Krystal

The Leader in **Redosable Gene Therapy** for Rare Disease

Topline GEM-3 Trial Results Call

Forward looking statements

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Call Agenda

1 **Introductory Comments**
Krish Krishnan – Chairman and CEO

2 **Dystrophic Epidermolysis Bullosa Background**
Dr. Peter Marinkovich

3 **GEM-3 Results and Next Steps**
Suma Krishnan – Founder and COO

4 **Commercial Preparations**
Andy Orth – Chief Commercial Officer

5 **Q&A**

Krish Krishnan

Chairman and CEO

Novel viral vector platform positively differentiated from other viral vector technologies

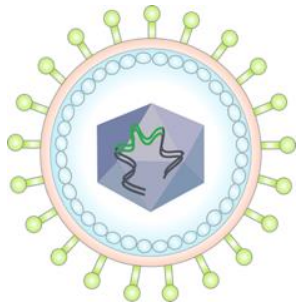
1 Robust tropism to target cells of interest upon local administration

2 Large payload capacity allows for delivery of two copies of large gene

3 Immune evasive properties of proprietary vectors enables redosability

GEM-3 results provide significant platform validation

Engineered HSV-1 Vector Platform



GEM-3 Study

Platform fully integrated from research to development to manufacturing to commercialization

1 Confirms safety and efficacy of VYJUVEK™* (beremagene geperpavec) for dystrophic EB

- Most advanced clinical application of platform

2 Validates therapeutic vector in dermatologic applications

- Skin pipeline covers rare and aesthetic conditions (via wholly owned subsidiary Jeune Aesthetics)
- Potential to deliver diverse genetic cargo

3 Validates therapeutic vector for broader redosable gene delivery

- Tropism to lung and additional types under exploration
- Potential to deliver diverse of genetic cargo with a variety of delivery mechanisms

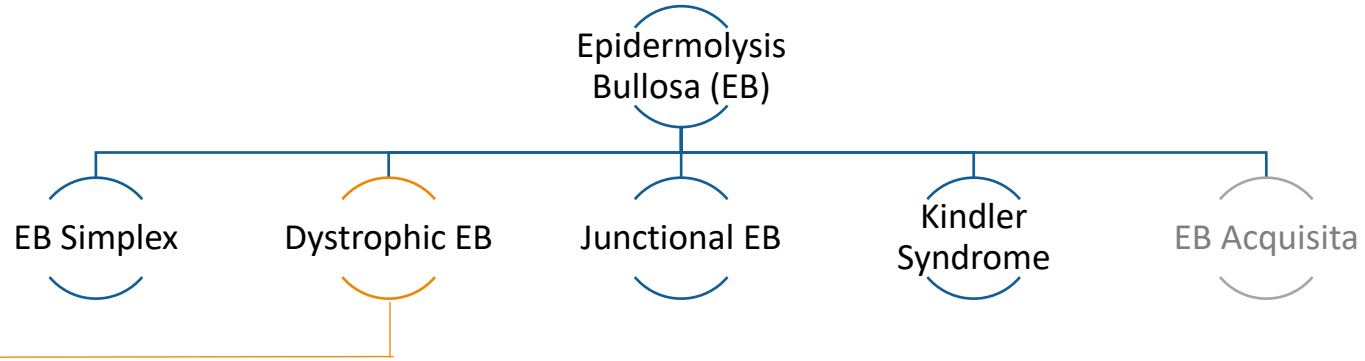
*VYJUVEK is the current proprietary name for beremagene geperpavec, formerly known as B-VEC
VYJUVEK is an investigational therapy being studied in clinical trials

Dr. Peter Marinkovich

Associate Professor of Dermatology at Stanford University
Blistering Disease Clinic Director

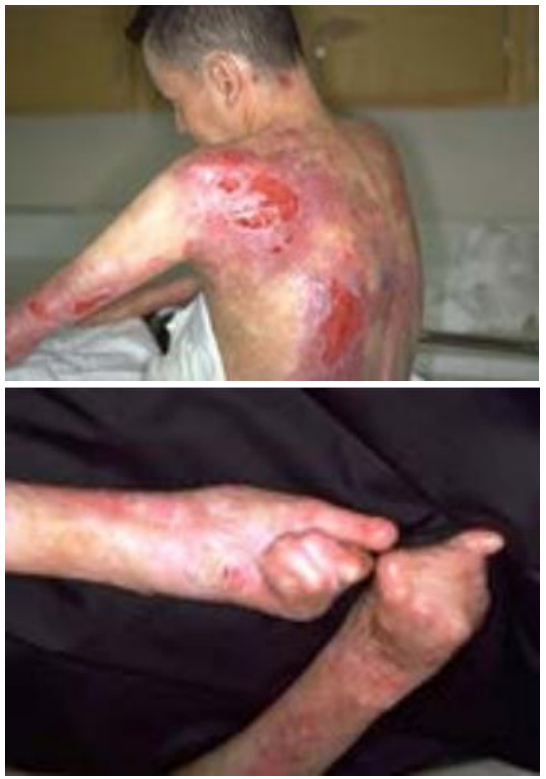
Disclosures: Principal investigator in GEM-3 trial

Epidermolysis Bullosa is a group of rare diseases associated with fragile skin, causing skin to blister easily



