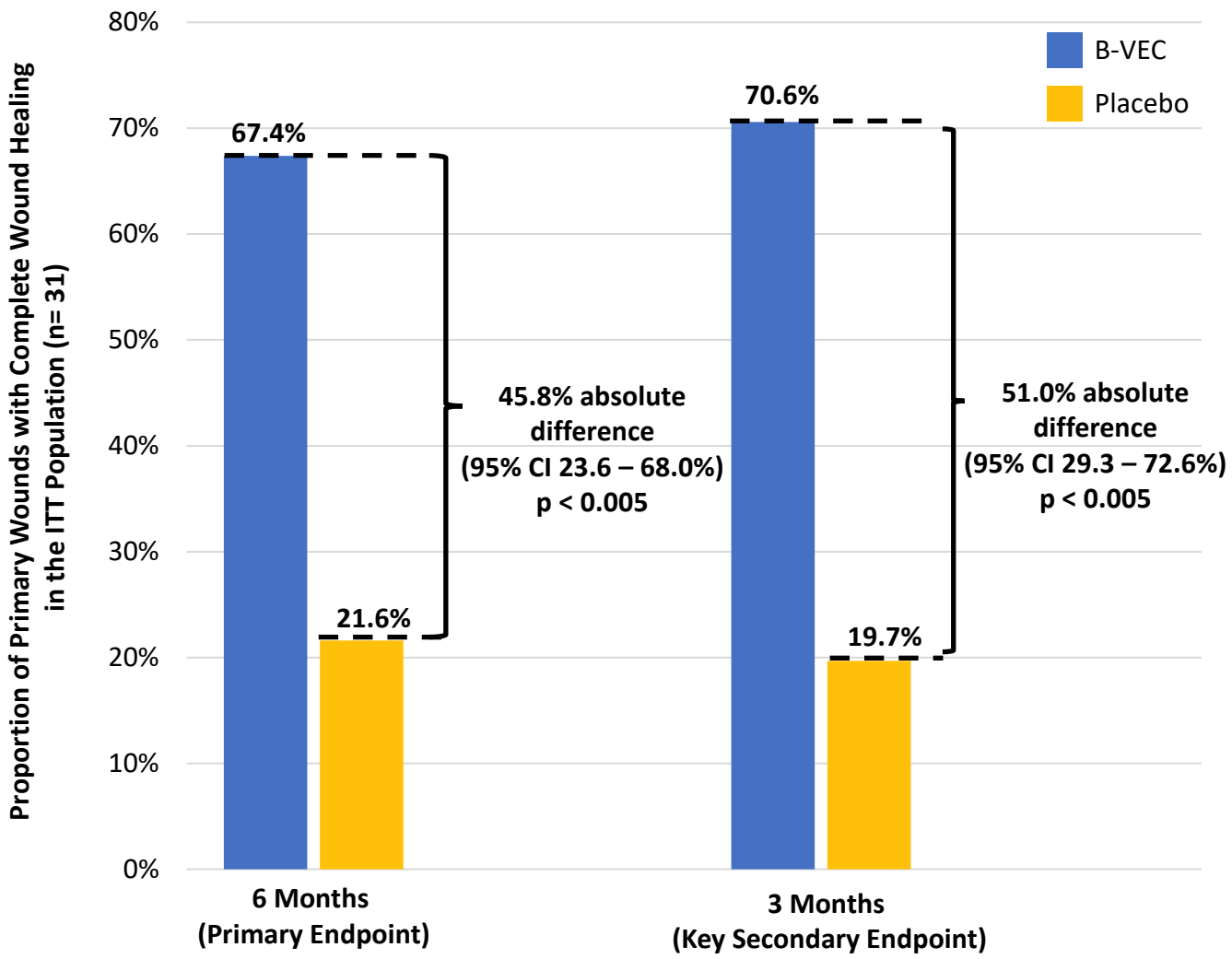
	Total patients (n=31)
Age, years	
Mean (SD)	17.2 (10.7)
Range	1 – 44
Age category, n (%)	
≤12 years	10 (32.3)
>12 and ≤18 years	9 (29.0)
>18 years	12 (38.7)
Sex, n (%)	
Male	20 (64.5)
Female	11 (35.5)
Race, n (%)	
White	20 (64.5)
Asian	6 (19.4)
American Indian or Alaska Native	5 (16.1)

