Krystal

Medicines for Skin Diseases and Conditions –
A Gene Therapy Company

GEM-2 bercolagene telserpavec (B-VEC, KB103)
Phase I / II Clinical Study Update
October 29, 2019

Forward-Looking Statements

This webcast and the slides accompanying it contain data from Krystal's Phase I/II trial evaluating B-VEC in patients suffering from Dystrophic epidermolysis bullosa, or DEB. Statements made in the webcast and slides may contain "forward-looking statements" regarding matters that are not historical facts, including statements relating to the Company's clinical trials and product development pipeline. There can be no assurance that the data contained in these results will be replicated in additional patients enrolled in this or any future trial, or that these results will prove clinically meaningful in the development of B-VEC as a potential drug. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Words such as "anticipates," "plans," "expects," "intends," "will," "potential," "hope" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon current expectations of the Company and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties. Detailed information regarding factors that may cause actual results to differ materially from the results expressed or implied by statements in this press release relating to the Company may be found in the Company's periodic filings with the Securities and Exchange Commission..

bercolagene telserpavec (B-VEC, KB103)

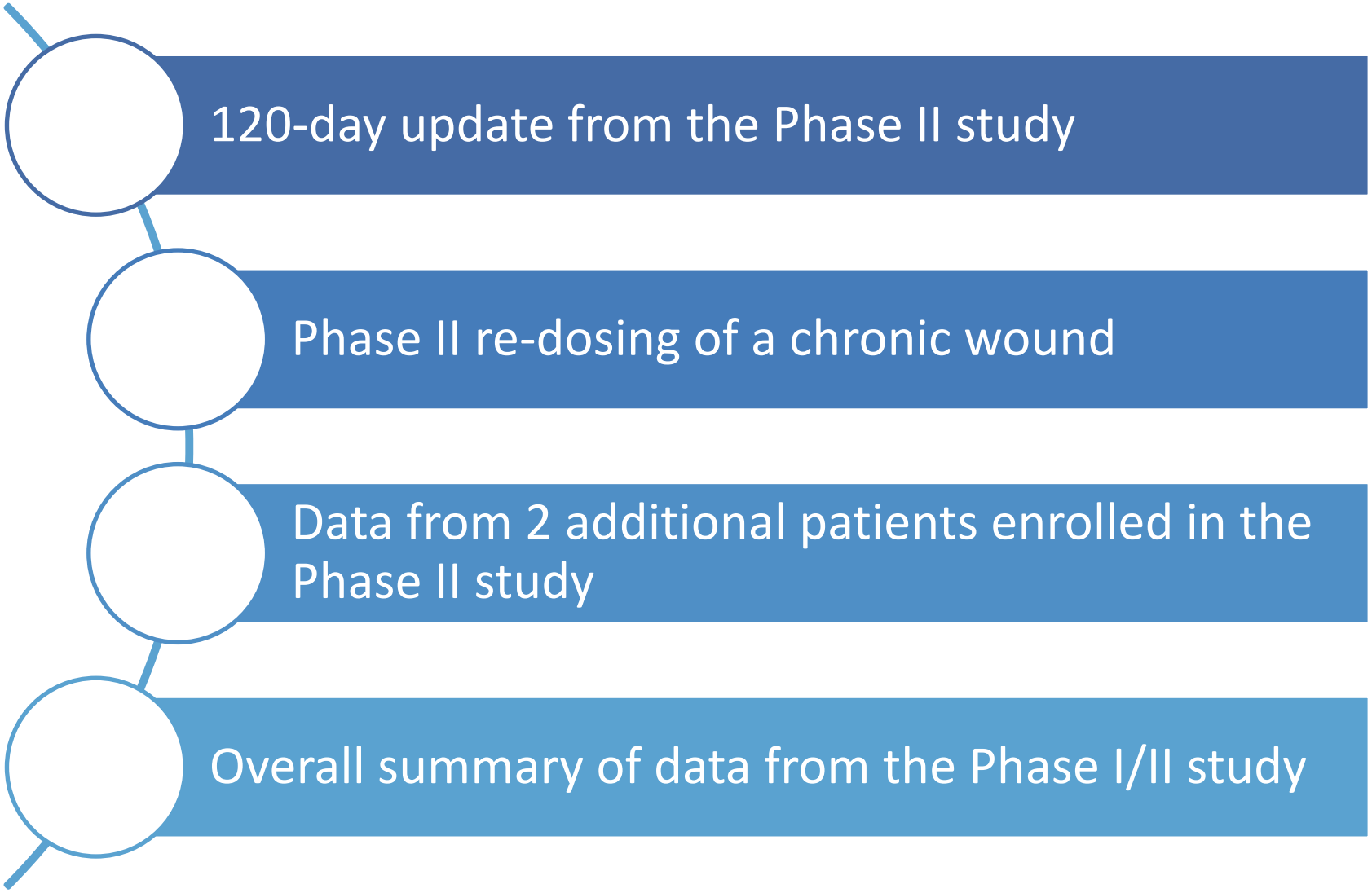
For the treatment of dystrophic epidermolysis bullosa