Dystrophic EB

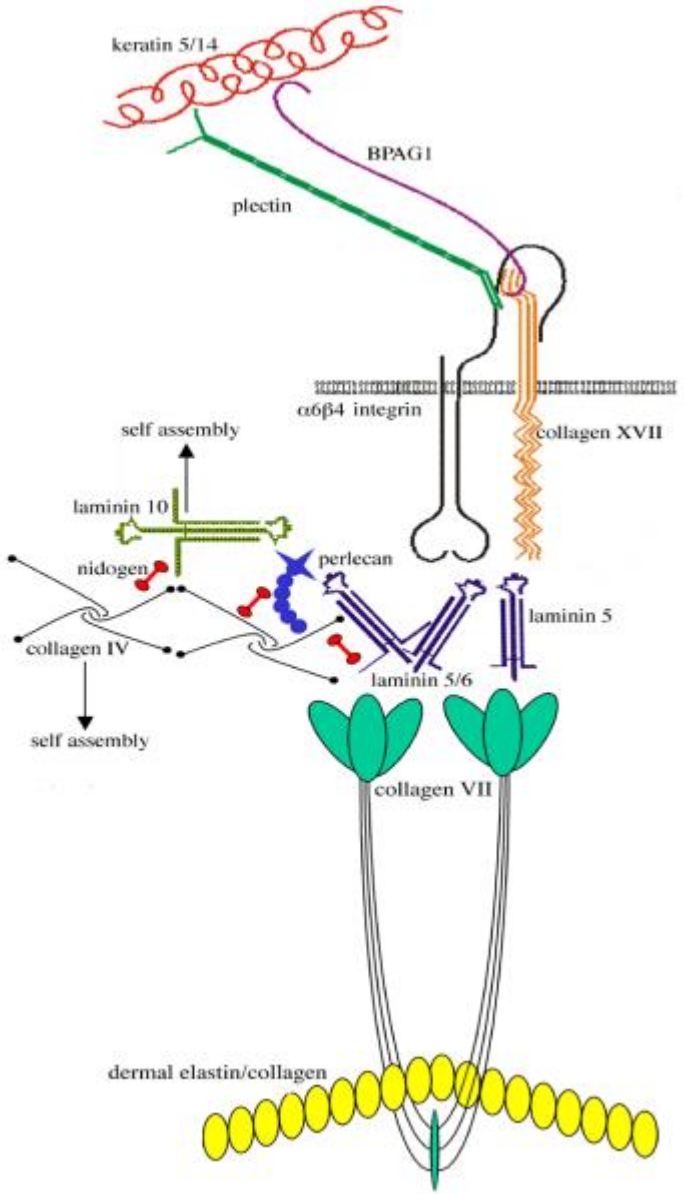
- One of four inherited forms of EB
- Dystrophic EB can be inherited dominantly (DDEB) or recessively (RDEB); the recessive form of Dystrophic EB is the most severe, chronic type of EB
- Blisters occur in the lower layer of the skin, just beneath the lamina densa in the most superficial portion of the dermis
- Produces debilitating scarring to hands and other parts of the body
- Constant cycle of blistering, wounding and re-healing greatly increases risk of squamous cell carcinoma (SCC) which can be fatal
- Diagnosis has traditionally been made based on skin biopsy and is often incorrect; genetic testing provides the most accurate diagnosis



Images courtesy of Dr. Peter Marinkovich

The dystrophic form of EB is caused by mutations in the *COL7A1* gene

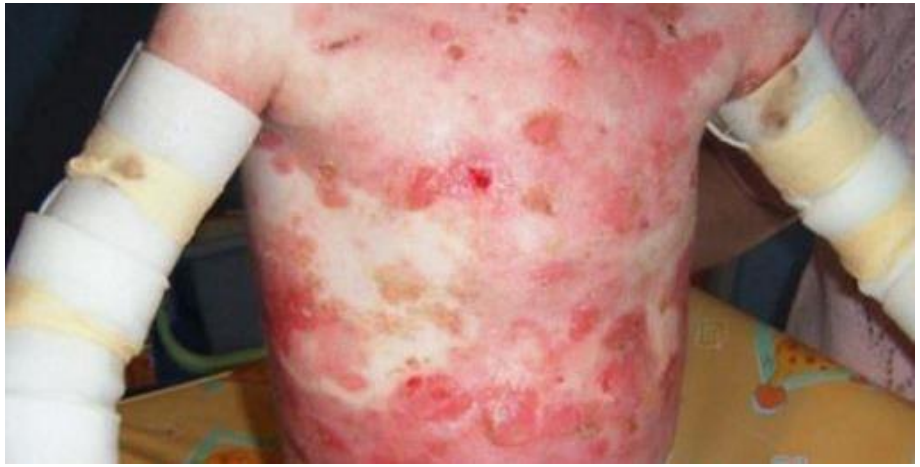
- The location of the blisters (below the lamina densa) corresponds to level of the “anchoring fibrils”
- Anchoring fibrils are the molecular glue that holds the dermis to the epidermis, and are mainly composed of type VII collagen protein (COL7)
- Mutations in the *COL7A1* gene lead to missing or dysfunctional forms of the protein; mutations can be dominant (DDEB) or recessive (RDEB)
- Without functional anchoring fibrils, the skin is fragile and easily shears with even slight friction (holding a pencil, putting on a shirt)



Images courtesy of Dr. Peter Marinkovich

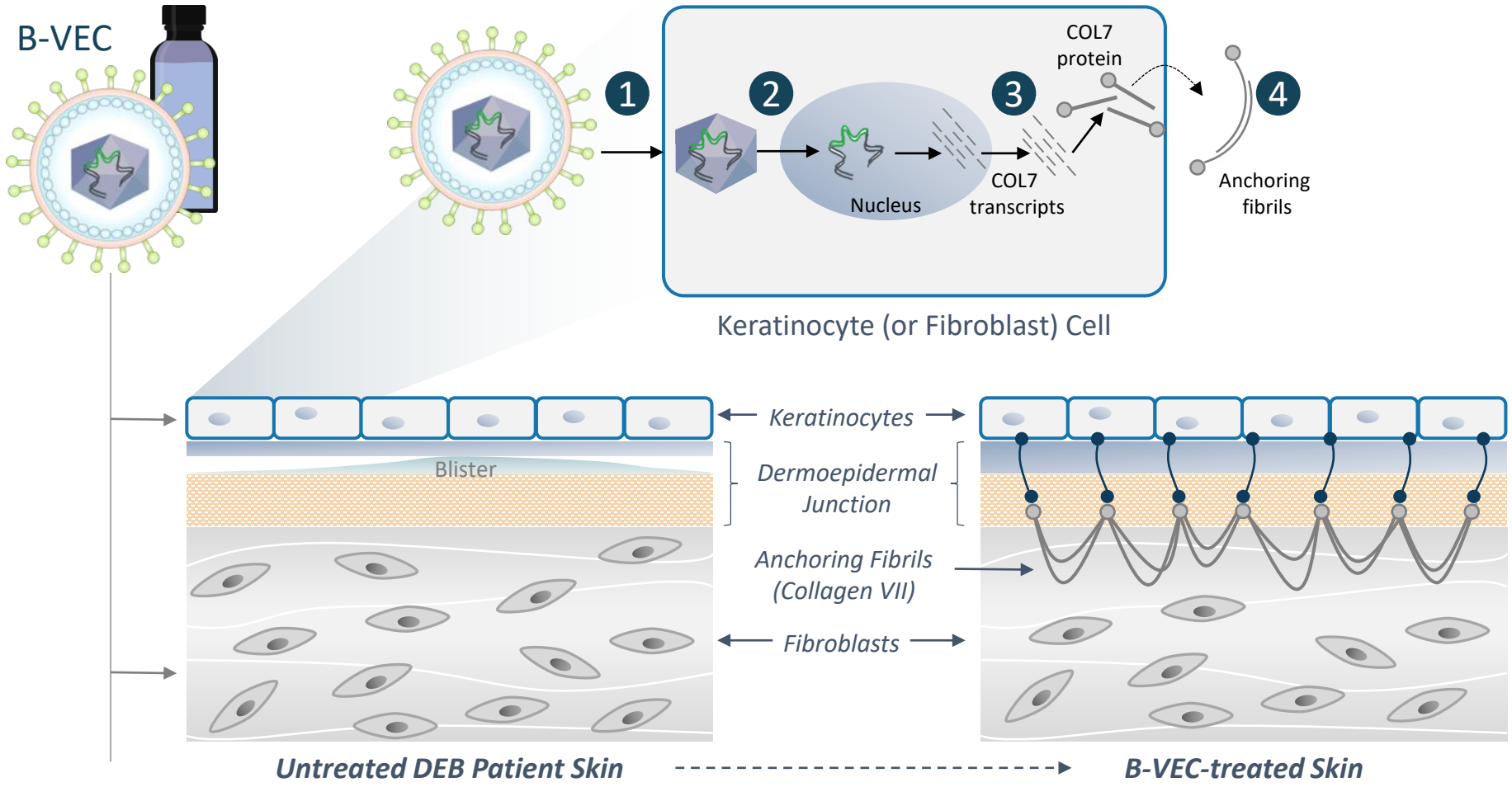
There are currently no approved corrective treatments for dystrophic EB