	Total patients (n=31)
Genotype, n (%)	
DDEB	1 (3.2)
RDEB	30 (96.8)

Primary wound	B-VEC (n=31)	Placebo (n=31)
Wound area/size, cm^2		
Mean (SD)	14.4 (12.7)	15.6 (12.1)
Range	2.3 – 57.3	2.3 – 51.5
Wound area/size category*, n (%)		
<20 cm^2	23 (74.2)	22 (71.0)
20 - <40 cm^2	6 (19.4)	8 (25.8)
40 – 60 cm^2	2 (6.5)	1 (3.2)

*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
B-VEC, beremagene geperpavec; DDEB, dominant dystrophic epidermolysis bullosa; RDEB, recessive dystrophic epidermolysis bullosa; SD, standard deviation

Significantly Greater Complete Wound Healing with B-VEC Treatment

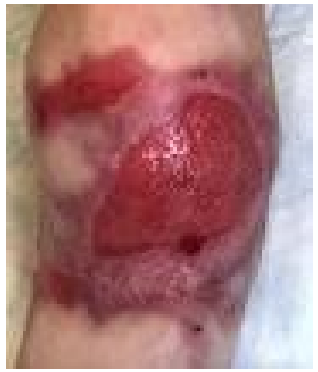
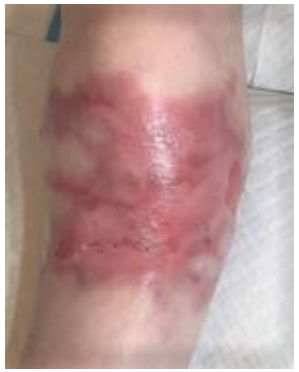
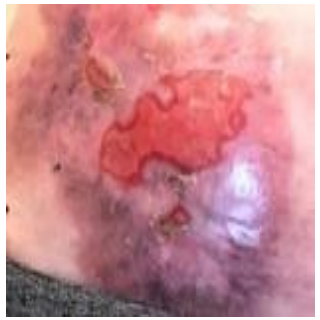
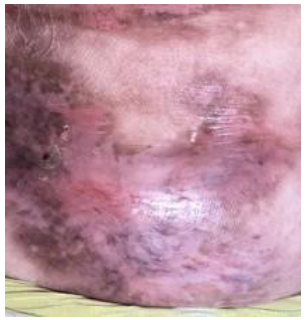
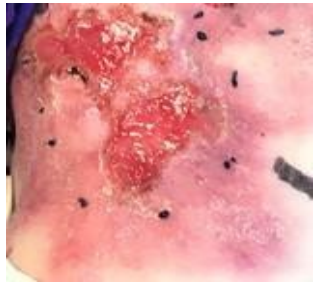
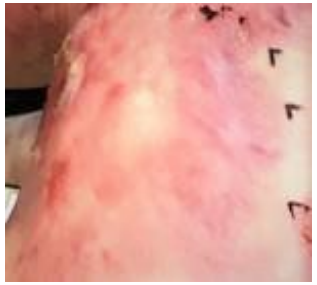


Data as of database lock on 19Nov2021; data in figure based on ITT population (imputed); p-values and CIs are based on exact McNemar's test
B-VEC, beremagene geperpavec; CI, confidence interval; DDEB, dominant dystrophic epidermolysis bullosa; ITT, intent-to-treat