- RMAT designation;
- Prime Eligibility;
- Fast Track Designation Granted;
- Orphan Drug Designation in US and EU;
- Rare Pediatric Disease Designation in US;
- Eligible for Priority Review Voucher.

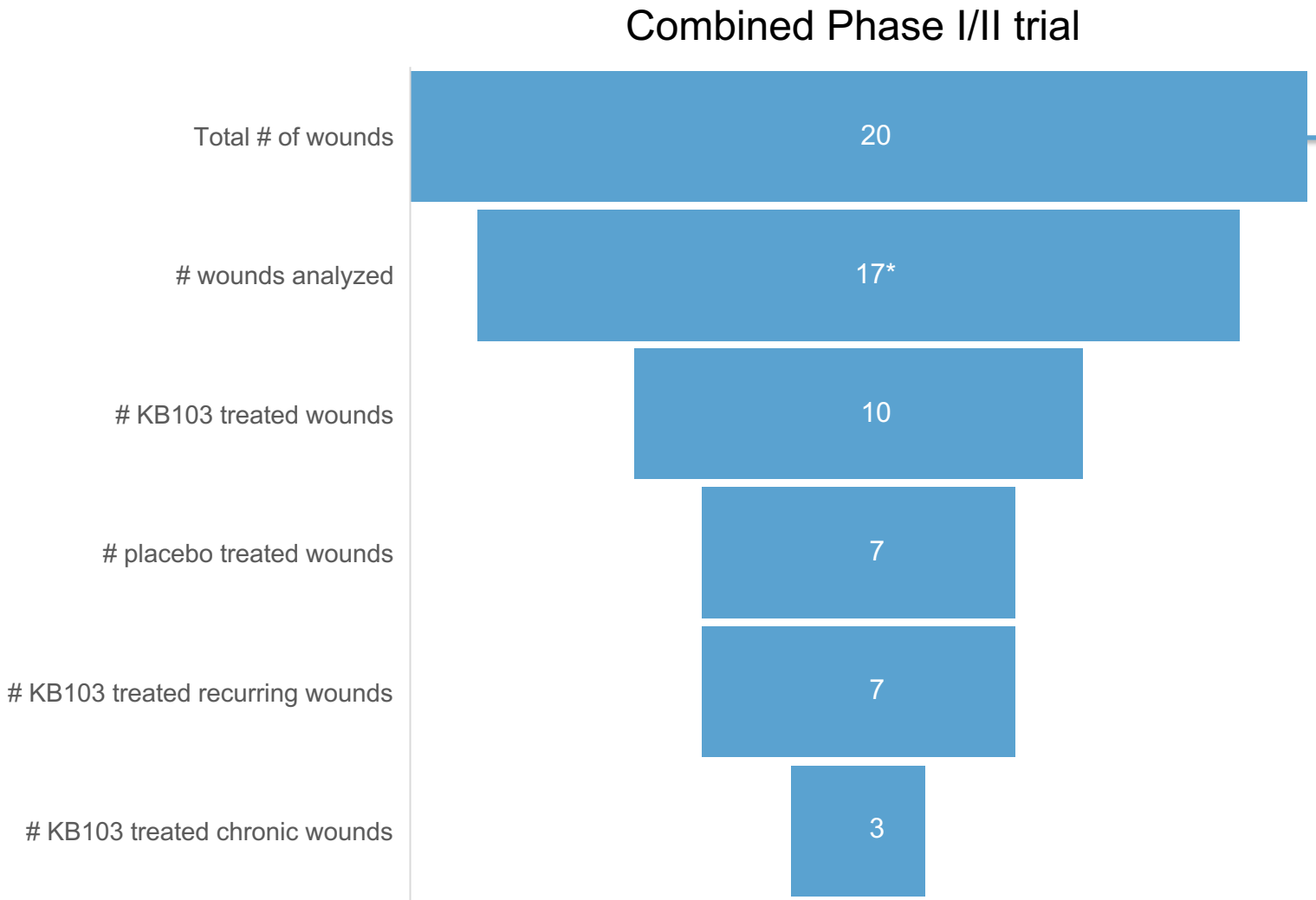
Summary of Prior Data Releases

- October 2018: Krystal announced interim Phase 1 data that is summarized below:
    - B-VEC continued to be well tolerated following initial and repeat dosing.
    - 100% wound closure (by area) was observed in 2 wounds treated with B-VEC.
    - Average time to wound closure was 12 days (median 12 days).
    - The duration of wound closure on two patients following 100% wound closure as of the last follow up was 184 days (6.6 months) and 174 days (6.2 months) respectively.
- June 2019: Krystal announced Phase II data out to Study Day 90 that is summarized below:
    - Four patients were dosed in the second half of December 2018 – one patient discontinued after 30 days due to an inability to travel.