- Current treatment options for dystrophic EB are largely palliative in nature, involving wound care regimens similar to the care provided to burn victims
- Blistered areas are wrapped in special bandages which must be changed frequently, often daily, which is time consuming and painful
- The goal of treatment is to promote wound healing, prevent infection, and protect the skin form trauma to minimize blister formation
- Multidisciplinary care is often needed, and includes pain management, nutritional support, physical therapy, and other supportive care
- Palliative treatments cost $200k – $400k annually[1,2]



1. 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
2. GENEGRAFT Report Summary. (2015, February 16). Retrieved December 13, 2016, from http://cordis.europa.eu/result/rcn/156078_en.html

B-VEC is an investigational, off-the-shelf, topical gene therapy designed to correct the underlying molecular defect in DEB wounds



1. B-VEC enters the compromised skin of DEB patients and transduces both keratinocytes and fibroblasts
2. Once in the nucleus of transduced cells the vector genome is deposited (episomally)
3. As a result, *COL7A1* transcripts are generated, allowing the cell to produce and secrete functional COL7 protein
4. The secreted COL7 protein assembles into anchoring fibrils which hold the epidermis and dermis together

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

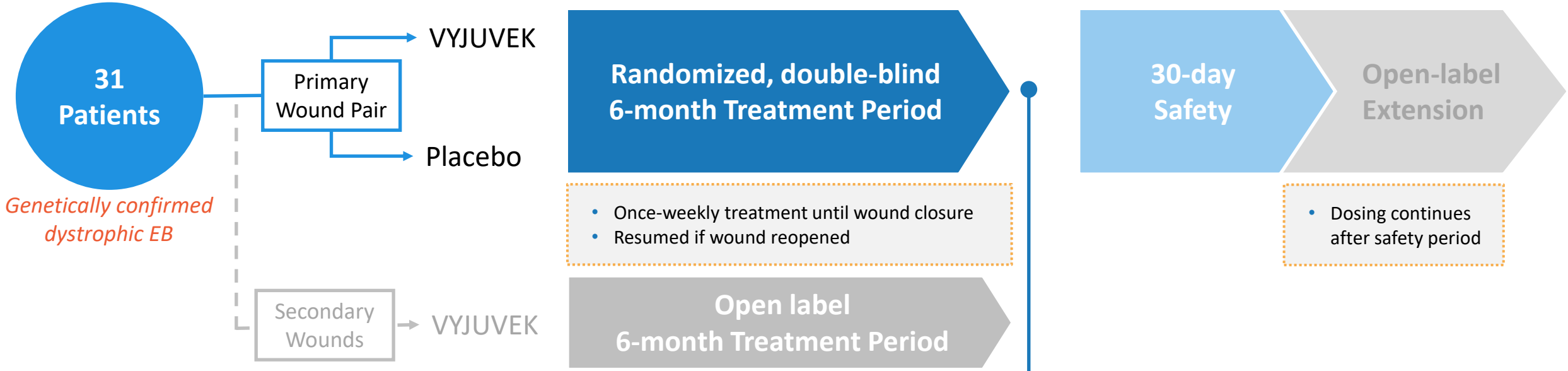
Suma Krishnan

Founder and COO

VYJUVEK™ represents important firsts

VYJUVEK is an investigational therapy being studied in clinical trials

GEM-3 evaluated weekly VYJUVEK™ or Placebo in dystrophic EB patients



Primary Efficacy Endpoints

- Complete wound healing at Week 22 and Week 24; or at Week 24 and Week 26 (six-month timepoints)

Secondary Efficacy Endpoints

- Complete wound healing at weeks 8 and 10, or 10 and 12 (three-month timepoints)
- Mean change in pain severity (VAS or FLACC-R Scale) associated with wound dressing changes

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)
- Less than ten percent 10% of enrolled patients had the dominant form of dystrophic epidermolysis bullosa (DDEB)

VYJUVEK is an investigational therapy being studied in clinical trials

Topline Ph3 safety data summary

1 **Topical VYJUVEK was well tolerated with a safety profile consistent with prior studies**

2 **No drug-related serious AEs or discontinuations due to treatment were reported**

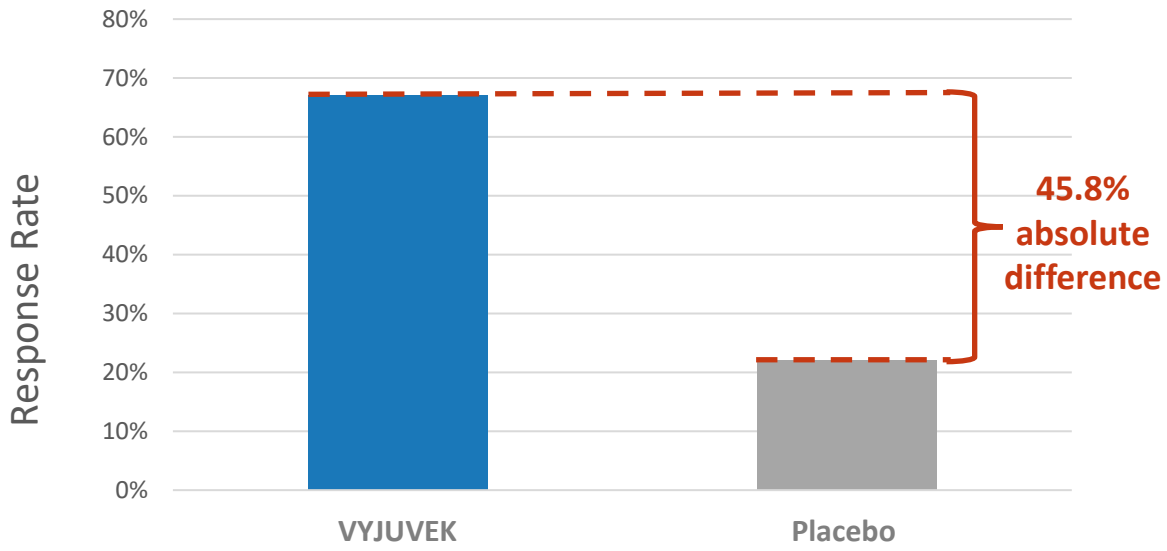
- One mild drug-related AE was reported during the trial

