Krystal

Medicines for Skin Diseases and Conditions –
A Gene Therapy Company

CORPORATE PRESENTATION
Q1 2019

Forward-Looking Statements

This presentation contains forward-looking statements and information. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify forward-looking statements. These forward-looking statements are predictions and involve risks and uncertainties such that actual results may differ materially from these statements. These risks and uncertainties include, among others: actions by the FDA and other regulatory agencies, results and timing of current and planned clinical trials, risks related to the commercialization of our products, our ability to manufacture sufficient quantities of products for clinical trials and commercial launch, and those other risks detailed from time to time under the caption “Risk Factors” and elsewhere in Krystal Biotech's Securities and Exchange Commission (SEC) filings included in our Annual Report on Form 10-K for the year ending December 31, 2017, and in future filings and reports of Krystal Biotech. The Company undertakes no duty or obligation to update any forward-looking statements as a result of new information, future events or changes in its expectations.

Company Overview

- NASDAQ: KRYS; Started operations in 2016 with headquarters in Pittsburgh, Pennsylvania.
- Established a proprietary fully-integrated HSV-1-based gene therapy Skin TARgeted Delivery platform (STAR-D) and a pipeline of clinical and non-clinical effectors to target skin diseases and conditions. Zero royalty burden.
- Interim data readout in GEM-Phase I/II trial targeting Dystrophic Epidermolysis Bullosa (DEB) met all primary and secondary endpoints. Full data readout anticipated in 1H 2019 and pivotal study anticipated to begin in 2H 2019 with BLA filing expected in 1H 2020.
- Multiple targets (5 additional indications) based on STAR-D platform currently in pipeline
- US Patents 9,877,990 (issued 1/16/18) and 10,155,016 (issued 12/18/18) covering pharmaceutical compositions and methods of their use
- First GMP In-house manufacturing facility in Pittsburgh, PA complete. Plans to build a second GMP facility in 2H 2019 in motion.
- Insider ownership (management, employees, directors): 33 percent of fully diluted shares outstanding (as of 12/31/18)

Skin TARgeted Delivery Platform

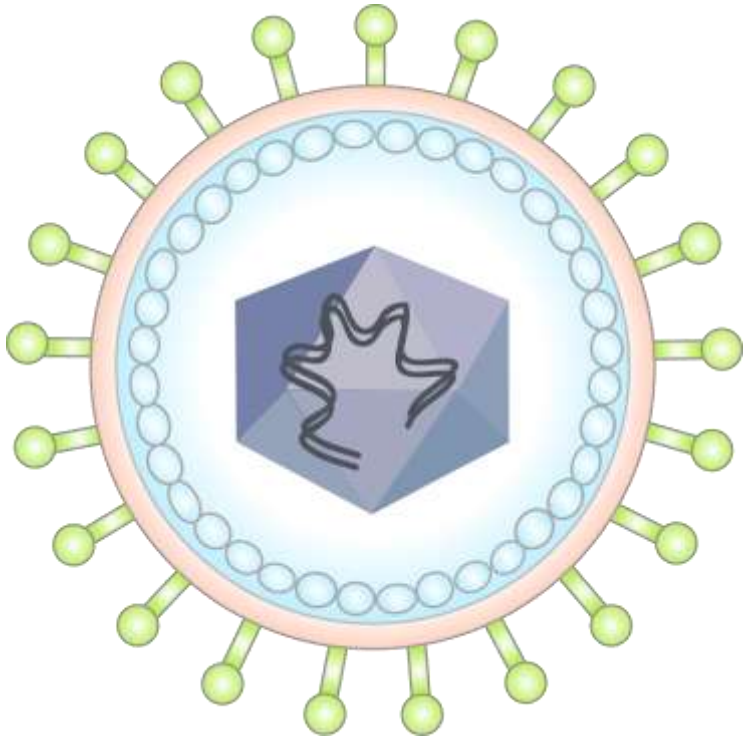
Modified Herpes Simplex Virus 1 (HSV-1) vector well suited to treat skin diseases

Proprietary Vectors
and underlying cell lines support robust and flexible drug production

Direct delivery
Topical administration for open wounds and intradermal for intact skin

Reproducible and Scalable Manufacturing
using internally developed and validated protocols

Non-integrating
into the DNA making it safer



Significant payload capacity
due to ~150Kb genome to accommodate multiple genes and effectors in the backbone

Stability
of vector beneficial to production and storage

High Transduction Efficiency
Transduces dividing and non-dividing skin cells

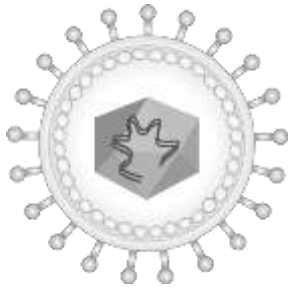
Non-Replicating
Safe for repeat administration; transient transgene expression, diluted by cell divisions

Regulatory precedent
HSV-1 used as backbone in Amgen's Imlygic®, which is approved for melanoma and administered weekly to patients

Krystal's Unique and Straightforward Approach

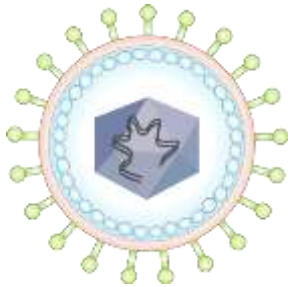
"Off-the-shelf" gene therapy with repeat administration

Wild-type HSV-1



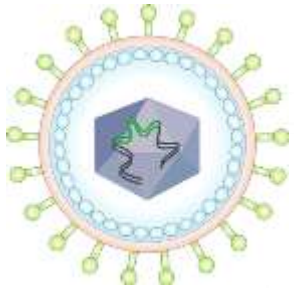
Targeted mutagenesis of HSV-1, resulting in platform that is both safe and effective for delivery of effector(s) to human skin

STAR-D Platform



Modify STAR-D platform via insertion of one or more therapeutic effectors of interest

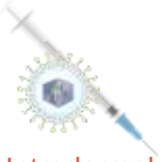
Therapeutic Vector



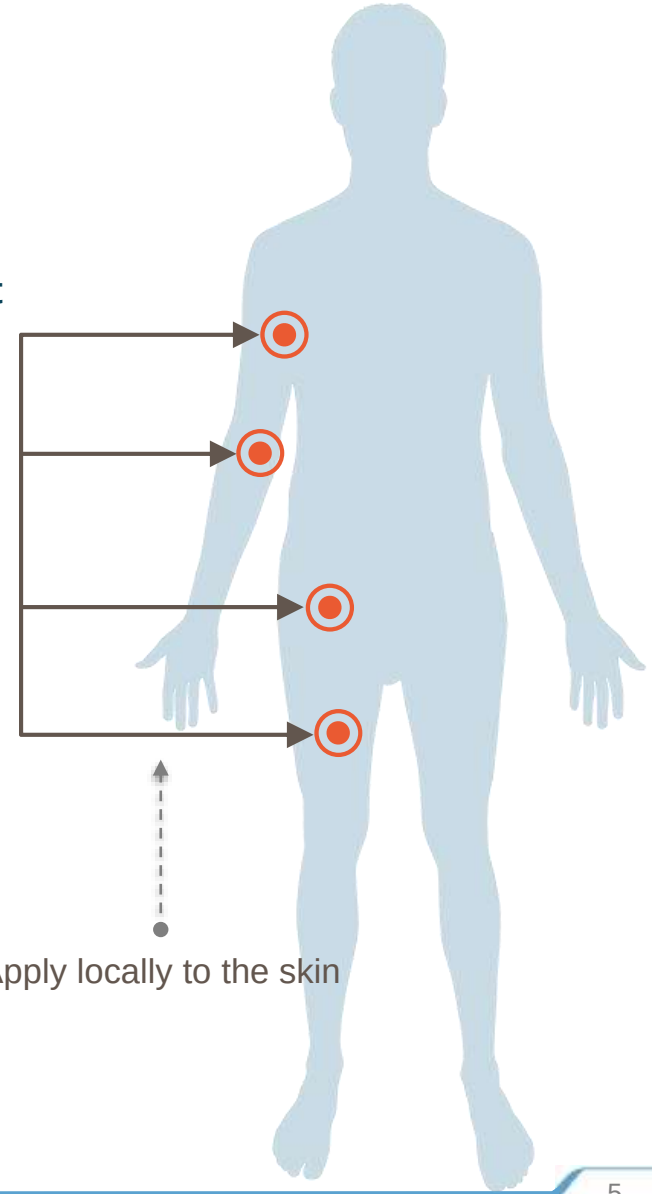
Formulate into a topical gel or intradermal solution

Drug Product

Topical



Intradermal

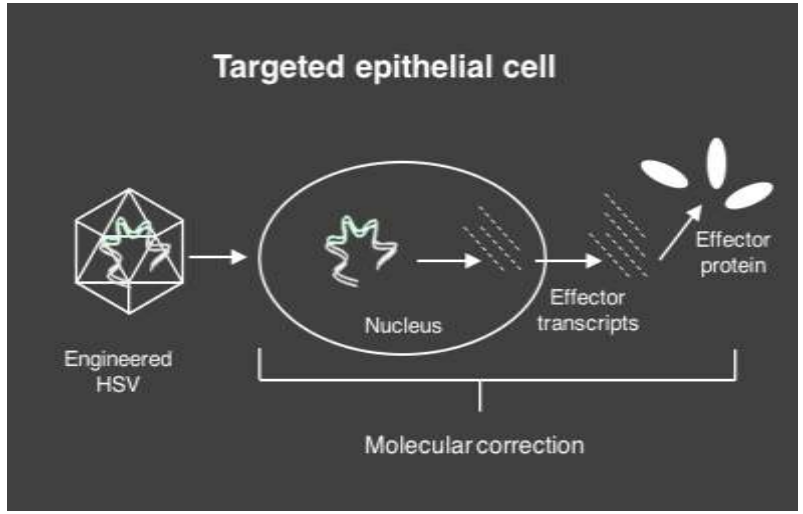


Apply locally to the skin

Krystal's Approach: Applicable to a Wide Range of Skin Diseases and Conditions

1. Severe monogenic skin diseases

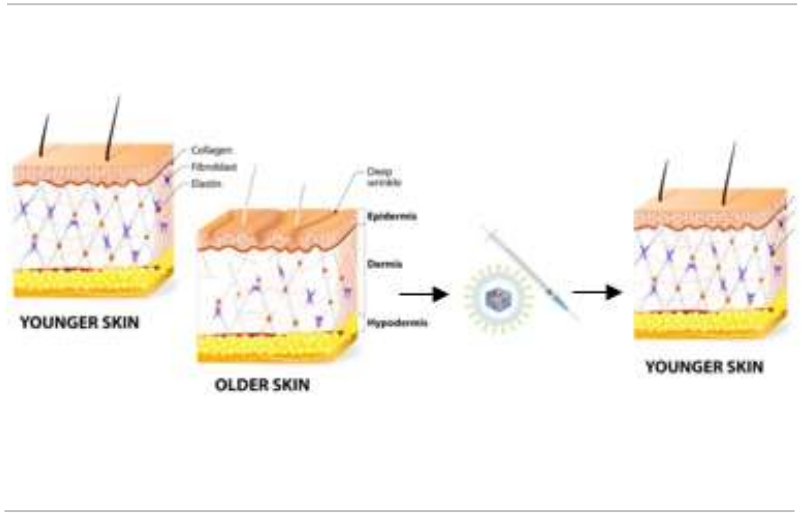
Indications: Dystrophic Epidermolysis Bullosa (DEB); Autosomal Recessive Congenital Ichthyosis (ARCI); Junctional Epidermolysis Bullosa (JEB); Netherton Syndrome (NS)



Effectors: *COL7A1* (type VII collagen); *TGM1* (transglutaminase-1); laminins; *SPINK5* (serine protease inhibitor kazal-type 5)

2. Aesthetic conditions

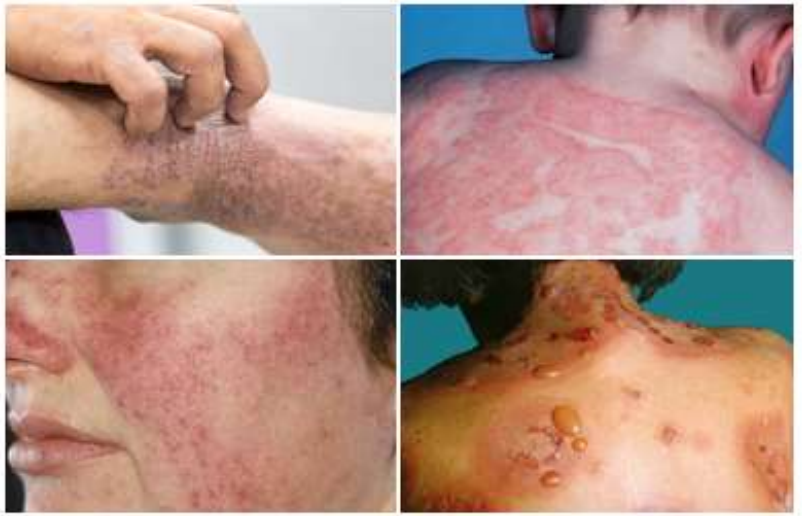
Indications: fine lines; nasolabial folds; glabellar lines; depressed scars; UV-induced skin damage



Effectors: Collagens

3. Chronic skin diseases

Indications: atopic dermatitis; psoriasis; rosacea; acne



Effectors: Anti-inflammatory antibodies and antibody fragments

Krystal's Current Pipeline

Product	Indication	Discovery	Preclinical	Phase I/II	Phase III	Marketed
KB103†‡•¤	**Dystrophic EB**					
KB104	**Netherton Syndrome**					
KB105†¤	**TGM1-deficient ARCI**					
KB107	**Junctional EB**					
KB301 / KB302	**Aesthetic Skin Conditions**				Two undisclosed targets	
KB5XX	**Chronic Skin Diseases**			Two undisclosed targets		

†: FDA Orphan Drug Designation;
‡: EMA Orphan Drug Designation;
•: Fast-track Designation;
¤: FDA Rare Pediatric Disease Designation.