    - B-VEC continued to be well tolerated following initial and repeat dosing.
    - 5 out of 6 wounds treated with B-VEC closed completely (100% wound closure).
    - The average time to 100% wound closure on 5 out of 6 wounds was 23.4 days. On recurring wounds, the average time to 100% wound closure was 19 days.
    - The average duration following complete (100%) wound closure on recurring wounds as measured on Day 90 was 71 days.

Presentation Summary



Wound Characterization in Phase II and Combined Trial



Phase	# of Wounds
1	4
2	12
2 (additional patients)	4

*One patient in Phase II trial dropped out of the study after 30 days due to an inability to travel resulting in 3 wounds not included in the analysis. Chronic wounds remain open for greater than or equal to 12 weeks while recurring wounds heal but easily open.

120-Day Update on the Phase II Study

GEM-2: Phase 2 Trial Design

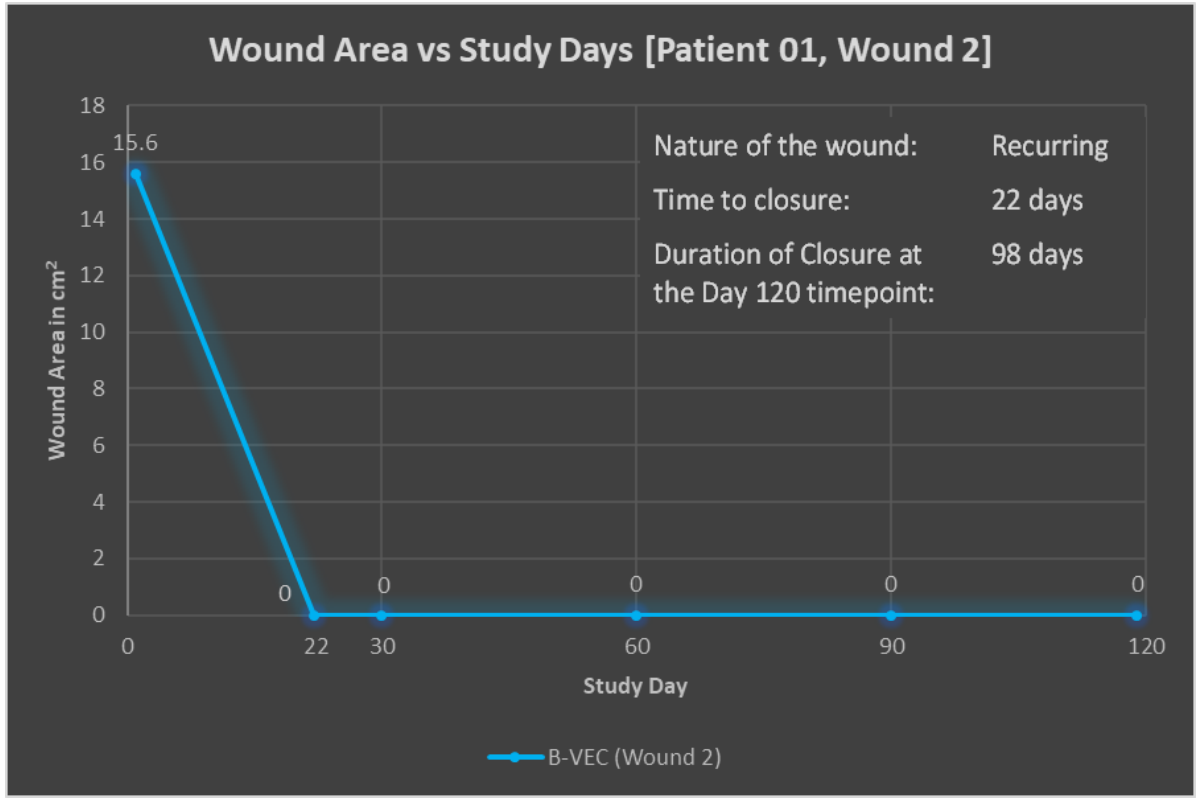
Four patients enrolled in December, 2018. Principal Investigator: Dr. Peter Marinkovich, Stanford University