3 **Immunogenicity profile (as measured by anti-HSV-1 and anti-COL7 antibodies) was consistent with prior studies**

VYJUVEK is an investigational therapy being studied in clinical trials

Topline Ph3 efficacy data summary

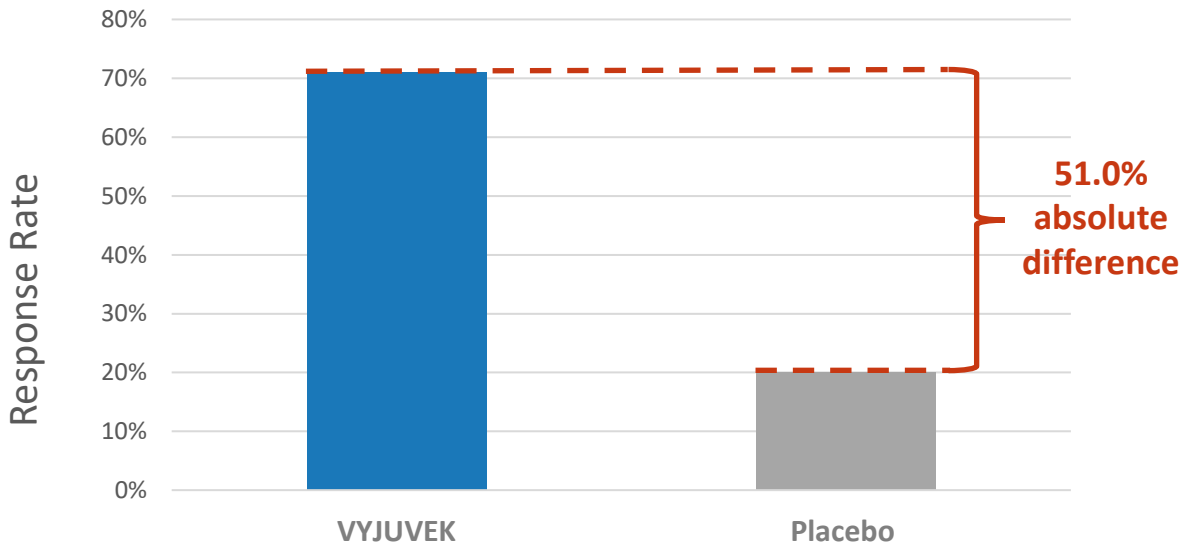
Met **primary endpoint** of complete wound healing at 6-month timepoints



Response Rate	67%	22%
Absolute Difference	45.8%	
95% Confidence Interval	23.6%-68.0%	
p-value*	**<0.005**	

*based on McNemar test

Met **secondary endpoint** of complete wound healing at 3-month timepoints



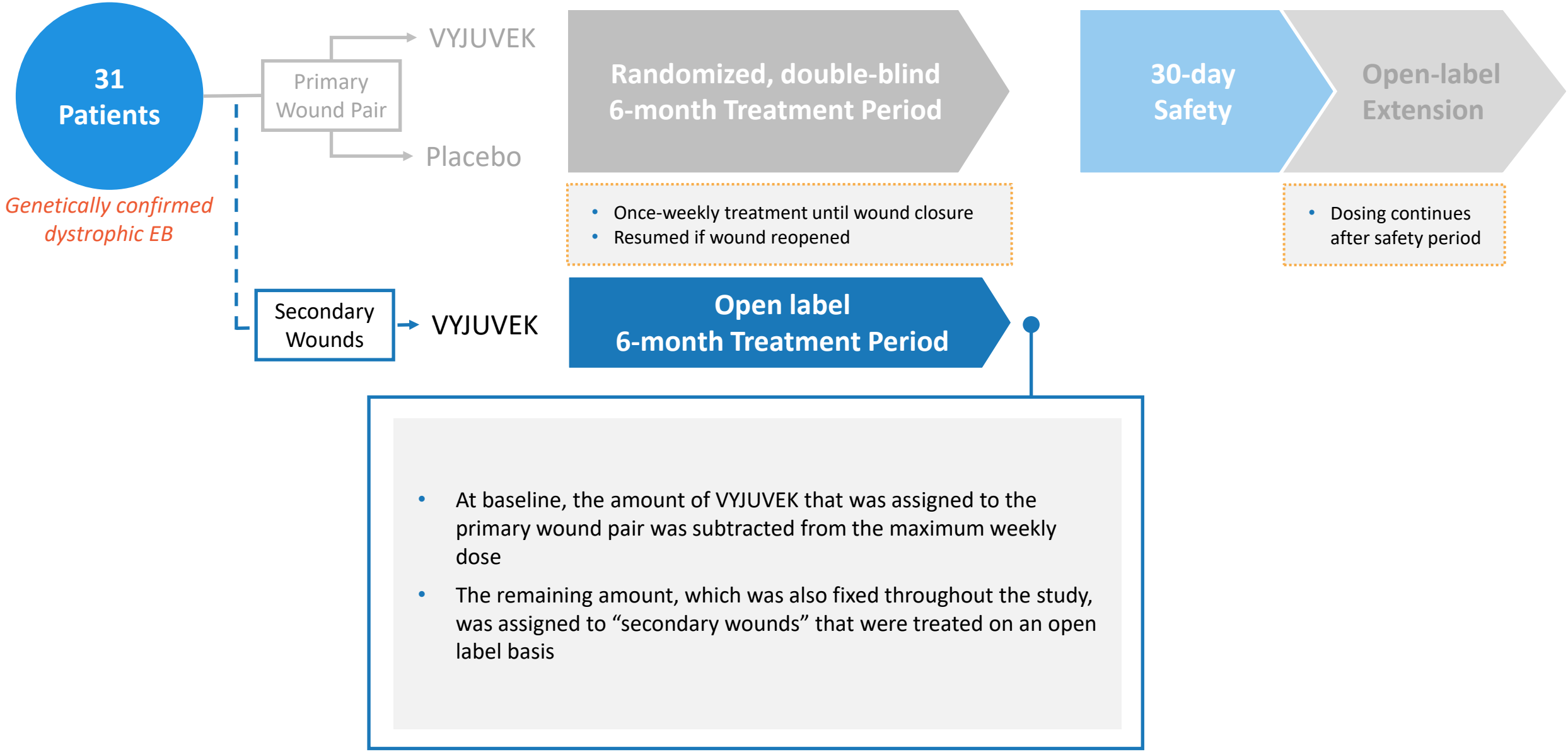
Response Rate	71%	20%
Absolute Difference	51.0%	
95% Confidence Interval	29.3%-72.6%	
p-value*	**<0.005**	