A Catalyst-rich 2019

- Announce final results for KB103 phase I/II trial; 1H 2019
- Commence pivotal phase III trial for KB103; 2H 2019
- Begin phase I clinical trials for two pipeline candidates in 2019
  - KB105 for ichthyosis in 1H 2019
  - KB301 for aesthetic condition in 2H 2019
- First GMP facility inauguration and operational in 1Q 2019. Break ground on second backup GMP facility in 2H 2019.
- Pre-clinical work in chronic skin diseases in anticipation of clinical program in 2020

A fully-integrated proprietary HSV-1-based gene therapy Skin TARgeted Delivery (STAR-D) platform and a pipeline of clinical and non clinical effectors to target skin diseases and conditions

KB103*

USAN: *bercolagene telserpavec*

For treatment of dystrophic epidermolysis bullosa (DEB)

* Fast Track Designation Granted;

  Orphan Drug Designation in US and EU;

  Rare Pediatric Disease Designation in US;

  Eligible for Priority Review Voucher.

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Dystrophic Epidermolysis Bullosa (DEB)

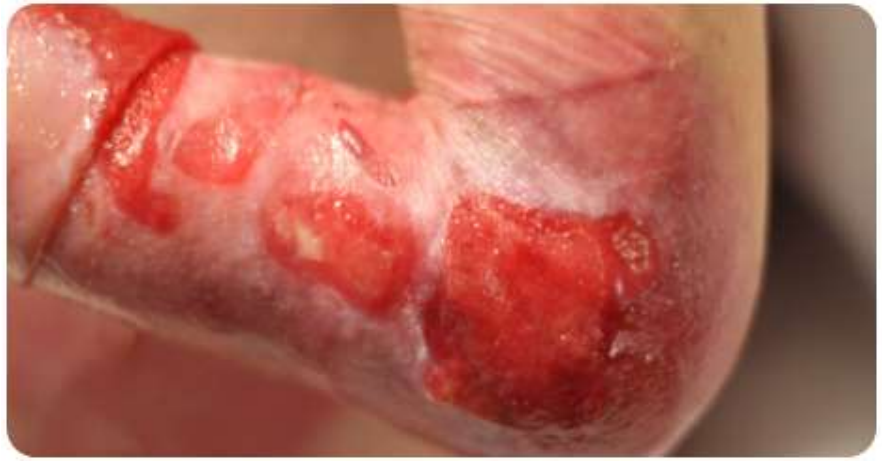
"Butterfly Children" is used to describe young DEB patients because their skin is as fragile as a butterfly's wings

Dystrophic Epidermolysis Bullosa

A rare, genetic connective tissue disease that causes skin to tear or blister from minor contact

Caused by a mutation in the COL7A1 gene that codes for the COL7 protein

Without COL7 the epidermis does not anchor to the dermis



Epidemiology

Prevalence: Up to 125,000 people are affected by DEB worldwide[1]

Incidence: The incidence of DEB is 6.5 per million births in the US[2]

Current Standard of Care

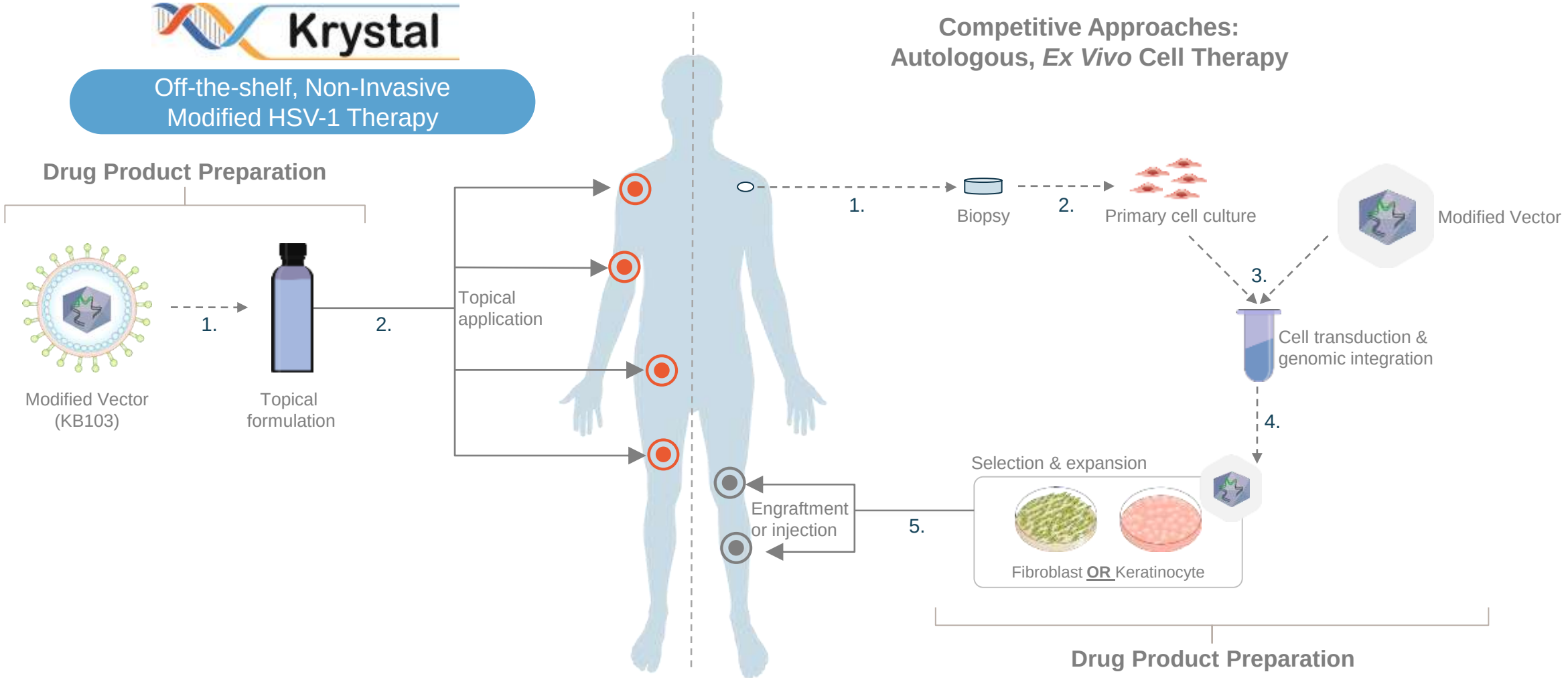
There are no approved treatments for DEB

Existing therapies limited to expensive and time-consuming palliative treatments

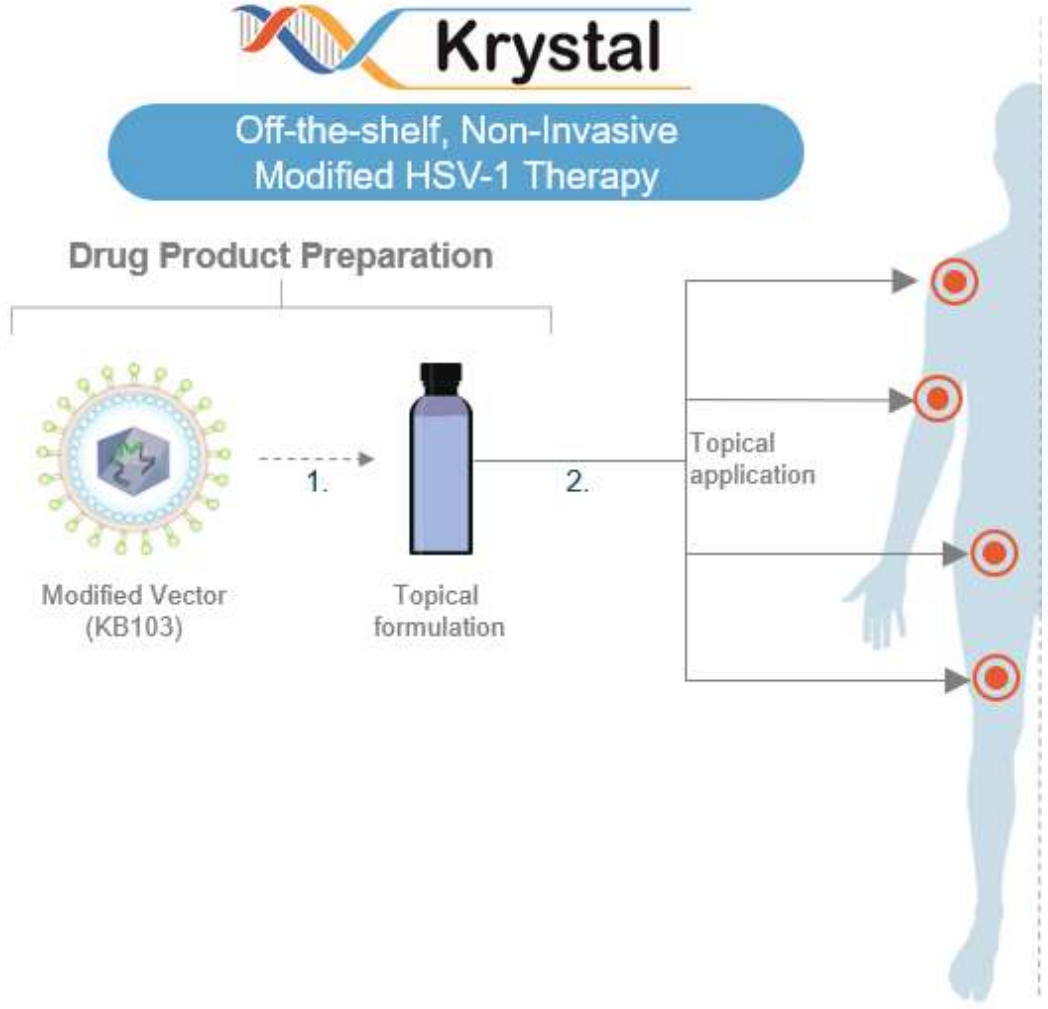
Palliative treatments cost $200k – $400k annually[3,4]

1. DEBRA International, http://www.debra-international.org/epidermolysis-bullosa/causes-and-subtypes.html; http://www.debra-international.org/what-is-eb/causes-and-subtypes/deb.html
2. Pfendner EG, Lucky AW. Dystrophic Epidermolysis Bullosa. 2006 Aug 21 [Updated 2015 Feb 26]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet].
3. 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
4. GENEGRAFT Report Summary. (2015, February 16). Retrieved December 13, 2016, from http://cordis.europa.eu/result/rcn/156078_en.html