- **Key objectives:** Demonstrate safety and wound healing of B-VEC
  - **Primary Clinical Objectives:** Safety and Wound healing (time to wound closure, % area of wound closure, duration of wound closure)
  - **Secondary Mechanistic Objectives:** Expression of COL7, Evidence of anchoring fibrils
- **Trial Design:**
  - Randomized, placebo-controlled study
  - 3 wounds treated topically in each patient: 1 placebo, 2 active
  - Initial front loaded dosing for 5 days (3e8 pfu/day)
  - Biopsies were based on PI discretion during site visits
  - Biopsied wounds were dosed one administration of 3e8 at site of biopsy, following a biopsy
  - Each patient is on-study for approximately six months; three months of on-site visits followed by a 3-month at-home imaging period

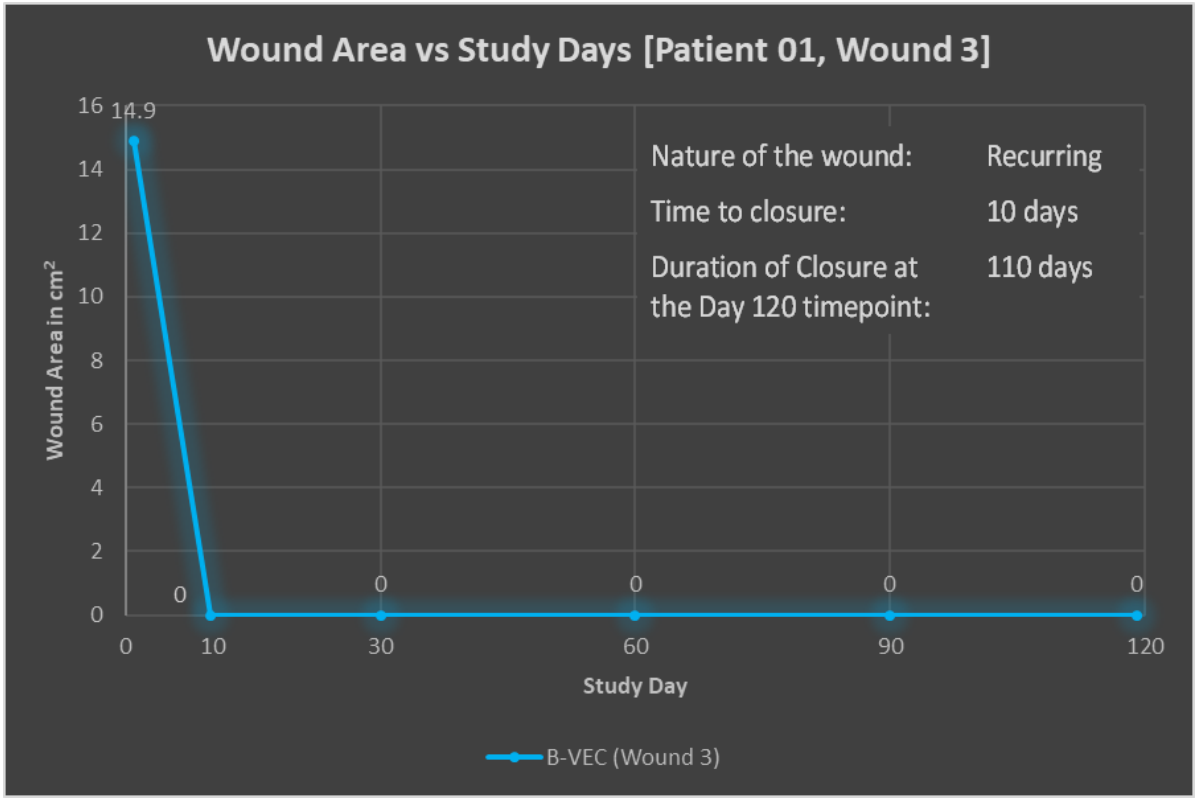
Phase II Study: 120 Day Update: Patient 1 (Age 13)