*based on McNemar test

- In an ad-hoc analysis, the trial also demonstrated a statistical difference between the active and placebo groups for wounds that demonstrated complete wound healing at both the three and six-month timepoints (p<0.005)

VYJUVEK is an investigational therapy being studied in clinical trials

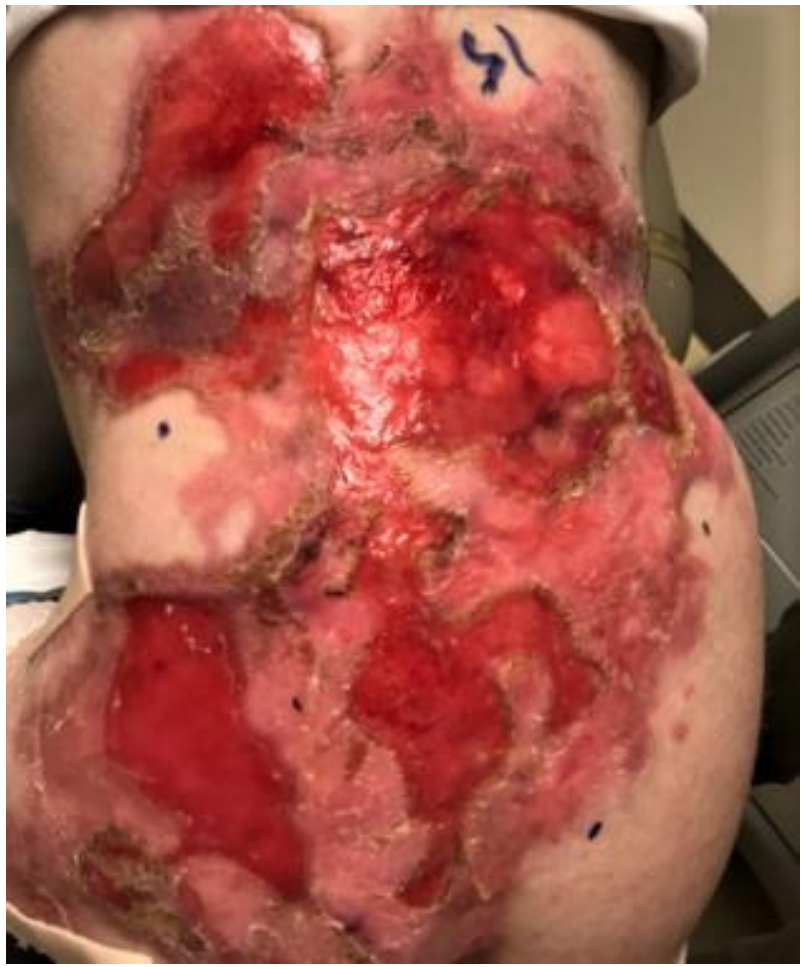
Secondary wounds received open-label VYJUVEK™ throughout the study



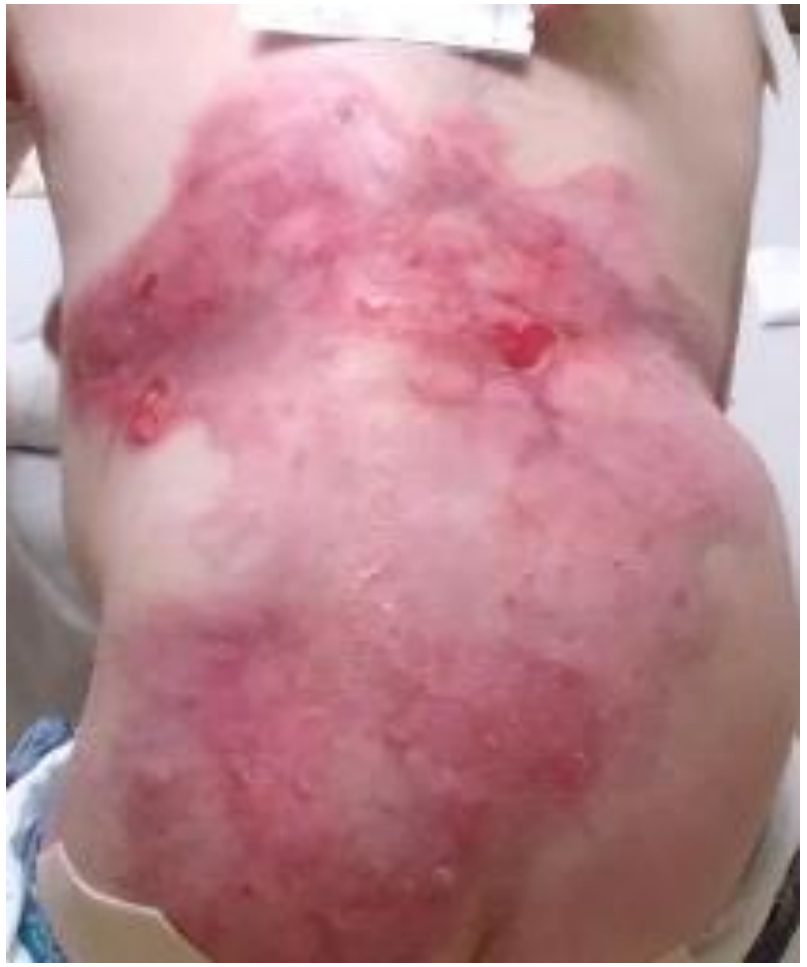
VYJUVEK is an investigational therapy being studied in clinical trials

Secondary wound (Illustrative)