Simple, Painless and Easy to Administer



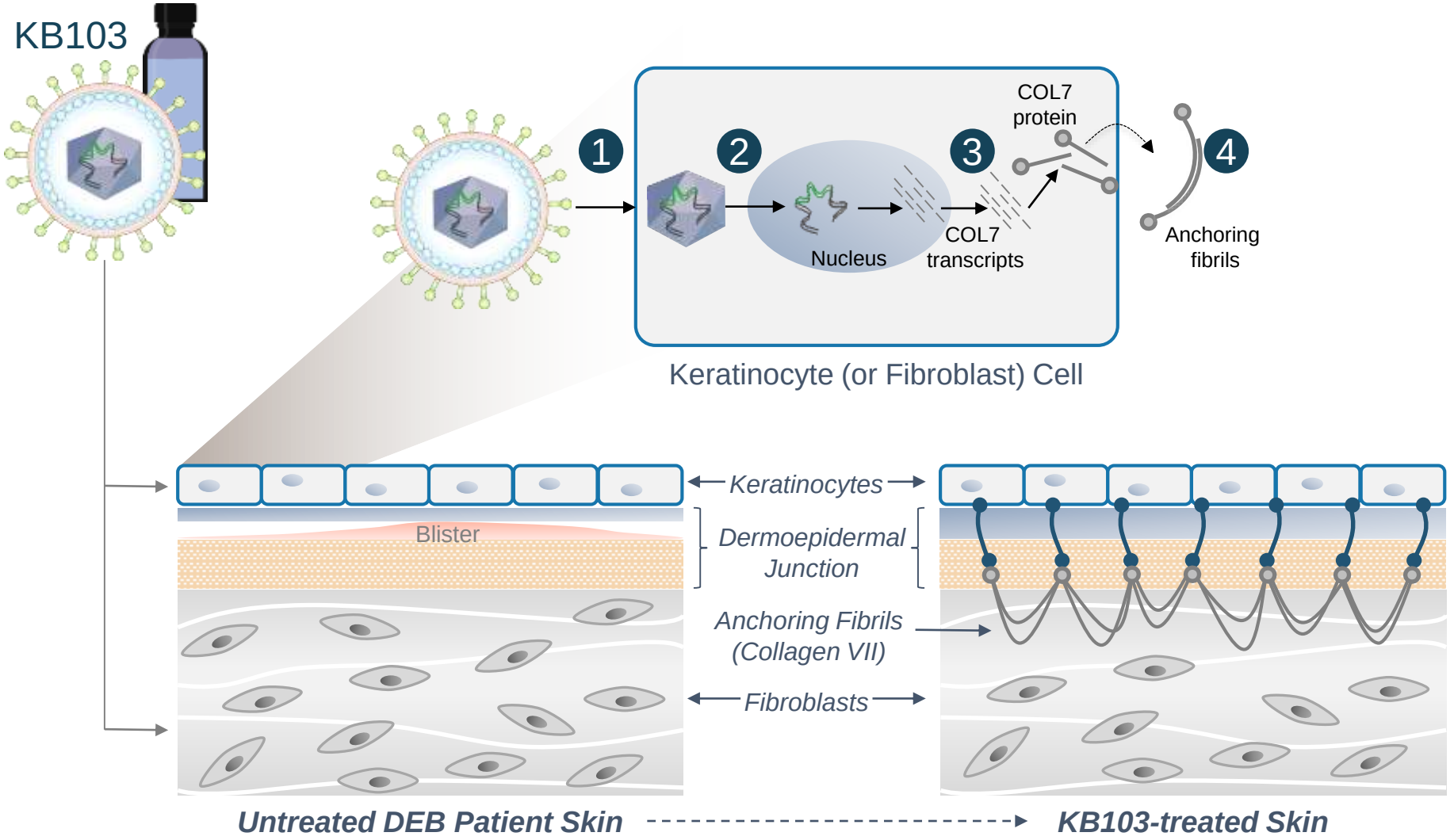
Simple, Painless and Easy to Administer



Benefits of Krystal's approach vs. autologous therapy:

- Drug product ready for use in multiple patients
- Manufacturing and supply chain costs are lower
- Therapy can be administered by any dermatologist
- Outpatient; no hospitalization needed
- Does not require expensive, invasive, and time-consuming procedures or sophisticated medical teams

KB103 Mechanism of Action



1. KB103 enters the compromised skin of DEB patients and transduces both keratinocytes and fibroblasts
2. The drug enters the nucleus of transduced cells and the vector genome is deposited (episomally)
3. *COL7A1* transcripts are generated, which allows 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

KB103 Status

- Interim Phase I data announced
- Four additional patients (total of 6) dosed in Phase II study
- Announce final Phase I/II data
- Initiate pivotal Phase III study
- File Biologics License Application (BLA)

KB103 Phase I/II Interim Clinical Data

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Phase I Trial Design

A Phase I Study of KB103, a Non-Integrating, Replication-Incompetent HSV Vector Expressing the Human Collagen VII Protein, for the Treatment of Dystrophic Epidermolysis Bullosa (DEB)

- Key objectives: Demonstrate efficacy and safety of KB103
- Primary Objectives: Expression of COL7, presence of anchoring fibrils, and safety
- Secondary Objectives: Change in wound area, duration of wound closure, time to wound closure
- Principal investigator: Dr. Peter Marinkovich, MD, Dermatologist, Stanford University
- Trial Design:
  - Randomized, open-label, placebo controlled
  - 2 wounds treated topically: 1 placebo, 1 active
  - 1 intact site treated intradermally
  - Patients were evaluated for COL7 expression by immunofluorescence and for the presence of anchoring fibrils by electron microscopy
  - Initial dosing at Day 0 and a repeat dose a month later; Patient 02 was additionally dosed on Day 14 and Day 42 by PI to understand impact of incremental dose escalation

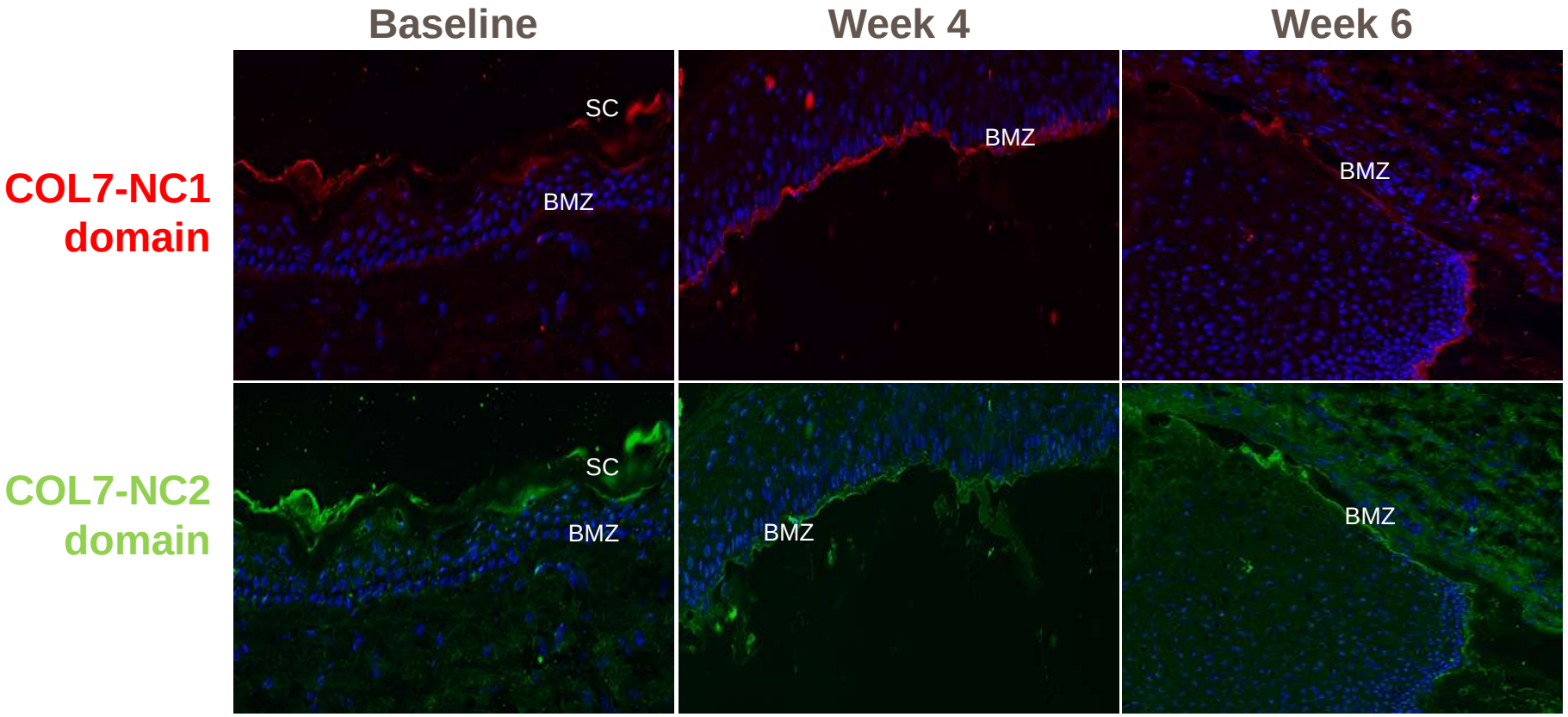
Patient Characteristics

Two patients have completed the study per phase I protocol

Characteristic	Patient 01	Patient 02
Age, y	35	28
Sex	Male	Male
Clinical and genetic diagnosis	Recessive DEB	Recessive DEB
Type VII collagen expression		
By immunofluorescence of skin biopsy	Trace NC1 detected NC2 undetected	Trace NC1 detected NC2 undetected
By Western blot	Positive for NC1	Positive for NC1
Electron microscopy of skin biopsy	No mature anchoring fibrils; sublamina densa split	No mature anchoring fibrils; sublamina densa split
Circulating autoantibodies	Negative	Negative

Patient 01: COL7 Immunofluorescence

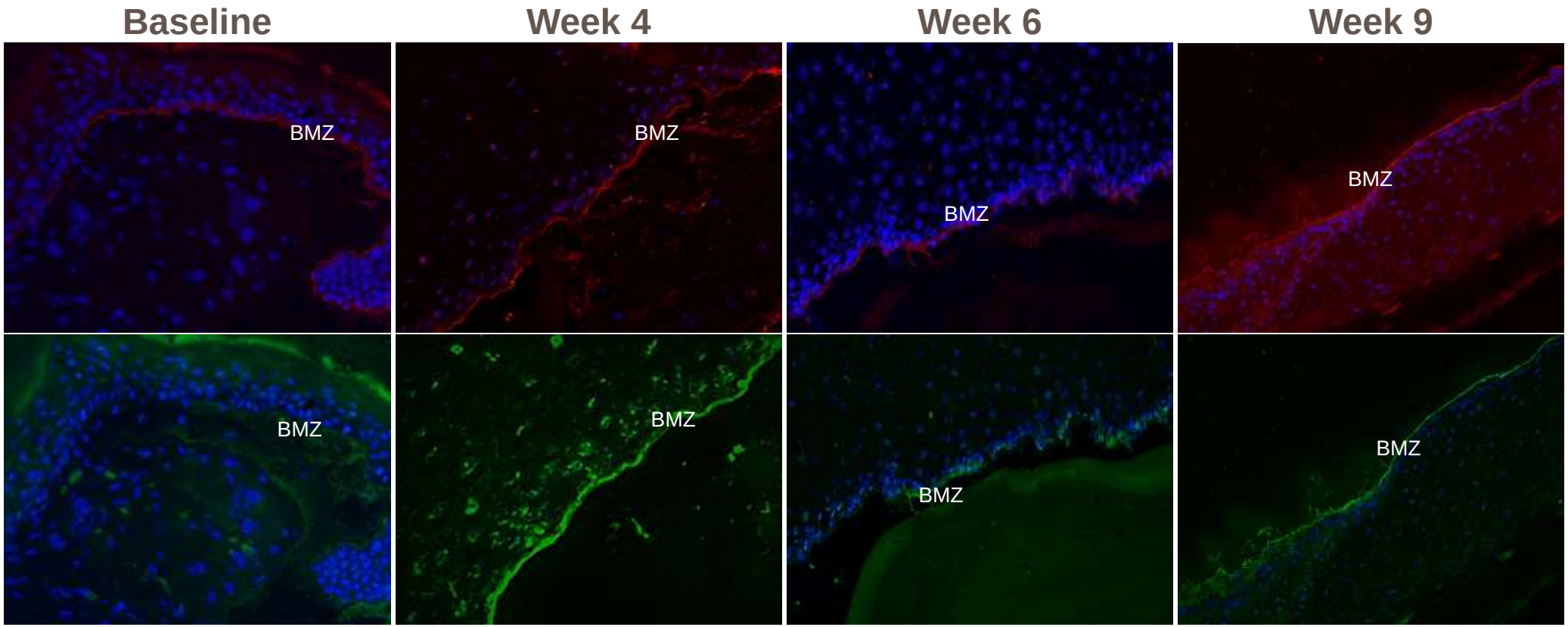
Full-length COL7 (NC1 and NC2) was detected at Weeks 4 and 6



SC: stratum corneum; BMZ: basement membrane zone

Patient 02: COL7 Immunofluorescence

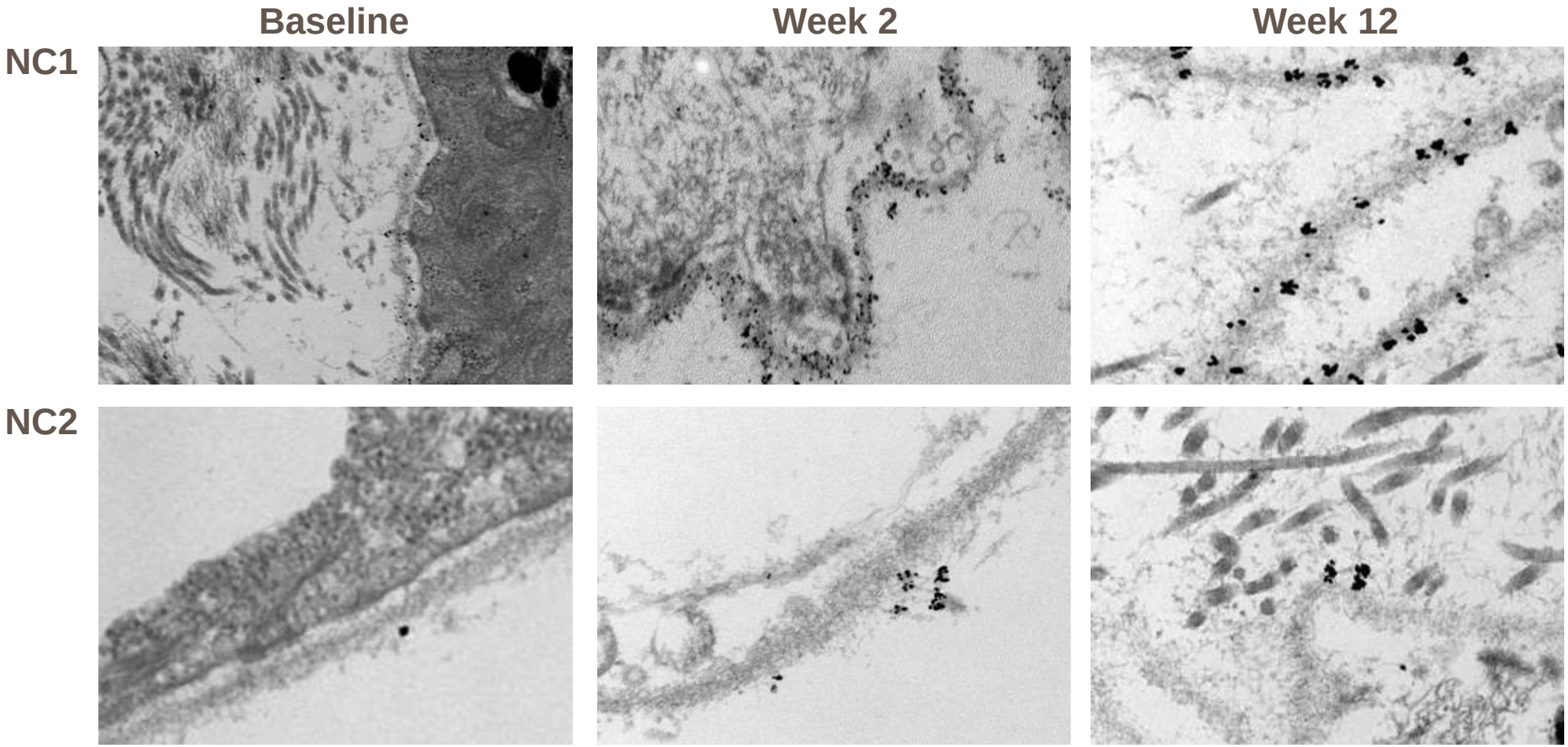
Full-length COL7 (NC1 and NC2) was detected at Weeks 4, 6, and 9