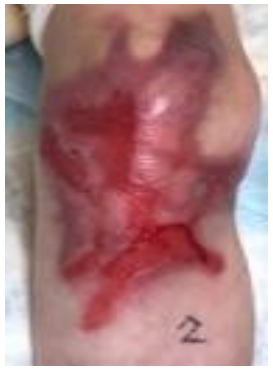
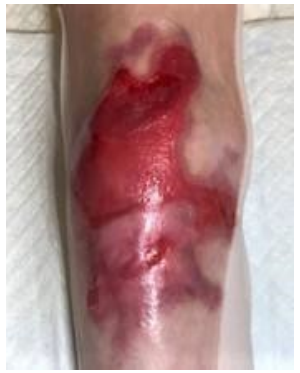
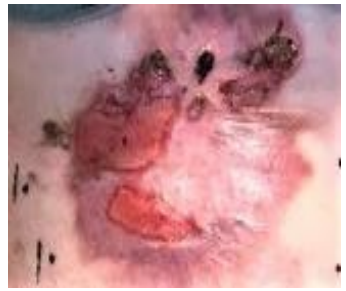
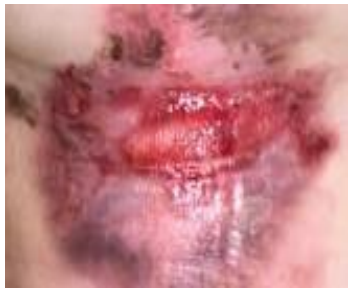
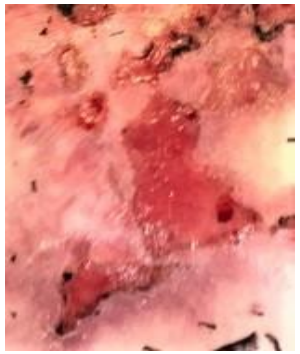
- The proportion of primary wounds with complete wound healing was significantly greater with B-VEC than placebo at both 3- and 6-month timepoints ($p < 0.005$)
- In the patient with DDEB, primary endpoint of complete wound healing at 6 months was achieved by the B-VEC treated wound, but not by the placebo treated wound
- At 6 months, 15 of 17 discordant pairs showed response to B-VEC but not placebo
  - Discordant pair defined as when one wound meets complete wound healing responder definition and other does not

Primary Wound Pairs (15 – 30 cm^2) at Baseline and 6 Months

B-VEC

	Baseline	6 Months
Patient A Knee		
Patient B Lower abdomen		
Patient C Lower trapezius		

Placebo

	Baseline	6 Months
Patient A Knee		
Patient B Sternum		
Patient C Upper paraspinal		

B-VEC, beremagene geperpavec

Treatment with B-VEC Demonstrated Durability of Response

- 49.7% of B-VEC treated wounds compared to 7.1% of placebo treated wounds demonstrated durability of response, defined as wounds that met complete wound healing at both 3 months (key secondary endpoint) and 6 months (primary endpoint)
- Nearly half of all B-VEC treated wounds demonstrated complete wound healing for three consecutive visits

	Responder, n (%)		Absolute Difference, % (95% CI)
	B-VEC (n=31)	Placebo (n=31)	
Durability of response†	15.4 (49.7)	2.2 (7.1)	42.6 (22.6, 62.6)
Complete wound healing			
Weeks 8, 10, and 12	14.8 (47.7)	5.1 (16.5)	31.3 (10.6, 51.9)
Weeks 22, 24, and 26	13.4 (43.2)	2.0 (6.5)	36.8 (19.8, 53.7)

†Durability of response was defined as meeting the responder definition for complete wound healing both at 3 months (Weeks 8 & 10 or Weeks 10 & 12) and at 6 months (Weeks 22 & 24 or Weeks 24 & 26)
Percentages are based on the number of subjects in the intent-to-treat (ITT) population; CIs are based on McNemar's test
Missing endpoint data were imputed assuming the data are missing at random and using multiple imputation methodology

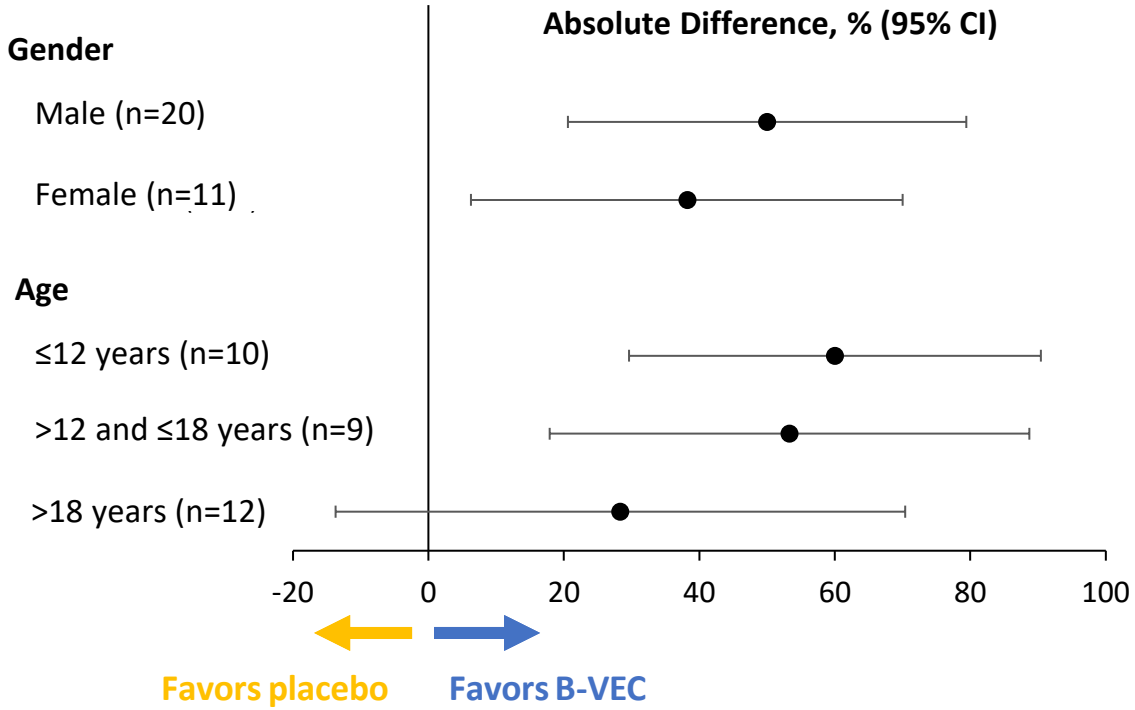
- Of the total B-VEC wounds closed at 3 months, 66.7% (14/21) of B-VEC-treated wounds were also closed at 6 months, as compared to 33.3% (2/6) for placebo treated wounds (p=0.02)