B-VEC administered wounds: (Wound Area over Study Days)

Wound 2: Lower right leg



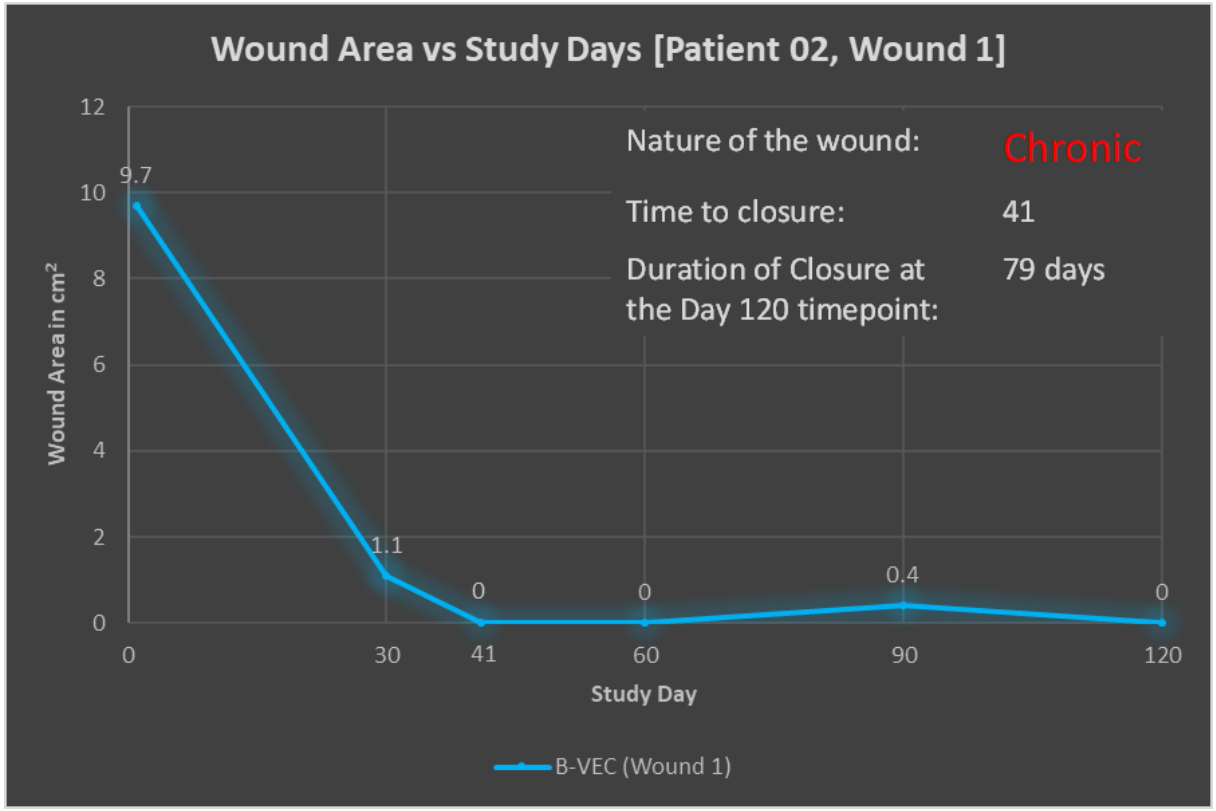
Wound 3: Right foot