BMZ: basement membrane zone

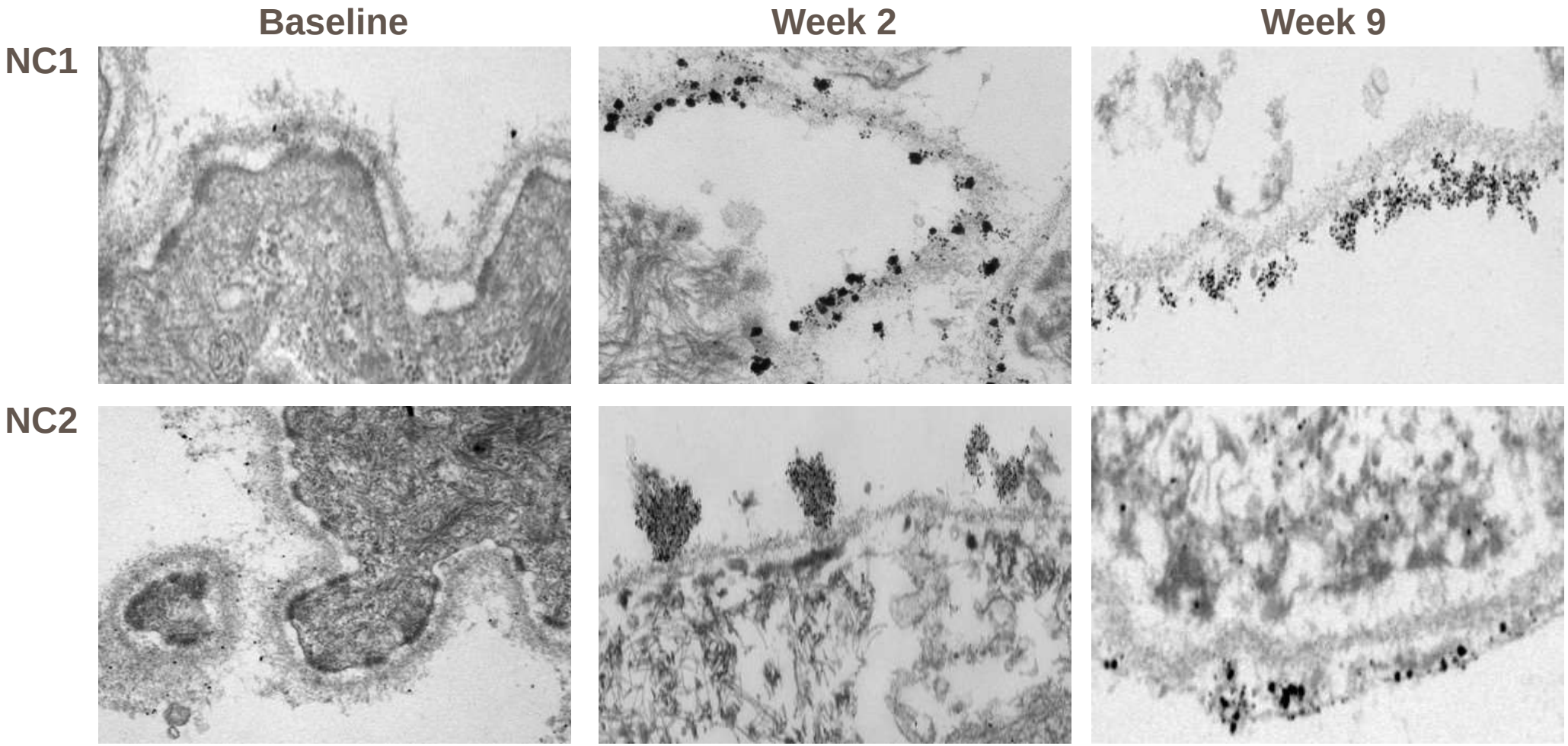
Patient 01: Anchoring Fibrils Using Immunoelectron Microscopy

NC1 and NC2-reactive anchoring fibrils detected as early as Week 2, and throughout study



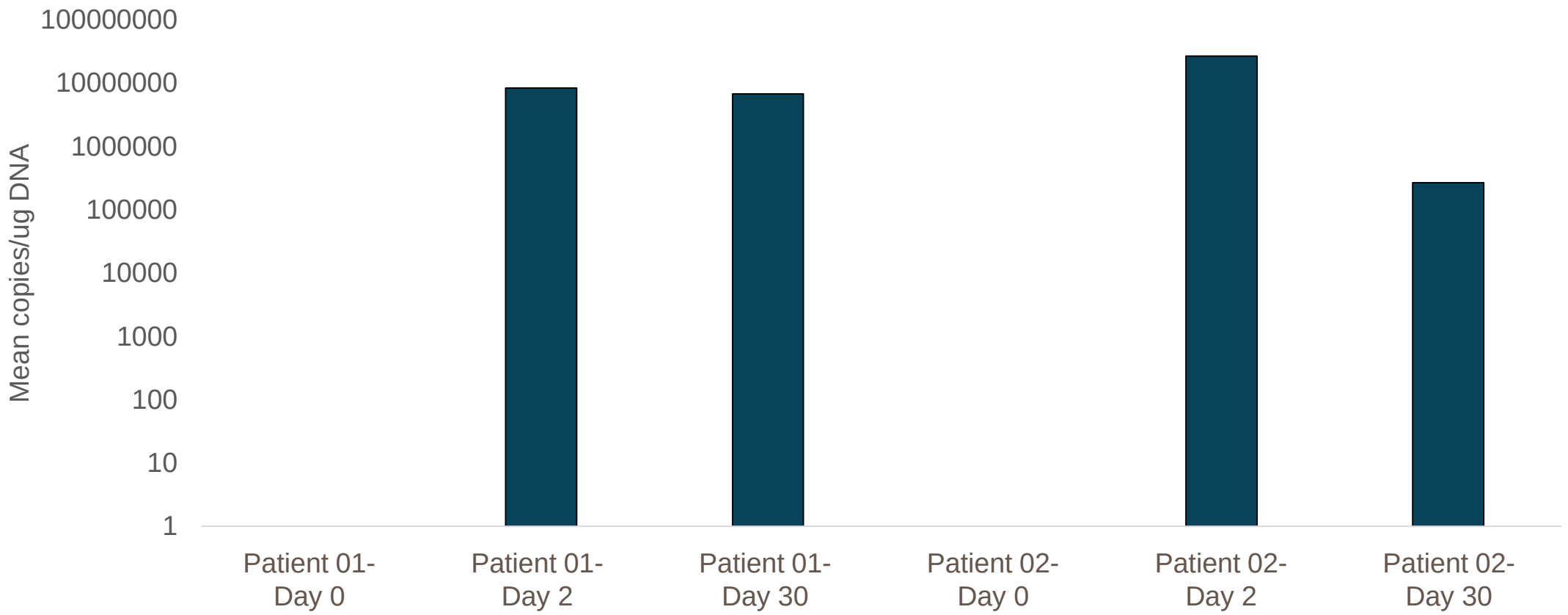
Patient 02: Anchoring Fibrils Using Immunoelectron Microscopy

NC1 and NC2-reactive anchoring fibrils detected as early as Week 2, and throughout study



Patients 01 and 02: Vector DNA Copies by qPCR

Post-dose KB103 DNA copies



- Dosing on Days 0 and 28. Measurements at Days 2 and 30
- The ability to re-administer KB103 was confirmed

Wound Monitoring

KB103-treated wounds closed by Week 2

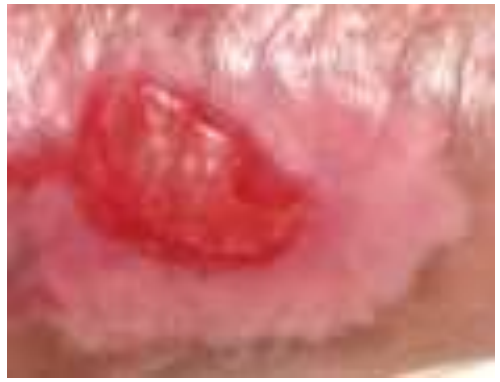
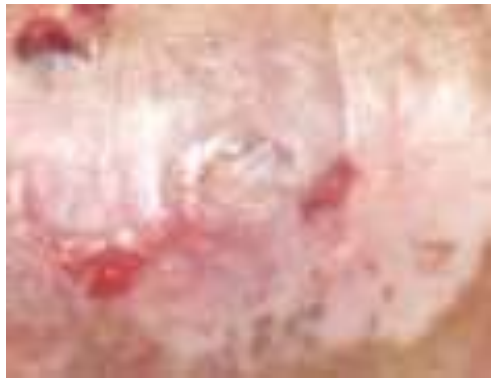
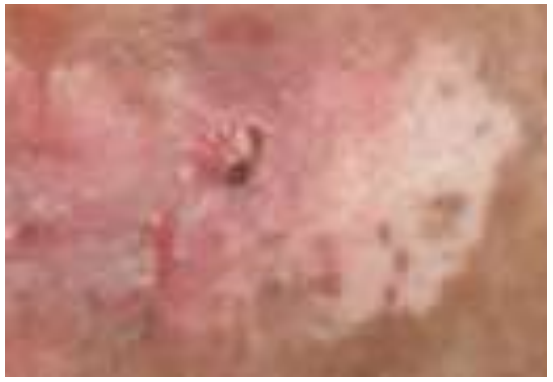
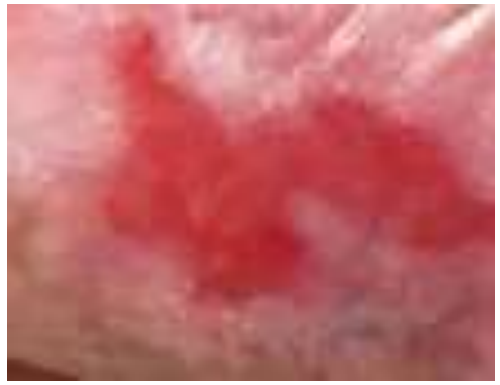
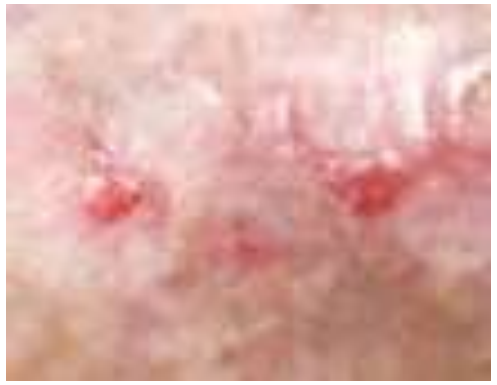
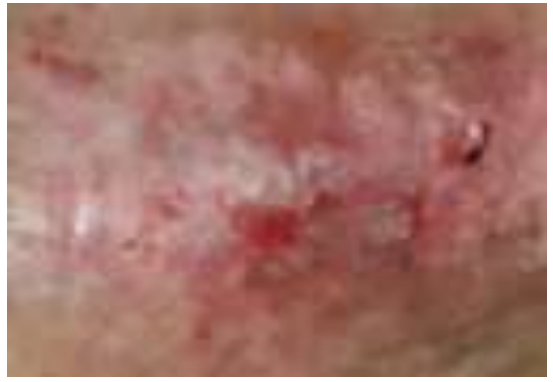
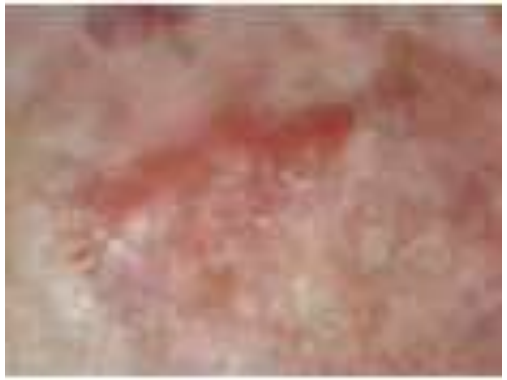
Parameters	Patient 01		Patient 02	
	KB103	Placebo	KB103	Placebo[1]
Number of wounds treated	1	1	1	1
Time to complete wound closure (weeks)	2.0	10	2	-
Duration of wound closure (months)	4.5[2]	2.5	3.5[2]	-
% wound closure at 1 month	100%	85%	100%	34%

[1]Patient 02's placebo wound did not fully close throughout the study
[2]Both wounds treated with KB103 continue to remain closed

Update: KB103-treated wounds remained closed through the last timepoint representing 5.7 and 6.6 months of closure, respectively, for Patients 01 and 02.