Data as of database lock on 19Nov2021
B-VEC, beremagene geperpavec; CI, confidence interval

Consistent Evidence of a Treatment Response with B-VEC Across Subgroups

- Treatment response was in favor of B-VEC for all gender, age, and wound area/size subgroups, however the individual subgroups were not powered to demonstrate statistical significance

Complete Wound Healing at 6 Months by Gender and Age Subgroups



Complete Wound Healing at 6 Months by Baseline Primary Wound Area/Size Category

Baseline primary wound area/size category*	B-VEC		Placebo	
	N	Complete wound healing at 6 months, n (%)	N	Complete wound healing at 6 months, n (%)
<20 cm²	23	14 (60.9)	22	5 (22.7)
20 - <40 cm²	6	4 (66.7)	8	1 (12.5)
40 – 60 cm²	2	1 (50.0)	1	0 (0)

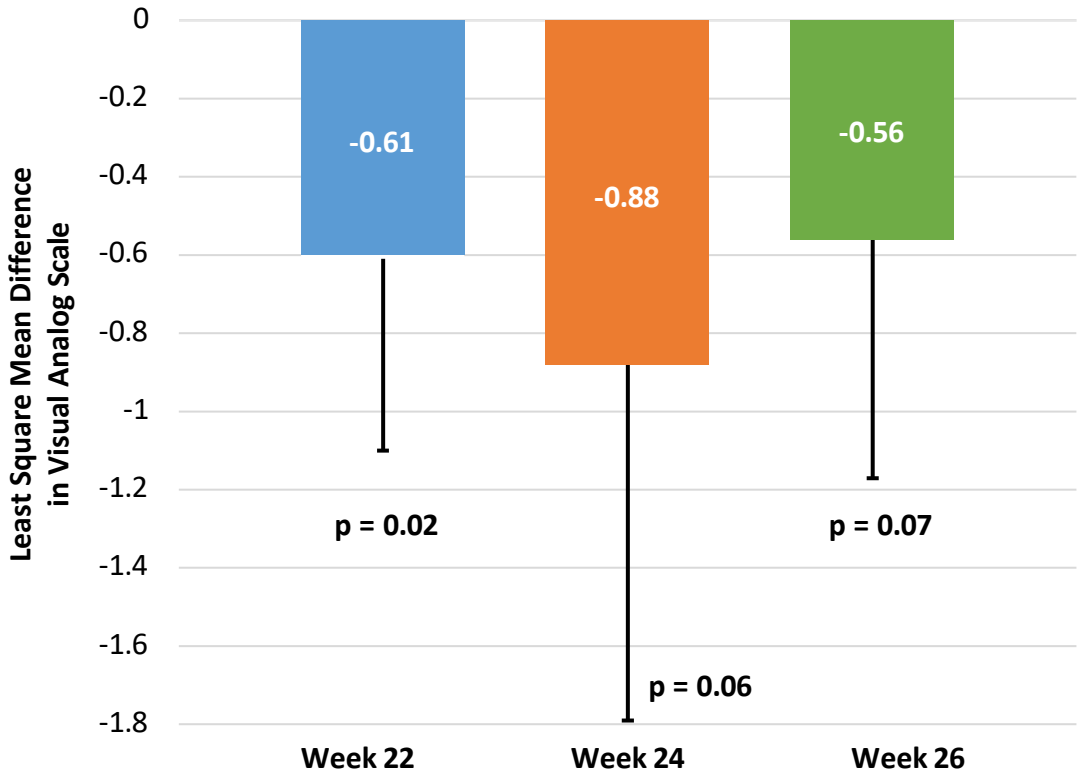
*In a small number of patients, the pre-defined threshold values for wound area/size category fell in between the size of the two wounds