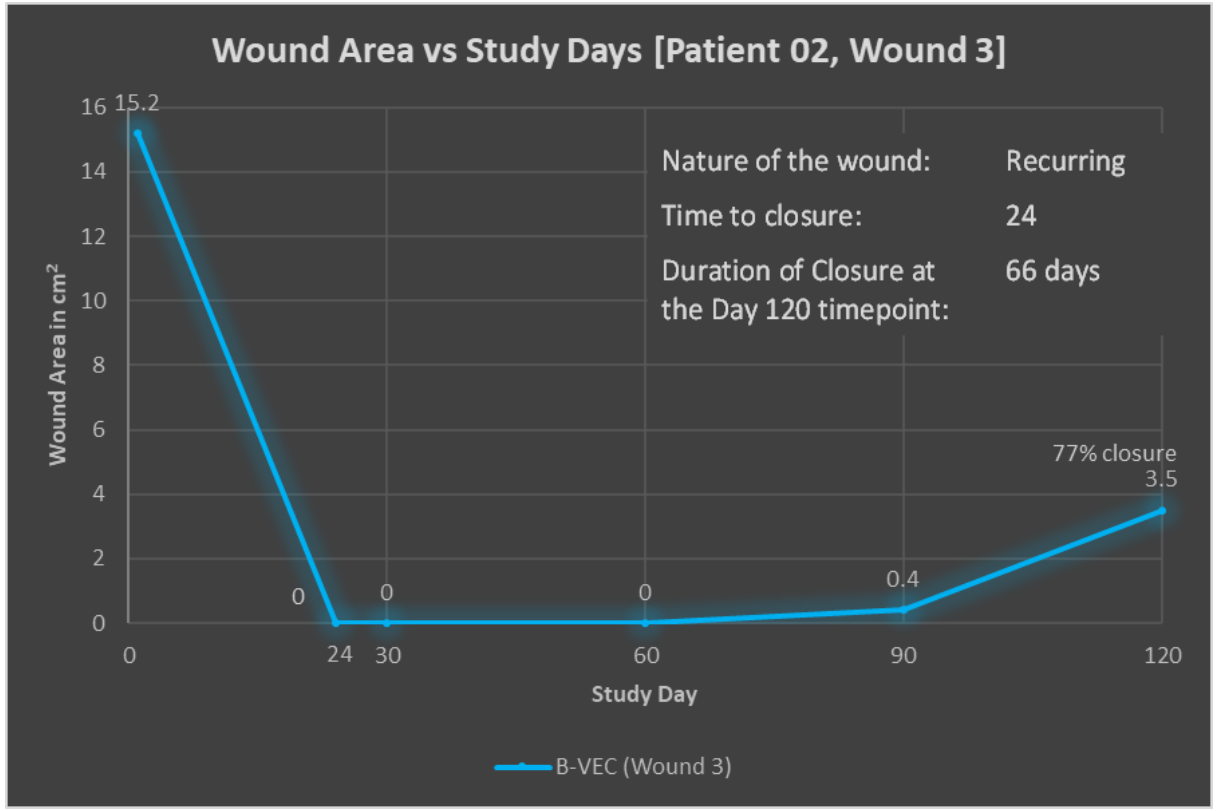
Phase II Study: 120 Day Update: Patient 2 (Age 15)

B-VEC administered wounds: (Wound Area over Study Days)