Large, chronic back wound in 21 year old RDEB patient



Baseline

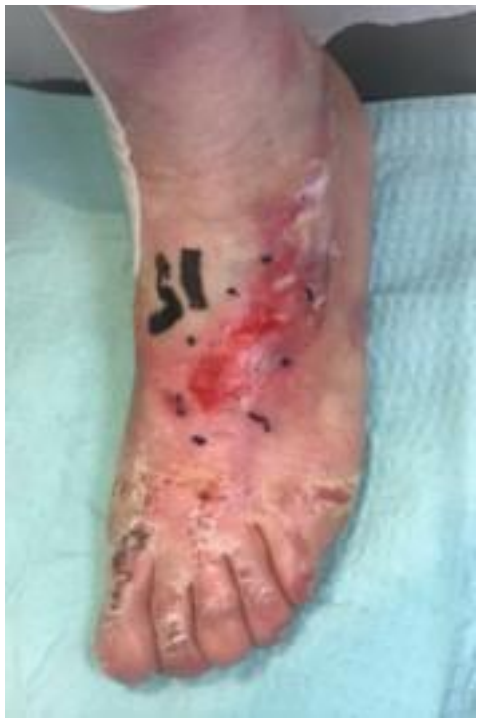


End of Study

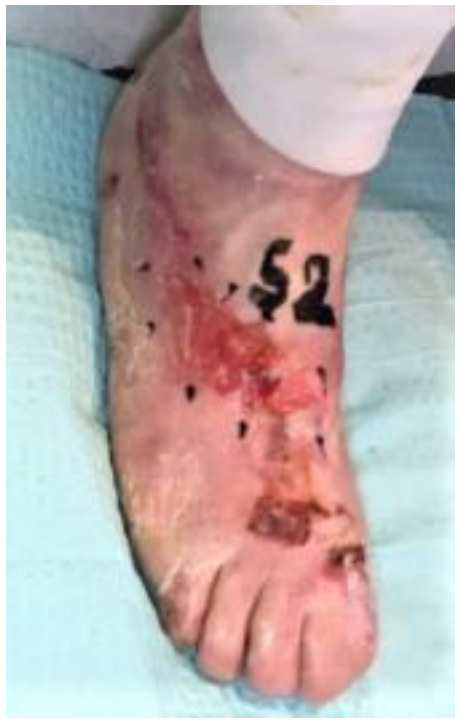
VYJUVEK is an investigational therapy being studied in clinical trials

Secondary wound (Illustrative)

Recurring foot wound in 34 year old RDEB patient

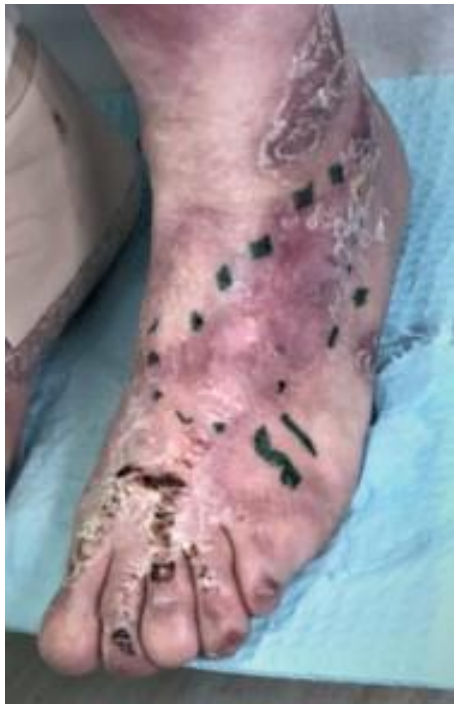


left foot



Right foot

Baseline



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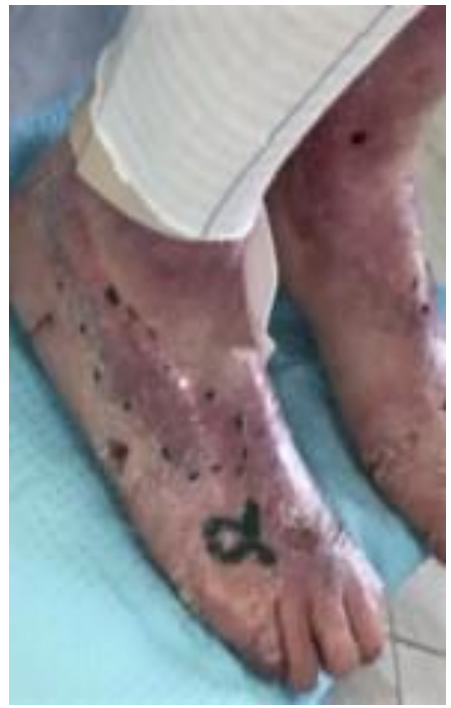
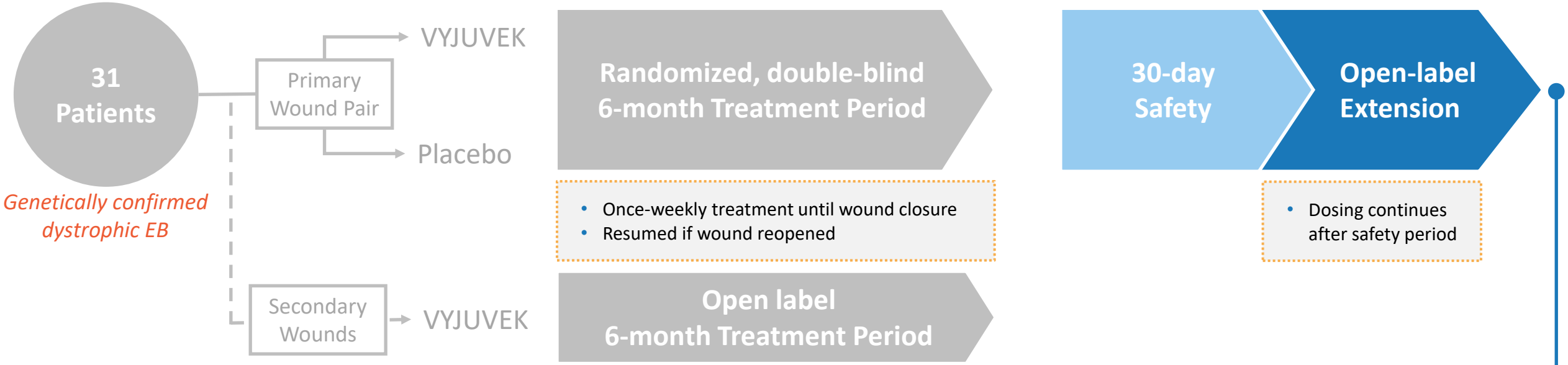