Data as of database lock on 19Nov2021; data in figures based on ITT population (imputed); p-values and CIs are based on exact McNemar's test; gender and age subgroups were pre-specified
B-VEC, beremagene geperpavec; CI, confidence interval; ITT, intent-to-treat

Pain and PRO Assessments Demonstrated Improvement Consistent with a Wound Healing Response

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

Change from Baseline in Pain following B-VEC Treatment



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

Data as of database lock on 19Nov2021
B-VEC, beremagene geperpavec; ITT, intent-to-treat; PRO, patient reported outcomes; VAS, Visual Analog Scale

B-VEC was Generally Well-Tolerated

- The majority of AEs were mild; there were no AEs leading to treatment discontinuation or death
- One AE, mild erythema, was considered possibly related to study drug as assessed by the investigator
- Three patients experienced a total of 5 SAEs during the study: cellulitis, anemia (2 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 B-VEC was not associated with HSV-1 serostatus at baseline or with COL7 seroconversion

	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)

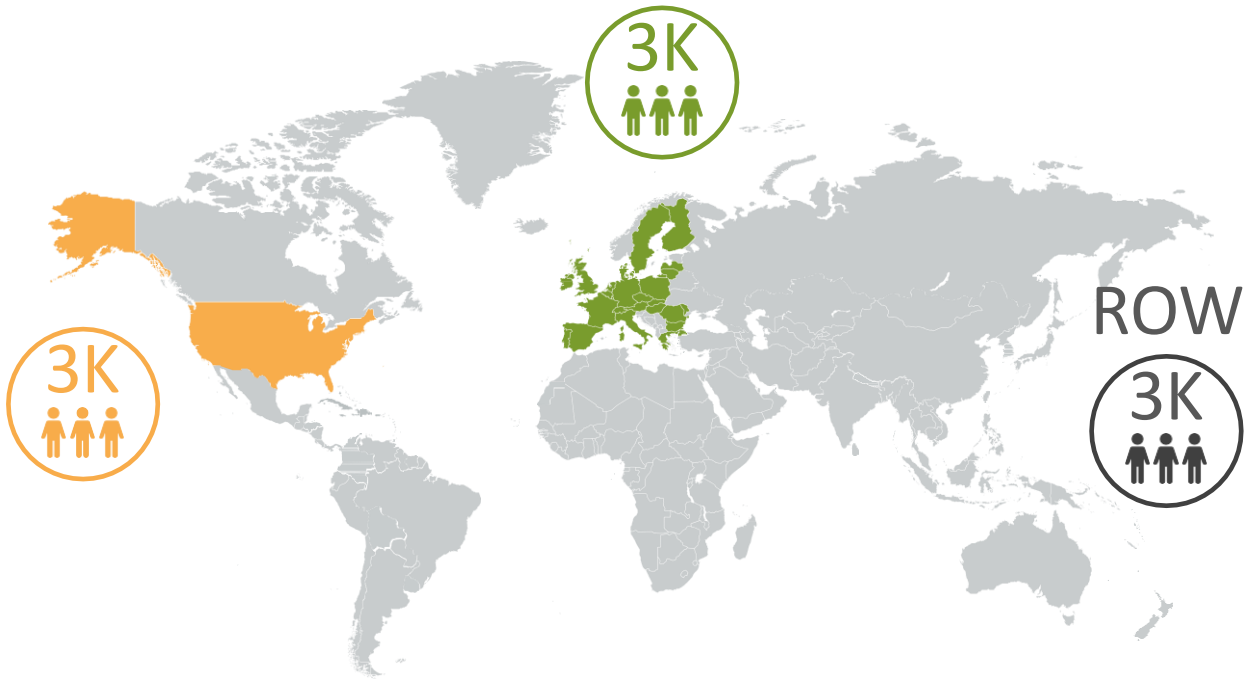
Data as of database lock on 19Nov2021
AEs, adverse events; B-VEC, beremagene geperpavec; COL7, type VII collagen; HSV-1; herpes simplex virus type 1; SAEs, serious adverse events