Wound 1: Right upper arm



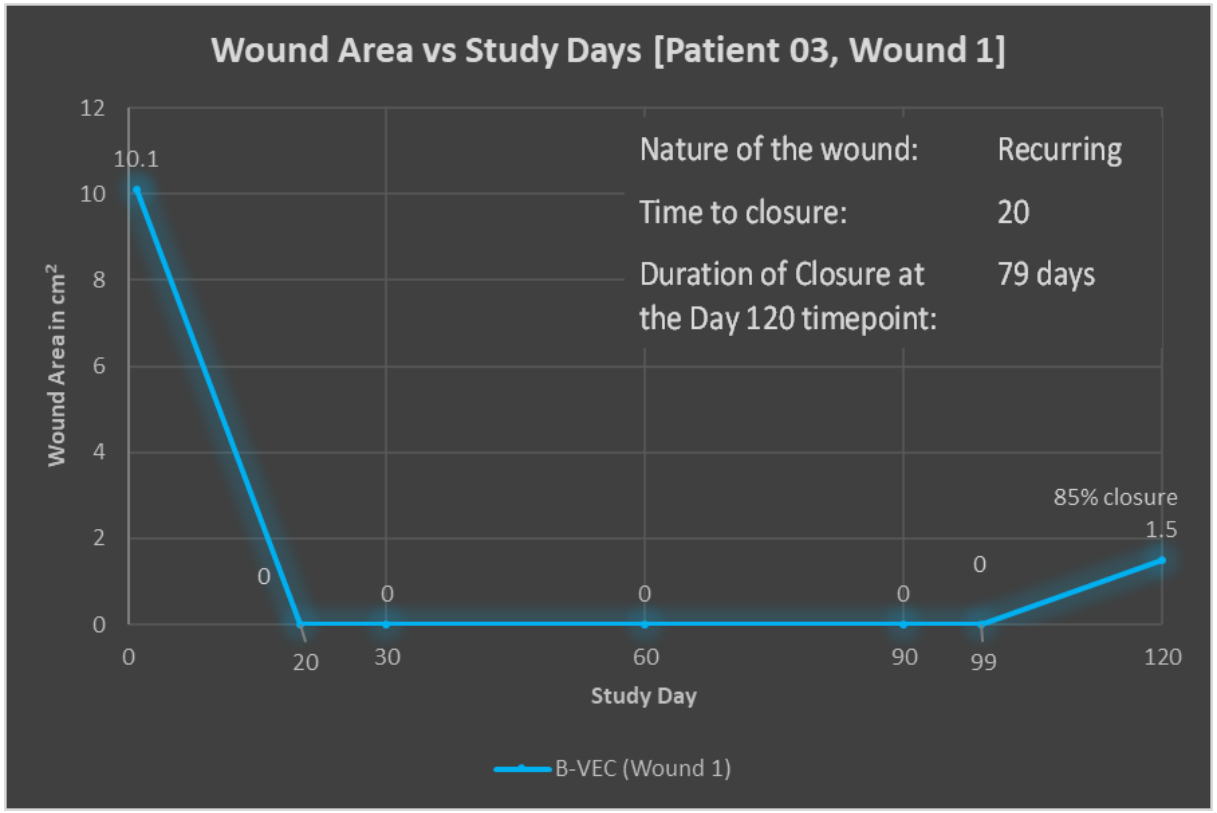
Wound 3: Right back



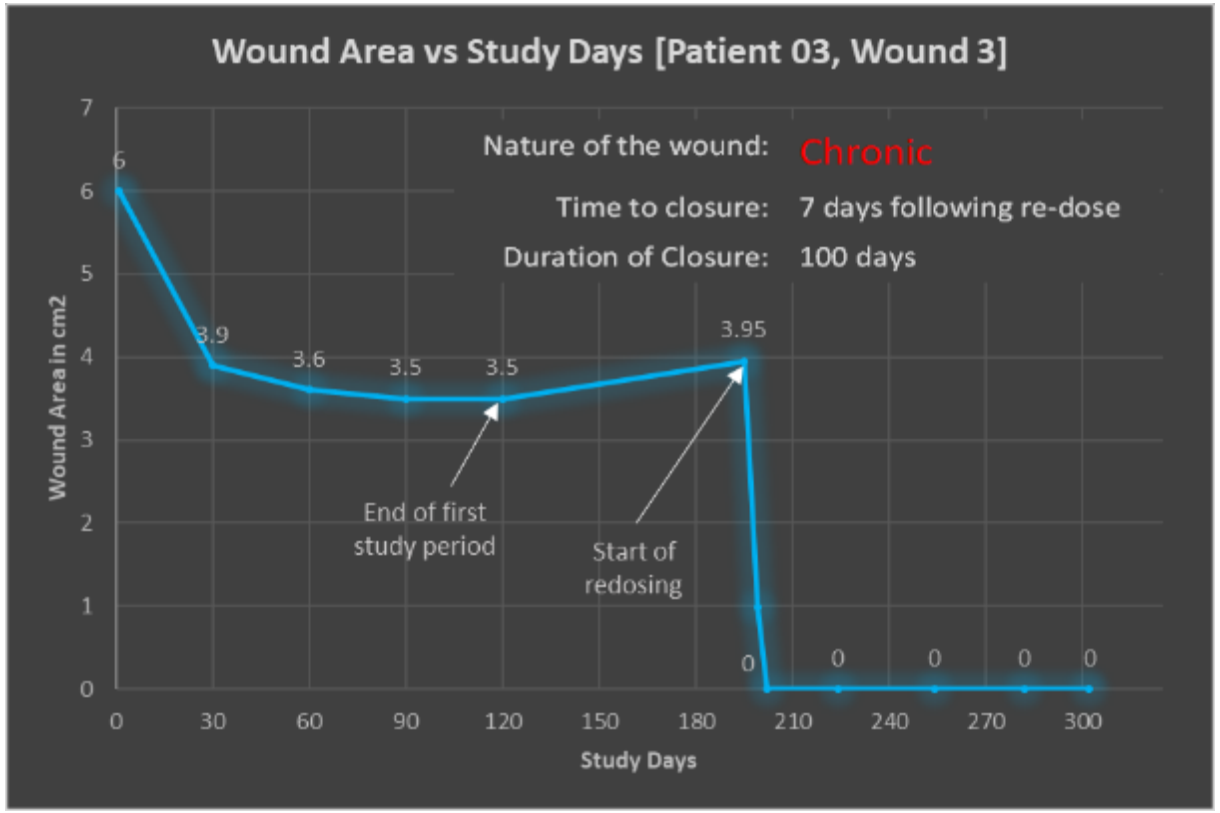
Phase II Study: 120 Day Update: Patient 3 (Age 22)