Right foot

End of Study

VYJUVEK is an investigational therapy being studied in clinical trials

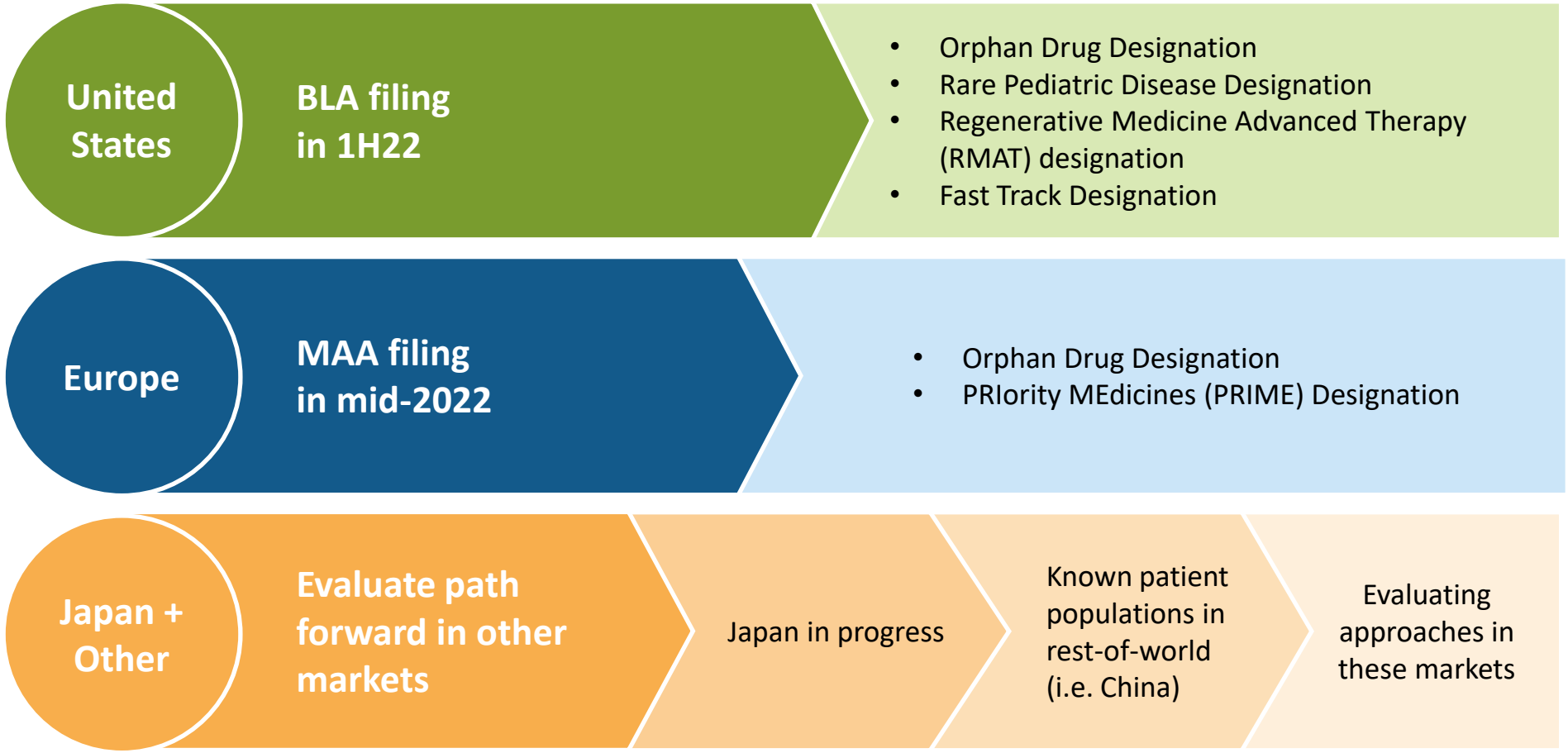
Open-label extension ongoing



- Patients who completed the Phase 3 trial have option to enroll
- Also opening three new sites where new patients who meet Ph3 entry criteria - but did not complete the Phase 3 trial – are eligible to enroll

VYJUVEK is an investigational therapy being studied in clinical trials

VYJUVEK™ regulatory next steps

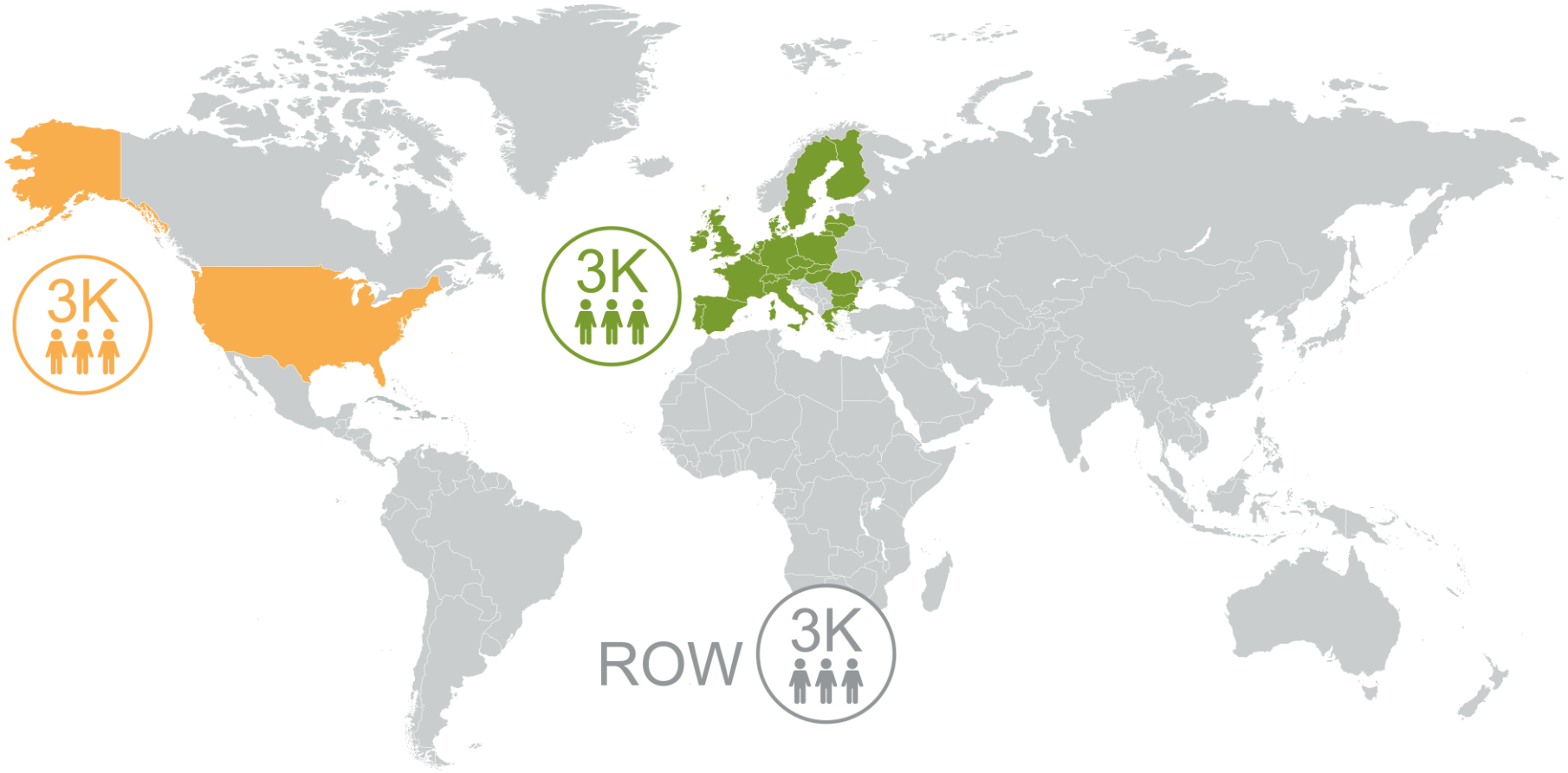


VYJUVEK is an investigational therapy being studied in clinical trials

Andy Orth

CCO

Dystrophic EB patient population and VYJUVEK™ opportunity



VYJUVEK is an investigational therapy being studied in clinical trials

Launch readiness / efforts

Education + Awareness

- 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
- Exploring all access pathways in Europe