Andy Orth

Chief Commercial Officer

Dystrophic EB Patient Population and B-VEC Opportunity

~9,000 patients across global reimbursable markets



Dystrophic EB represents a >$500M Global Market

- Genetic prevalence suggests ~3,000 patients in the US
  - Initial claims data mining points to >1,000 known patients diagnosed with DEB in the US and >2500 patients worldwide
- Payer mix expected to be ~80% commercially insured in the US
- Palliative care alone costs the healthcare system $200,000-$400,000 today
- B-VEC vial pricing to be informed by significant variability in patient level vial consumption; driven by disease severity and duration of treatment
- Patient costs (vial consumption) to the payer expected to decrease over time until they reach steady state. Proactively partnering with US payers for budget predictability

B-VEC is an investigational therapy being studied in clinical trials

Preparing for U.S. Launch

Pre-Launch Preparations

Education

- Patient and Caregiver facing Community Educational Liaisons in the field
- Health Care Professional and Patient focused Disease State Awareness programming underway
- Medical Affairs Key Opinion Leader engagement underway
- Payer education and engagement

Internal Preparation

- Profiling HCPs to ensure we know where the patients are and raise awareness/educate
- Laying groundwork for site-of-care strategy (goal to allow patients to get treatment in their own zip code)
- Building experienced team with strong culture
- Krystal Connect– our patient services and reimbursement hub

Launch

Initial Launch

- Focused on >1,000 patients identified by claims database analytics
- Primarily treating more severe patients at Centers of Excellence
- Access to treatment at convenient sites of care

Krystal CONNECT™
Personalized Support Services

Longer-term Launch

- Identifying and educating HCPs and patients in order to identify remaining Dystrophic EB patient population
- Patient finding activities - focusing on individuals currently not diagnosed or with localized -to-moderate diagnosis
- Drive patient disease awareness via sponsored genetic testing and disease education

Launched Decode DEB™ in October 2021 – Getting the Right Diagnosis

No-charge genetic testing program available to eligible U.S. residents who are suspected of having EB and have not yet been genetically confirmed

Comprehensive testing panel to identify Dystrophic EB or conditions with similar phenotypes, including other EB types and some non-EB genetic blistering conditions