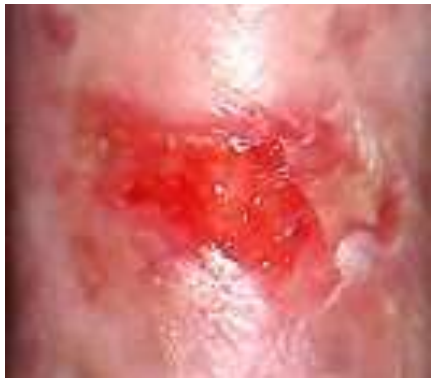
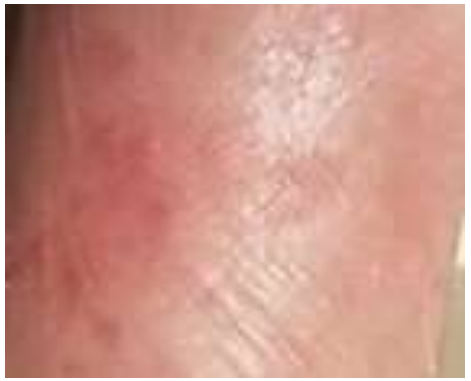
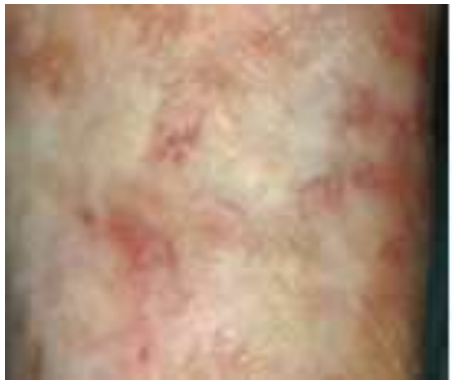
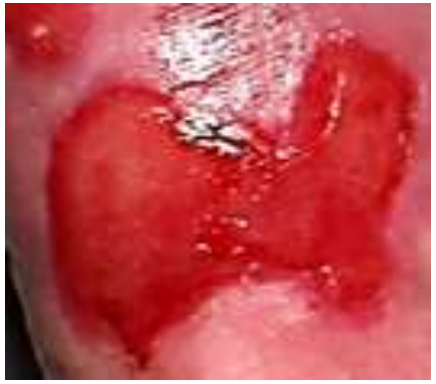
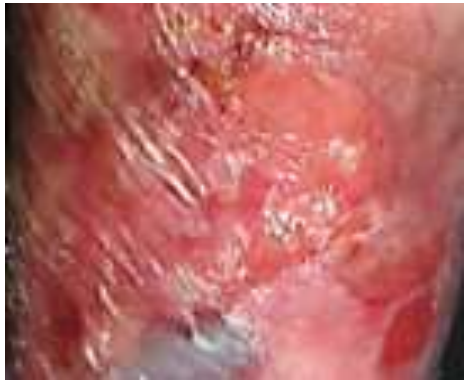
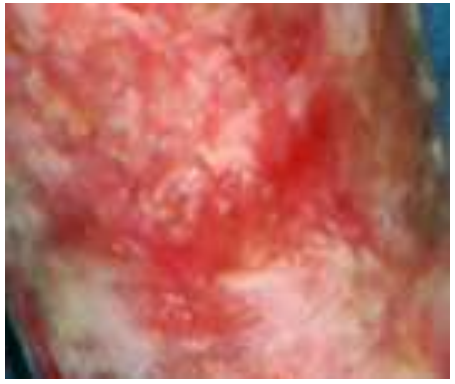
Patient 01: Wound Closure Images

Patient 01: KB103- and placebo-randomized wounds

	Baseline	1 Month	1.5 Months	2.5 Months
KB103				
Placebo				

Patient 02: Wound Closure Images

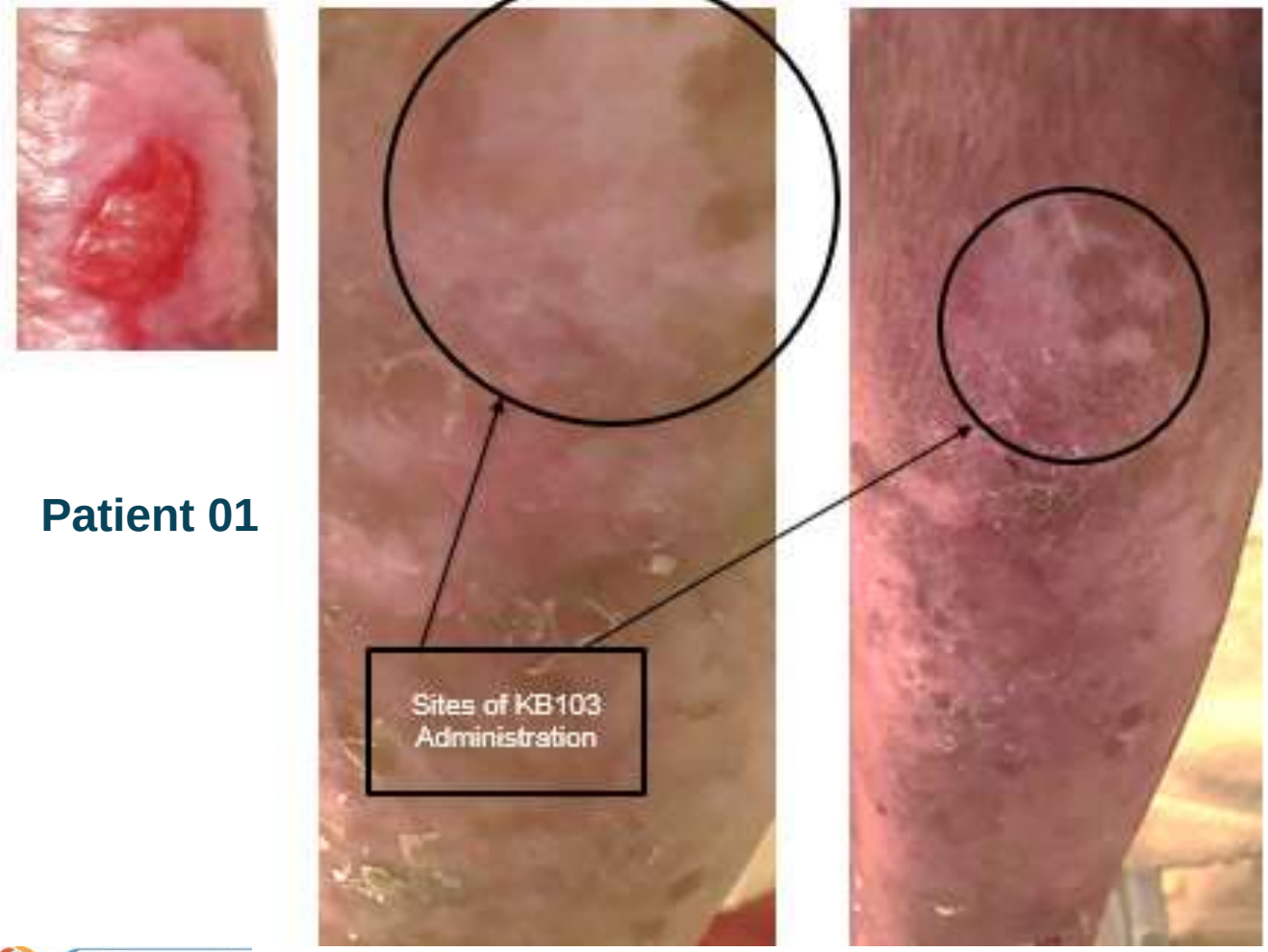
Patient 02: KB103- and placebo-randomized wounds

	Baseline	1 Month	2 Months
KB103			
Placebo			

Patients 01 and 02: Long-term Wound Closure Images

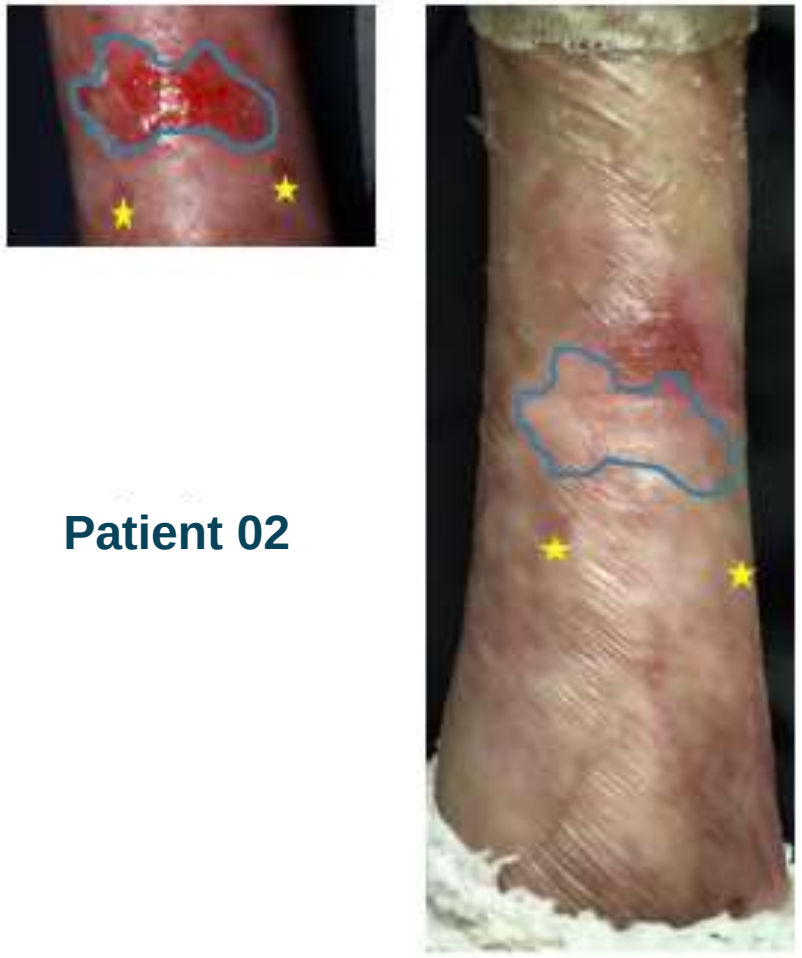
Post-study, at-home wound imaging of the KB103-administered site

Baseline | **3.5 months of closure** | **4.5 months of closure**



Patient 01

Baseline | **3.5 months of closure**



Patient 02

KB103 Safety Update in Wounds With Topical Application

Summary

KB103 continues to be well tolerated to date following first and repeat dose

- No treatment-related adverse events (serious or otherwise) were reported
- No immune response or blistering observed around the sites of administration following first and repeat dose
- Blood and urine samples collected throughout the study revealed:
  - No systemic viral shedding
  - No adverse events associated with routine labs (chemistry and hematology)
  - No antibodies to COL7 were detected

KB103 Efficacy Update in Wounds With Topical Application

Summary

- Results to date on 2 patients met all primary efficacy (presence of functional COL7 expression as early as Day 2 of treatment, observation of NC1 and NC2 reactive anchoring fibrils and continued expression following repeat administration) and safety endpoints (no adverse events, inflammation or irritation) in topically administered KB103 wounds.
- With respect to secondary endpoints – topically administered KB103 wounds closed in 2 weeks and remained closed through the last timepoint representing 5.7 and 6.6 months of closure, respectively, for Patients 01 and 02. Topically administered placebo treated wounds took 10 weeks to close in Patient 01 and did not completely close throughout the study in Patient 02.
- KB103 treated skin shows presence of functional COL7 expression and anchoring fibrils in both patients.
- Empirical observation that one patient discontinued use of bandages at the site of a KB103-treated area, an area which had required bandages for several months prior to administration.

Phase II Trial Design – Differentiators from Phase I

A Phase II Study of KB103, a Non-Integrating, Replication-Incompetent HSV Vector Expressing the Human Collagen VII Protein, for the Treatment of Dystrophic Epidermolysis Bullosa (DEB)

- Administration to children (vs adults only in Phase 1)
- Administration to larger wounds: up to 20 cm^2 (vs up to 10 cm^2 in Phase 1)
- Administration to 2 wounds per patient (vs 1 in Phase 1)
- A higher dose (up to 6 x 10^8 PFU) is administered per wound
- More frequent administrations allowed, contingent on wound characteristics
- Intradermal administrations were removed

Four patients have been dosed in phase II study

KB105*

For the treatment of Autosomal Recessive Congenital Ichthyosis associated with TGM1

* Orphan Drug Designation in US;

  Rare Pediatric Disease Designation in US;

  Eligible for Priority Review Voucher.