Krystal Decode DEB™

- No-charge genetic testing available to eligible US 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

Payer / Reimbursement

- Early engagement with US payer partners to educate on Dystrophic EB, Krystal and B-VEC
- Will pursue an aggressive and progressive value-based strategy to ensure timely and open access for B-VEC

VYJUVEK is an investigational therapy being studied in clinical trials

Platform supported by in-house manufacturing capacity and expertise

Established process conducted at Krystal's end-to-end GMP facility (Ancoris)

- Maintains control of IP/trade secrets relating to manufacturing process
- Adheres to internal process and production schedules, avoiding use of high demand gene therapy CMOs

Upstream process using stable producer cell lines has cost & regulatory benefits

- Stable complementary cell lines developed in-house are used in established methods for production of consistent batches
- Eliminates the need for multiple cGMP qualifications of plasmids and variability in transfection efficiency from batch to batch
- Scalable from clinical phase to commercial

Successfully developed a robust and reproducible downstream process

- Work conducted in an aseptic closed system process
- The same process is leveraged across pipeline with minimal redevelopment effort between product candidates
- Compliant with global regulatory requirements

Krish Krishnan

Chairman and CEO

Pipeline upcoming events

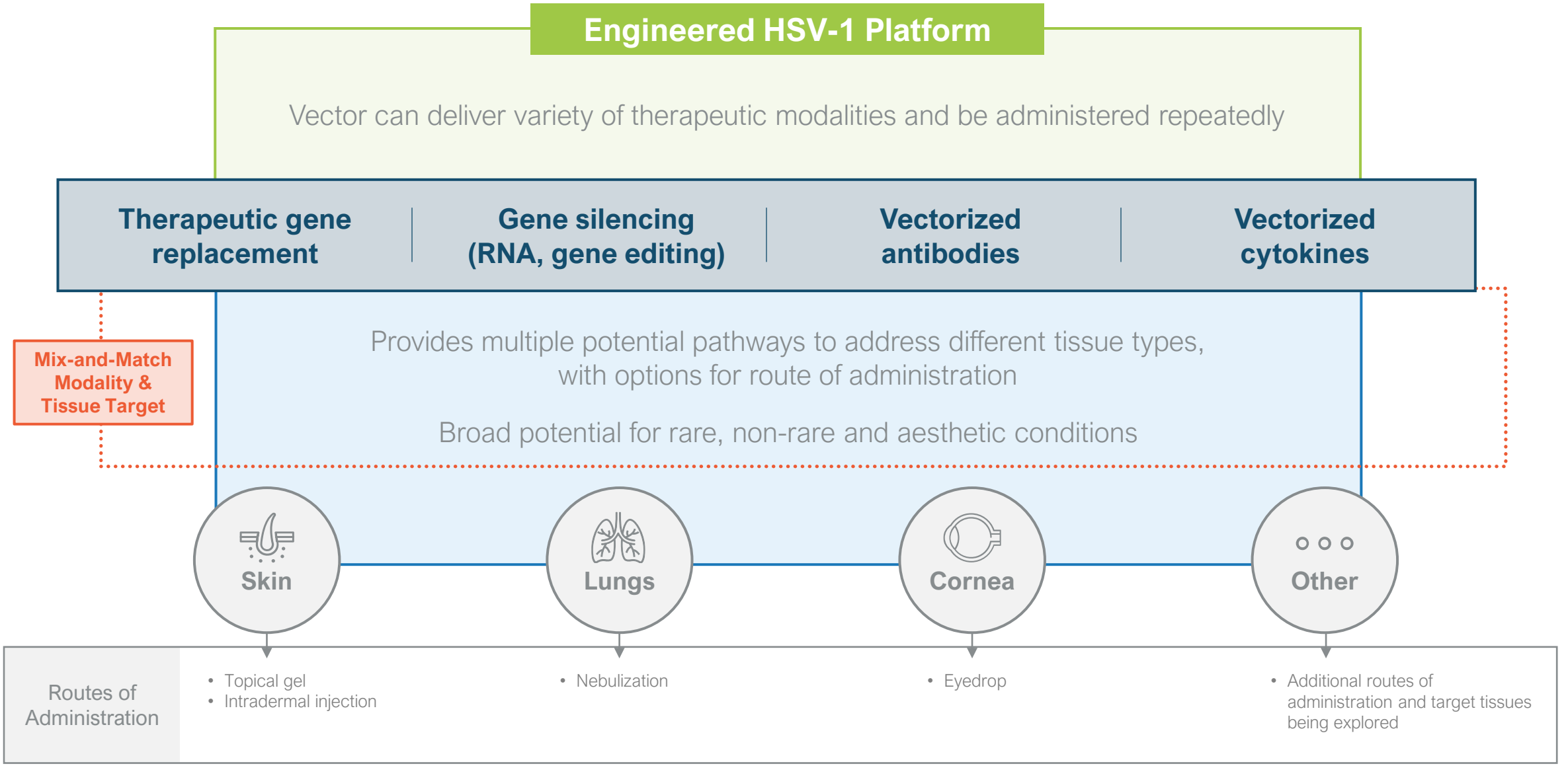
	Product	Protein	Indication	Key Upcoming Milestone	Ownership
Dermatology	VYJUVEK™ †¤•Δ‡§	Type VII collagen (COL7)	Dystrophic EB	File BLA in 1H22	Wholly owned
Dermatology	KB105†¤•‡	Transglutaminase 1 (TGM1)	TGM1-deficient ARCI	Initiate next Phase 2 cohort in 2022	Wholly owned
Dermatology	KB104¤	Serine Peptidase Inhibitor Kazal Type 5 (SPINK5)	Netherton Syndrome	File IND in 2022	Wholly owned
Dermatology	KB1XX	Undisclosed programs			Wholly owned
Dermatology	KB5XX	Vectorized antibodies	Chronic conditions		Wholly owned
Dermatology	KB301	Type III collagen (COL3)	Aesthetic skin conditions	Ph1 efficacy data in 1Q22	JEUNE
Respiratory	KB407†¤‡	Cystic fibrosis transmembrane conductance regulator (CFTR)	Cystic fibrosis	Initiate Ph1 study in 4Q21	Wholly owned
Respiratory	KB408	Alpha-1 antitrypsin (AAT)	Alpha-1 antitrypsin deficiency		Wholly owned
Respiratory	KB4XX	Undisclosed programs			Wholly owned

Discovery | Preclinical | Phase 1/2 | Phase 3

†: FDA Orphan Drug Designation;
¤: FDA Rare Pediatric Disease Designation;
•: Fast-track Designation;
Δ: FDA RMAT designation;
‡: EMA Orphan Drug Designation;
§: EMA PRIME Designation.

All pipeline compounds are investigational, being evaluated in clinical or pre-clinical studies.

Redosable gene delivery technology has broad potential



Questions & Answers