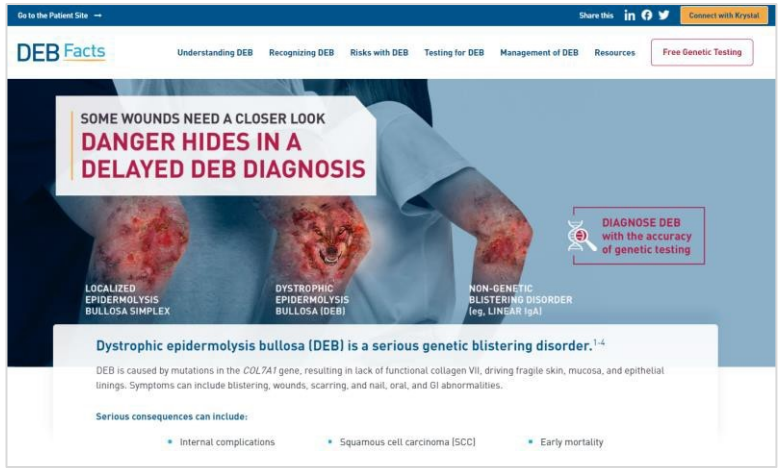
Excellent EB community response to date

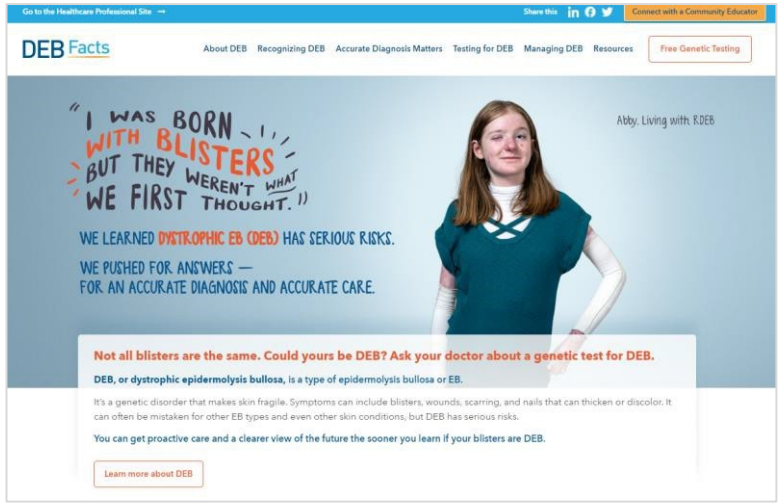
DEB Disease Awareness Update
DEBFacts Web Sites Launched early 2022

Importance of accurately diagnosing DEB Patients

DEB Caused by COL7 Dysfunction

Every Wound Matters/Has Consequences





>1,000 visits since launch.

Media investment and other websites traffic drivers launching early Q2

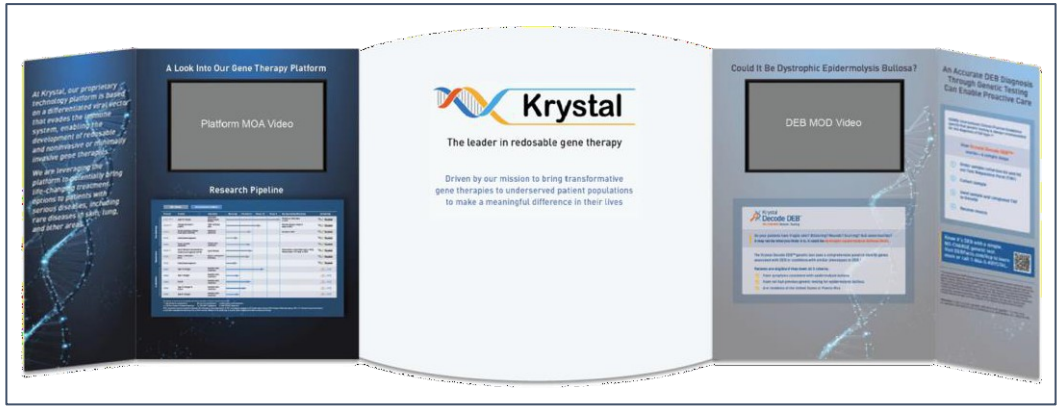
Proactive Education at American Academy of Dermatology

Medical affairs booth focused on disease state and Krystal Biotech awareness, highlighting:

- Patient journey cases
- Decode DEB genetic testing program
- Mechanism of disease and mechanism of action animations/videos
- Pipeline and clinical trial information

Engaging HCPs serving the dystrophic EB community

- Better understand practice dynamics, patient unmet needs, and dystrophic EB landscape
- Highlight Krystal scientific research



Learn More About

Dystrophic Epidermolysis Bullosa (DEB)

Significantly Expanding In-house Manufacturing Capacity and Expertise

Existing ANCORIS Facility

- ~10,000 sq ft GMP facility
- Process validation batches complete
- Designed to support B-VEC launch in U.S. and Europe+
- Comfortably within biologics gross margin range

New ASTRA Facility

- ~150,000 sq ft GMP facility
- Operational in 2022
- Introduces Automation
- Transition B-VEC commercial material to this facility eventually

Krish Krishnan

Chairman and CEO

Key Takeaways

B-VEC full Phase 3 data is compelling

Well-prepared to bring B-VEC to the DEB community

Robust upcoming catalysts for B-VEC and pipeline

Redosable gene delivery technology/platform has broad potential

Upcoming Milestones

Timing	Program	Event
2Q22	B-VEC for Dystrophic EB	Present more detailed GEM-3 safety results at SID (May 18-21)
2Q22	B-VEC for Dystrophic EB	File BLA with U.S. FDA
2Q22	KB407 for cystic fibrosis	Initiate Phase 1 clinical trial in Australia
2H22	B-VEC for Dystrophic EB	Fila MAA with EMA
2H22	KB407 for cystic fibrosis	File IND / Initiate clinical trial in U.S.
2022	KB105 for TGM1-ARCI	Initiate dosing in next Phase 1/2 cohort
2022	KB104 for Netherton	File IND and initiate clinical trial
4Q22	KB301 for aesthetic indications	Initiate one or more Phase 2 trials in aesthetic skin indications

Krystal

Questions & Answers