Krystal

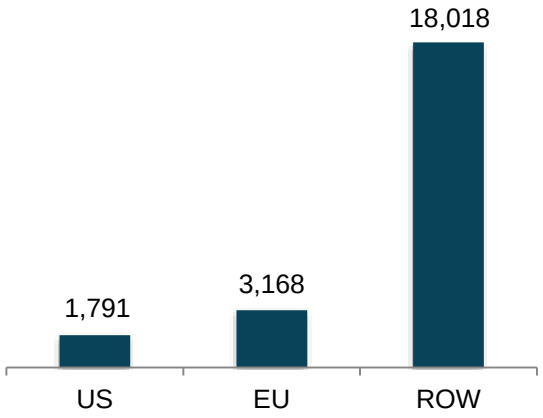
ARCI Associated With TGM1

Autosomal Recessive Congenital Ichthyosis (ARCI) associated with TGM1

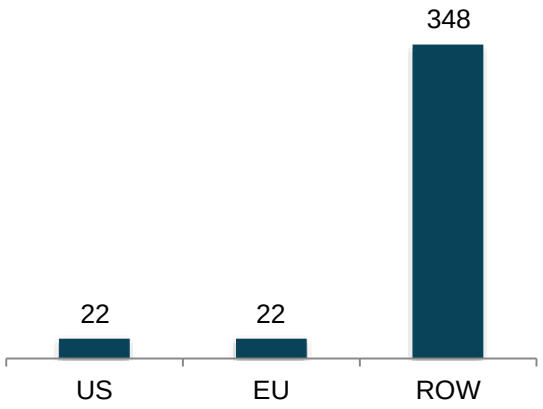
A condition characterized by thick dry scaly skin, increased trans-epidermal water loss (TEWL), risk for dehydration, sepsis, skin malignancies, *etc*.

Caused by a mutation of TGM1 gene required for epidermal barrier formation

Prevalence[1-8]



New Cases/Year



Current Standard of Care

There are no approved treatments for ARCI associated with TGM1

Existing approaches limited to time-consuming palliative treatments

1. Rodriguez-Pazos et al. *Actas Dermosifiliogr.* 2013 May;104(4):270–284;
2. Dreyfus et al. *Orphanet J Rare Dis.* 2014 Jan 6;9:1;
3. Hernandez-Martin et al. *J Am Acad Dermatol.* 2012 Aug;67(2):240–244;
4. Pigg et al. *Eur J Hum Genet.* 1998 Nov-Dec;6(6):589–596.
5. Pigg et al. *Acta Derm Venereol.* 2016 Nov 2;96(7):932–937;
6. Orphanet;
7. Foundation for Ichthyosis & Related Skin Types (FIRST);
8. National Organization for Rare Disorders (NORD).

ARCI Associated With TGM1

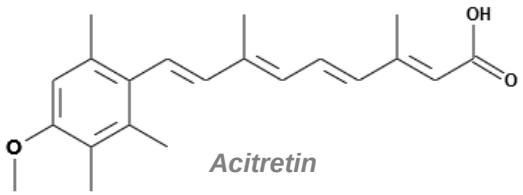
Current standard of care vs. Krystal's approach

Oral retinoids

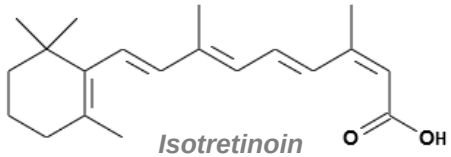
Does not address underlying genetic deficiency

Severe adverse effects

- Soft tissue calcification of the joints, *e.g.,* around the spine
- Increased blood triglycerides and cholesterol, potentially inducing or exacerbating atherosclerosis
- Acute and chronic toxicities associated with long-term exposure



Acitretin



Isotretinoin

Particularly ill-suited for certain patient segments

- **Children:** doctors delay retinoid therapy as long as possible due to the bone growth defects (including premature termination of bone elongation) induced by retinoids
- **Women of childbearing age:** retinoids are teratogens (cause fetal abnormalities, miscarriages and severe birth defects) with potentially long half-lives; must be avoided by pregnant women or women who intend on becoming pregnant

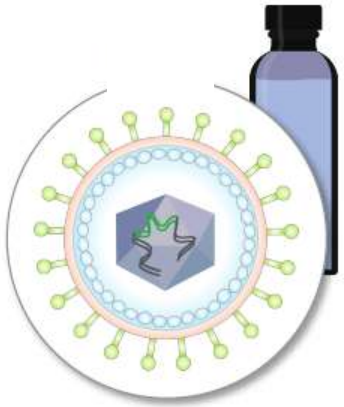
KB105

Corrects molecular defects of disease

- KB105 encodes and expresses multiple functional copies of TGM1
- Direct delivery of TGM1 to appropriate skin substrata

Improved safety

- Avoids severe adverse events associated with long-term retinoid therapy



No systemic exposure to the drug product

Engineered for topical application

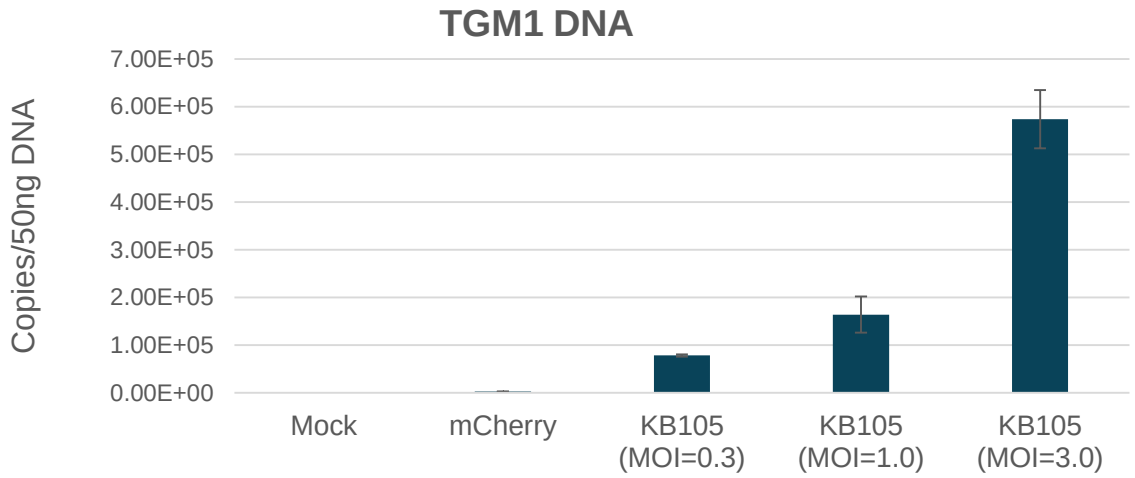
- Can be administered frequently

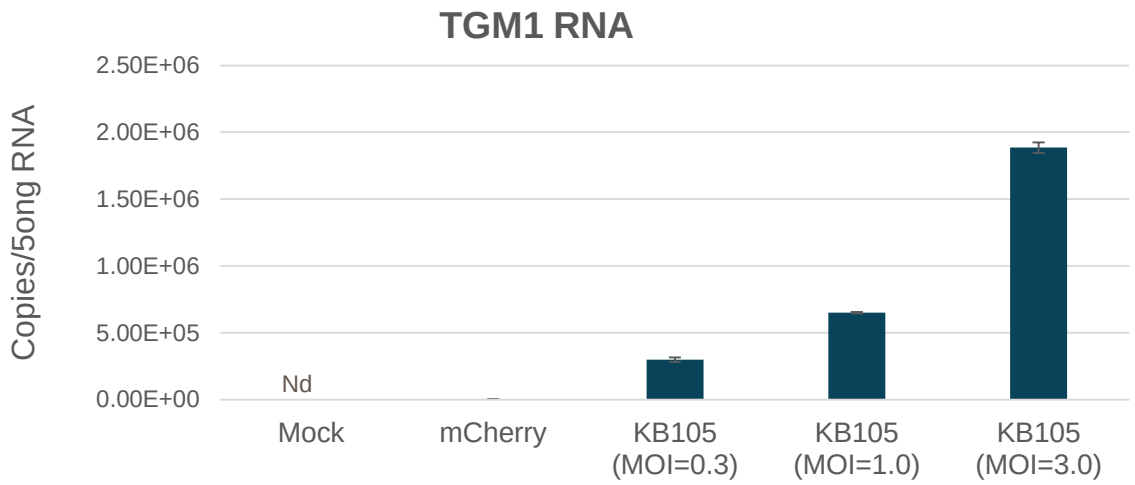
Suitable for all patient populations

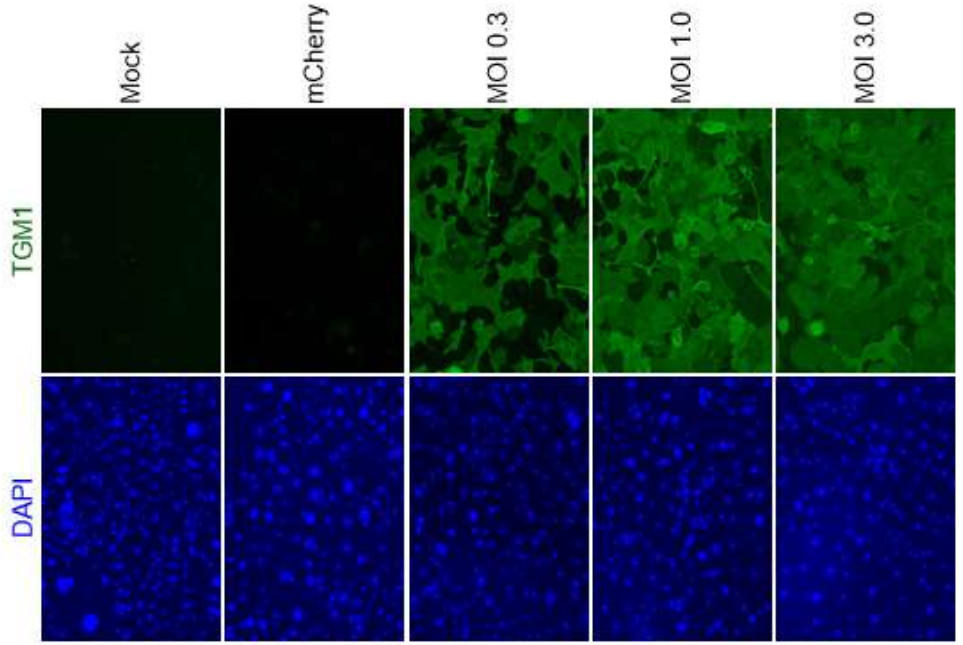
- Including children and women of childbearing age

KB105 *In Vitro* Data

KB105 efficiently transduces ***immortalized TGM1-deficient ARCI keratinocytes***

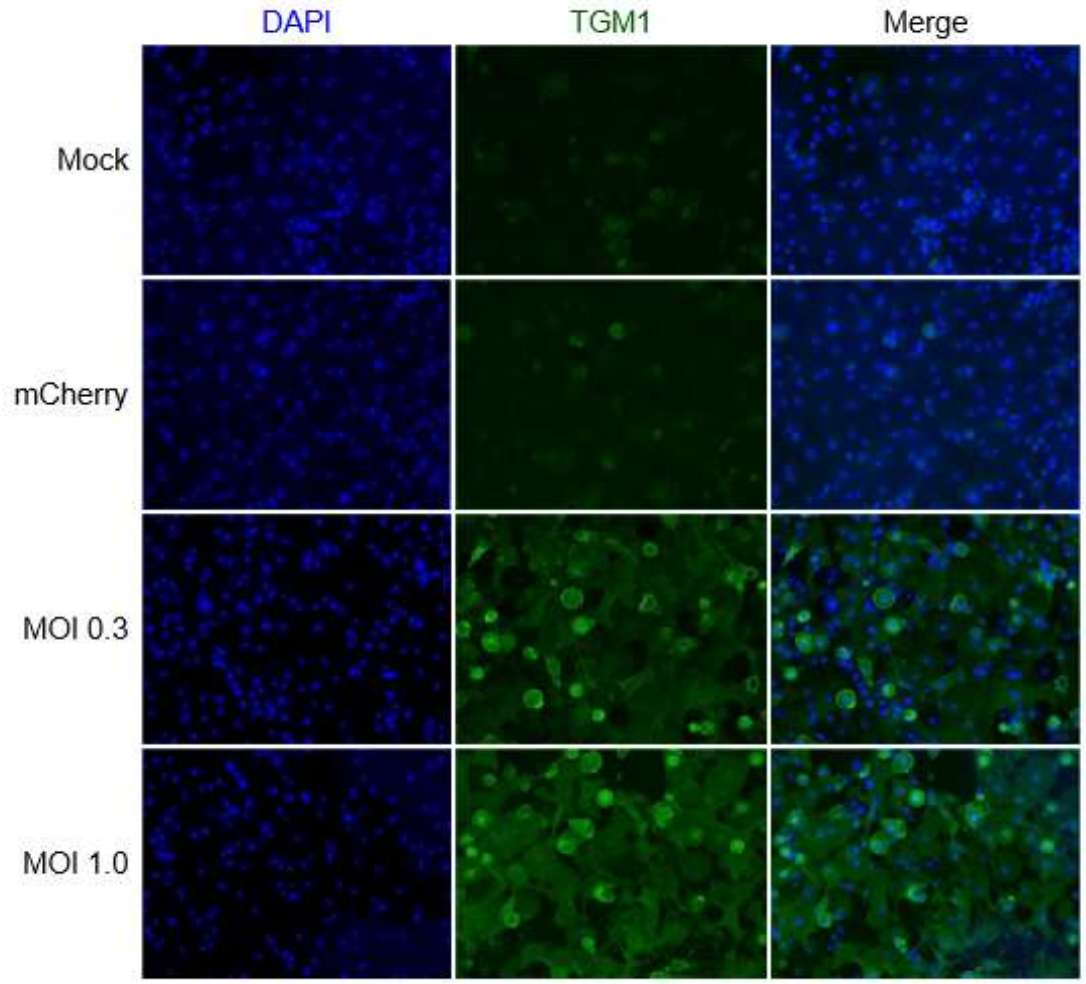


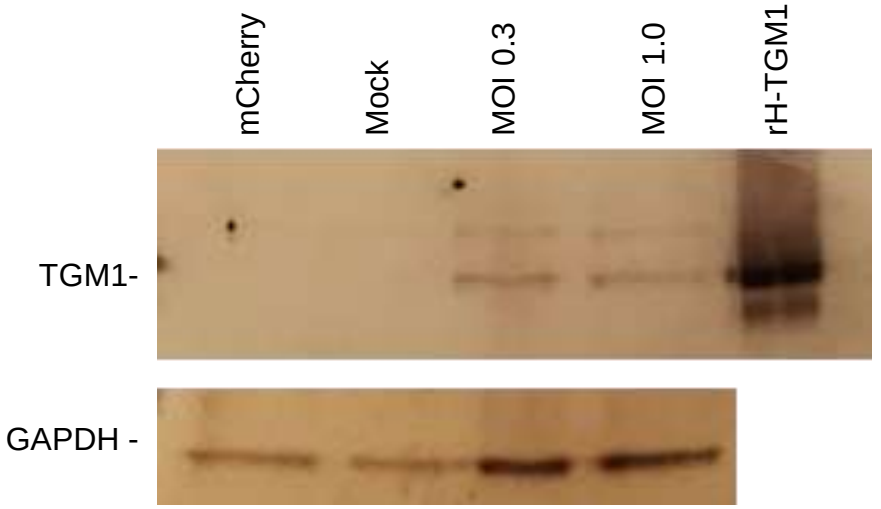




KB105 *In Vitro* Data

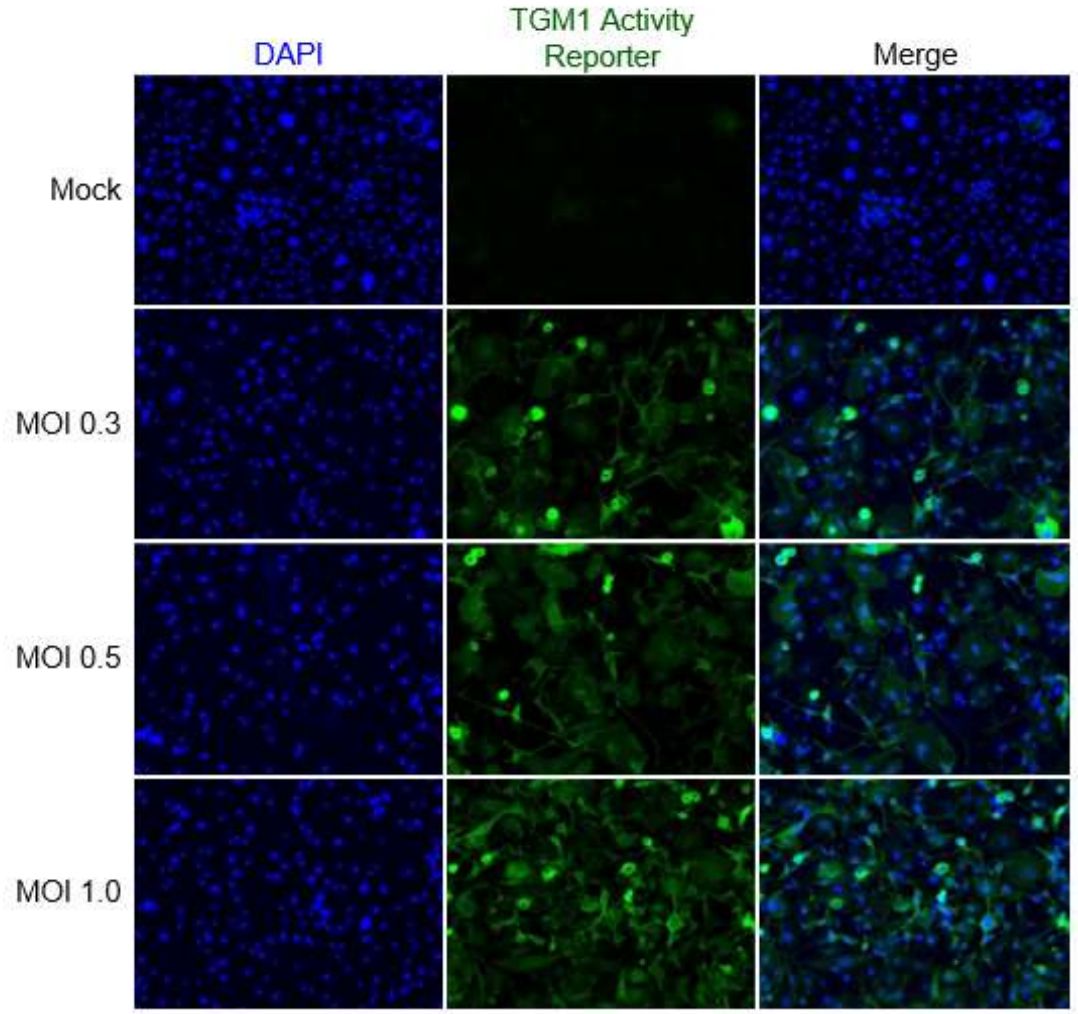
KB105 efficiently transduces ***primary TGM1-deficient ARCI keratinocytes***

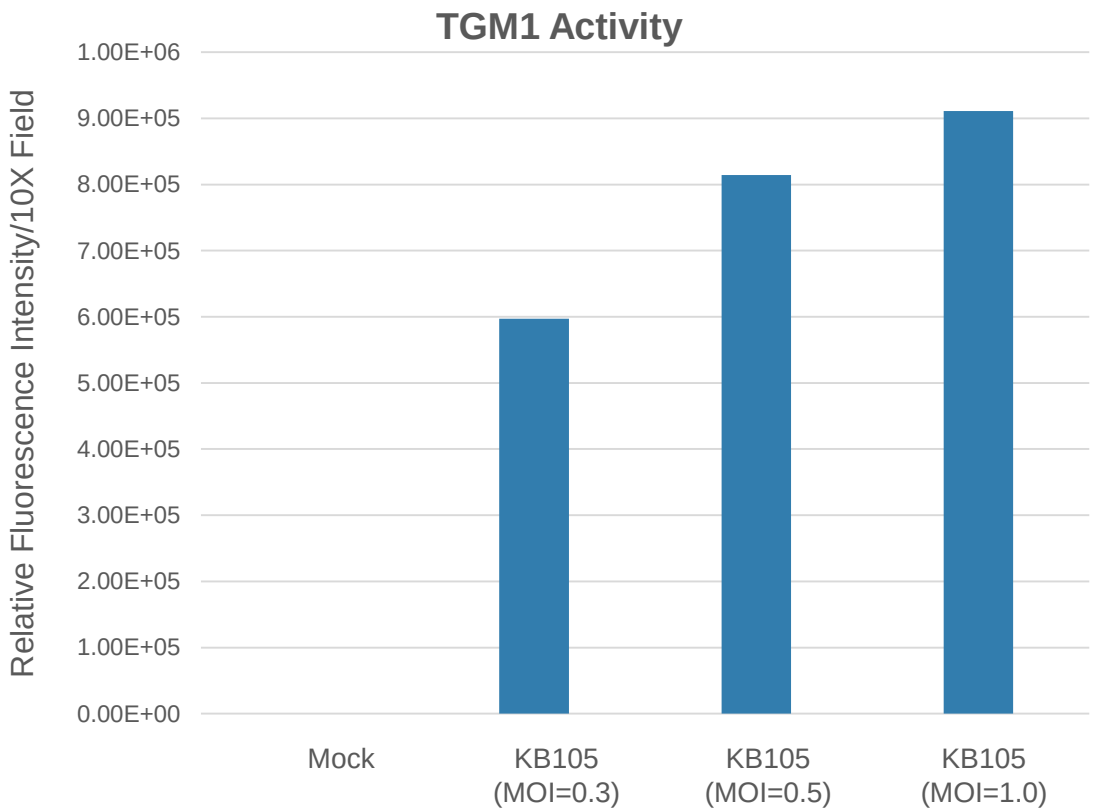




KB105 *In Vitro* Data

KB105 expresses ***functional TGM1*** in primary TGM1-deficient ARCI keratinocytes

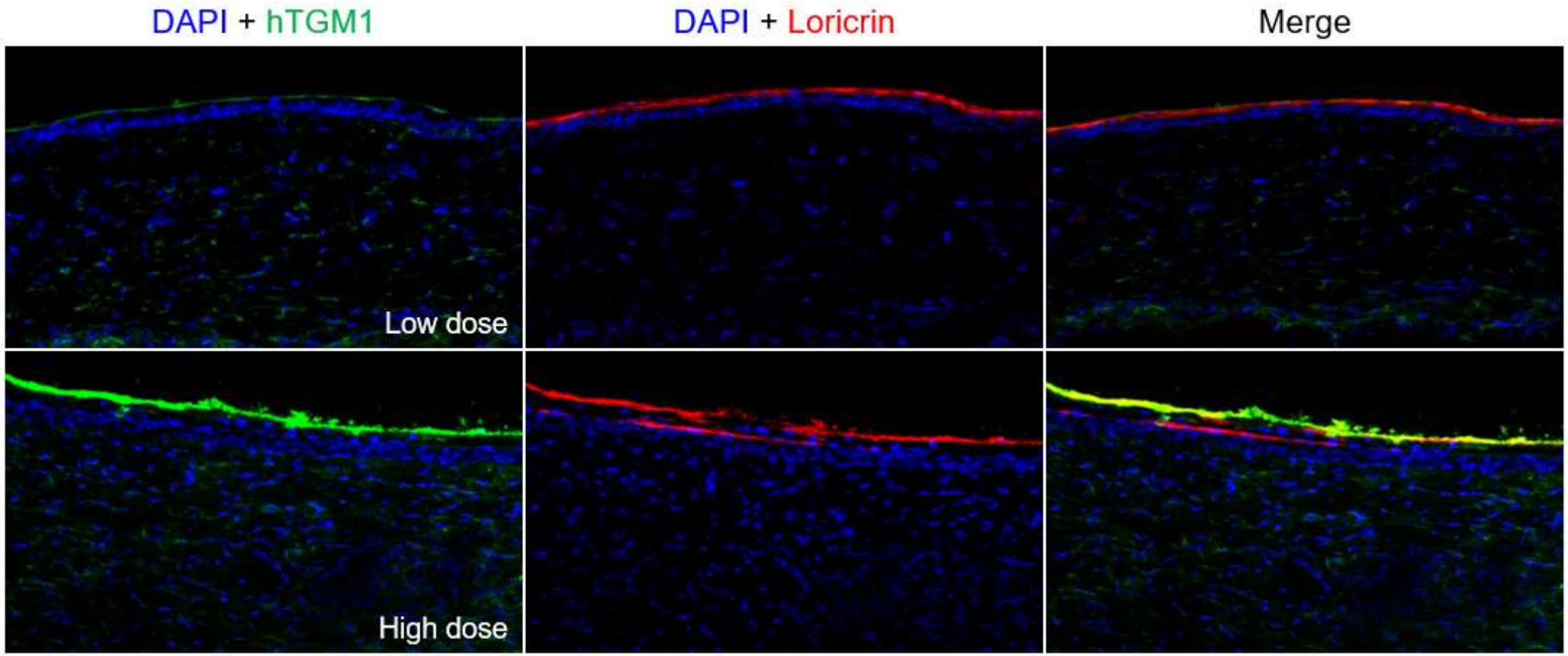




TGM1 activity determined using a fluorescent synthetic peptide reporter assay measuring TGM1-mediated glutamine conjugation

KB105 *In Vivo* Data

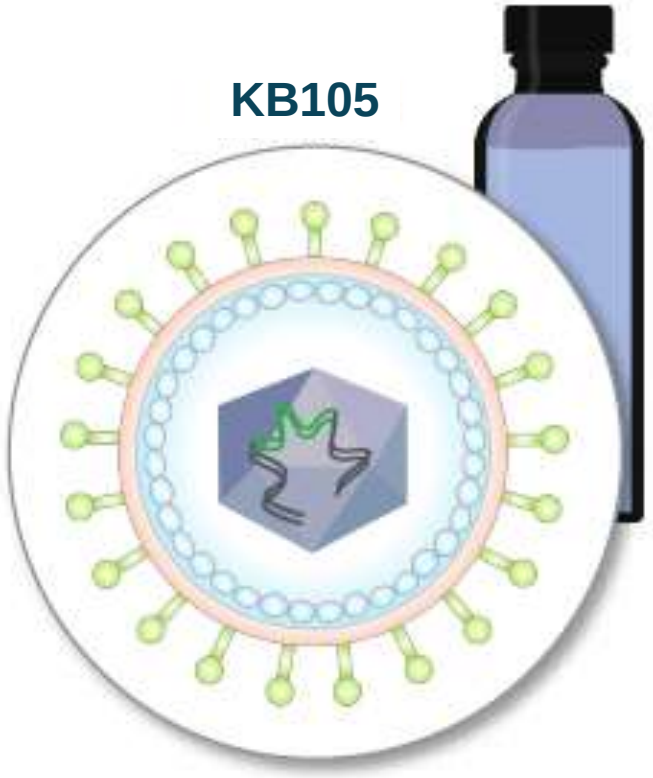
Properly localized, dose-dependent human TGM1 detected after topical application in BALB/c mice



Loricrin is both a substrate for TGM1 and serves as a marker for the Stratum Granulosum - indicates that TGM1 colocalizes with at least one native substrate and is expressed in the correct layer of skin

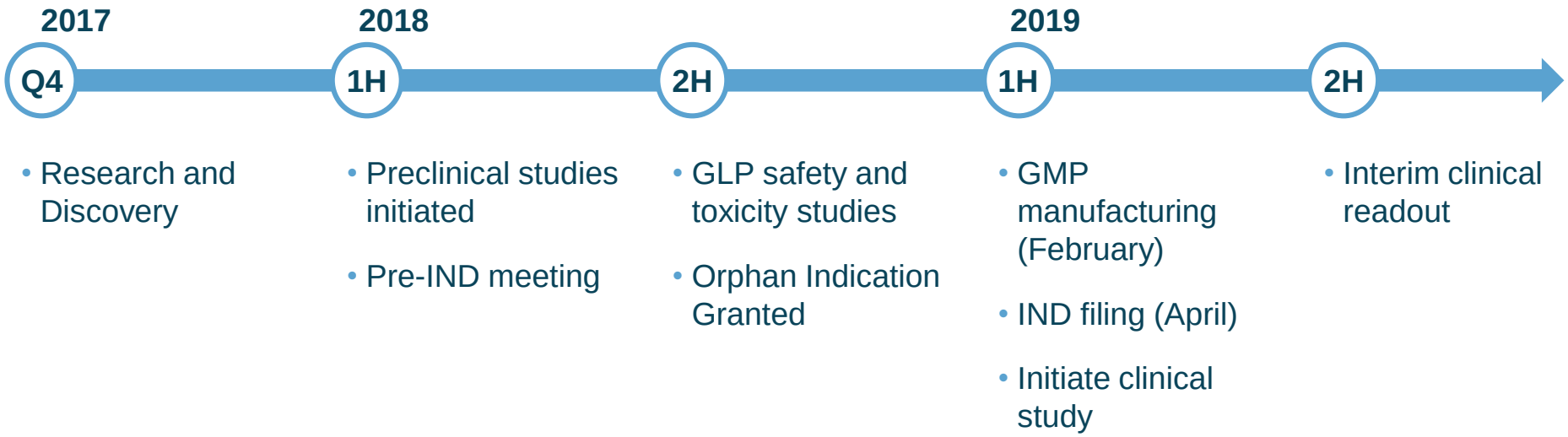
KB105 Conclusions

- Candidate viruses efficiently transduce target cells and express TGM1 *in vitro* and *in vivo*
- HSV variant shows reduced cytotoxicity
- Human TGM1 consistently expressed at high levels in immunocompetent mice
- KB105 rescues TGM1 expression in ARCI patient cells
- KB105's robust production of TGM1 *in vitro* and *in vivo* supports its use in ARCI patients



KB105 Timeline to Clinical Readout

Phase I/II clinical trial to begin 1H 2019



Krystal's Core Competency: CMC/Manufacturing

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

- 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 Production Process

- Proprietary engineered vectors (STAR-D) and complementary/supporting cell lines developed in-house are used in established methods for production of consistent batches
- Scalable from clinical phase to commercial

Downstream Purification Process

- Work conducted in an aseptic closed system process
- Process accommodates ever-expanding vector pipeline with minimal redevelopment effort between product candidates
- Compliant to global regulatory requirements

Key Opinion Leaders

Currently working with Krystal

Dr. Peter Marinkovich
Department of Dermatology
Stanford University
Serving as lead clinical investigator in KB103 phase I/II trial

Dr. Andrew South
Department of Dermatology,
Thomas Jefferson University

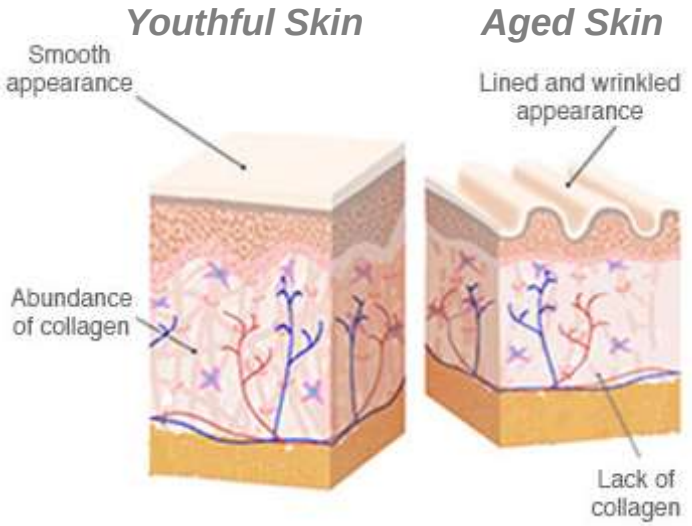
Dr. Joyce Teng
MD, PhD
Clinical Professor, Dermatology Clinical Professor, Pediatrics
Stanford University

Dr. Keith Choate
MD, PhD
Professor of Dermatology,Genetics, Pathology
Yale University School of Medicine

Dr. John McGrath
Professor of Molecular Dermatology
St. John's University of London

Beyond Severe Monogenic Skin Diseases

Application of STAR-D platform to treat aesthetic defects



The characteristic features of skin aging are largely due to aberrant collagen homeostasis, resulting in a net collagen deficiency

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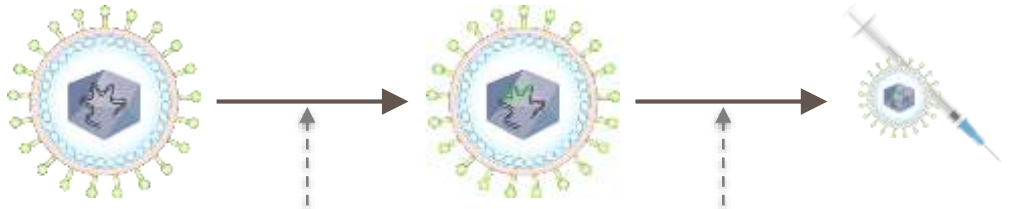
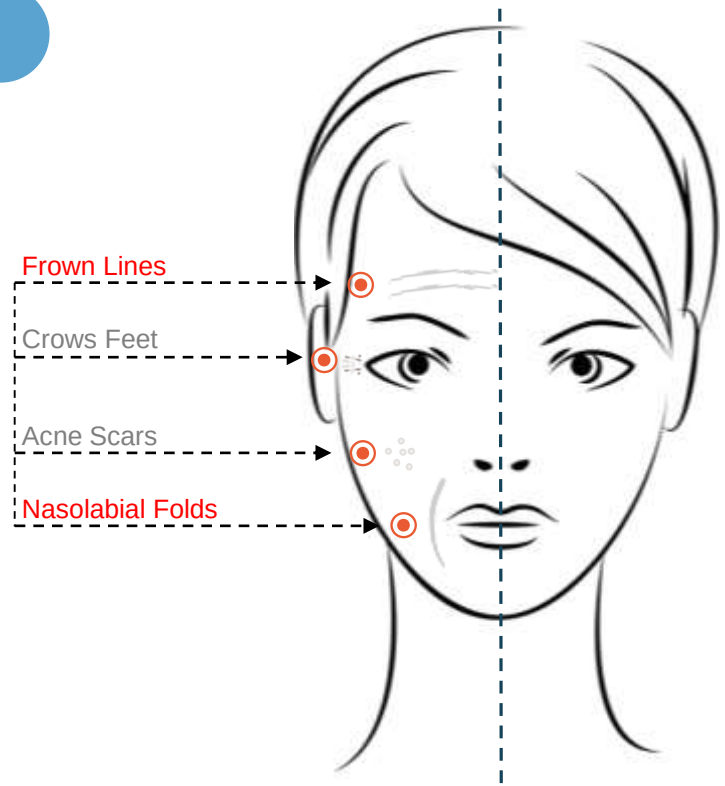
Off-the-shelf, Non-Invasive Modified HSV-1 Therapy

STAR-D Platform **KB301**



Modify STAR-D platform via insertion of human collagen gene(s)

Formulate into an intradermal solution



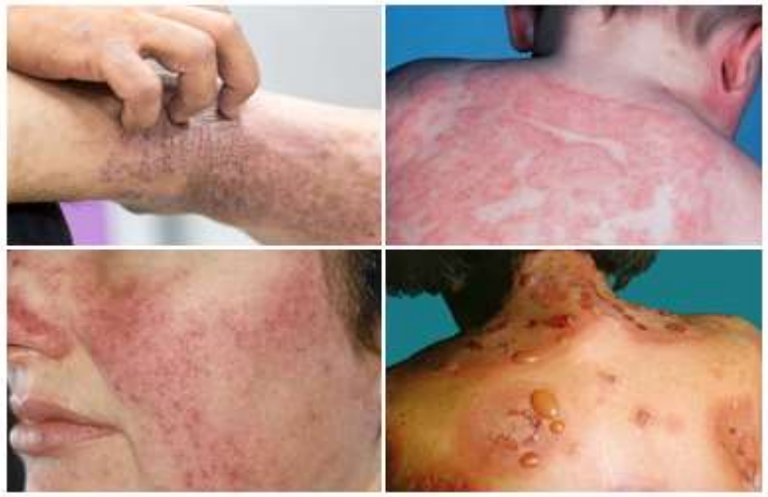
Fromowitz, J. “Update on Aging Skin”; Florida Society of Dermatology

Beyond Severe Monogenic Skin Diseases

Application of STAR-D platform to treat complex, chronic skin conditions

Chronic skin conditions

KB500 series (Antibodies) for Chronic Skin Diseases (Atopic Dermatitis, Psoriasis, *etc.*)



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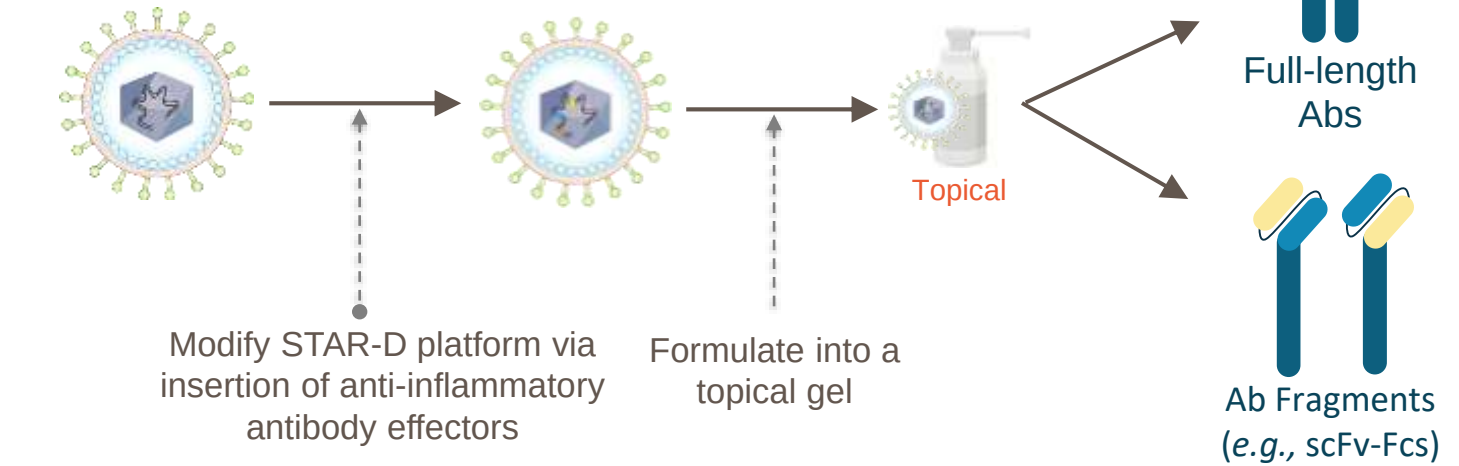
Off-the-shelf, Non-Invasive Modified HSV-1 Therapy



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Medicines for Skin Diseases and Conditions –
A Gene Therapy Company