B-VEC administered wounds: (Wound Area over Study Days)

Wound 1: Left upper arm



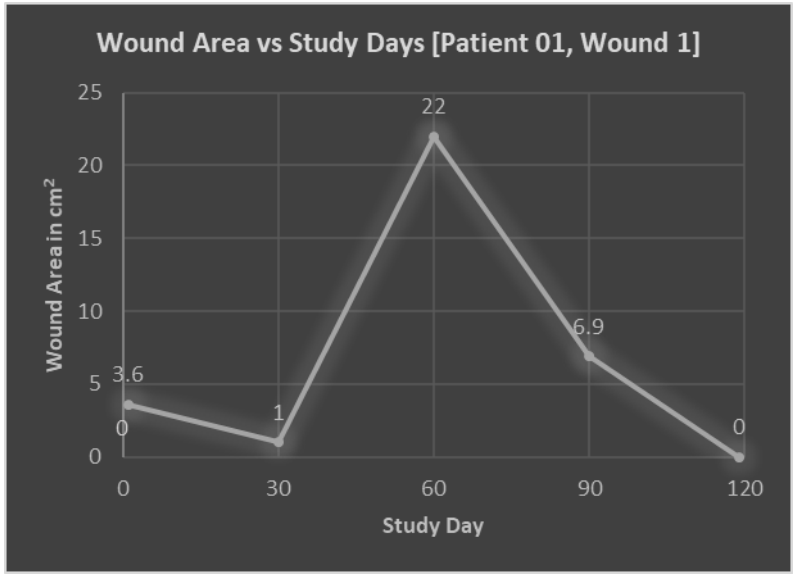
Wound 3: Right foot



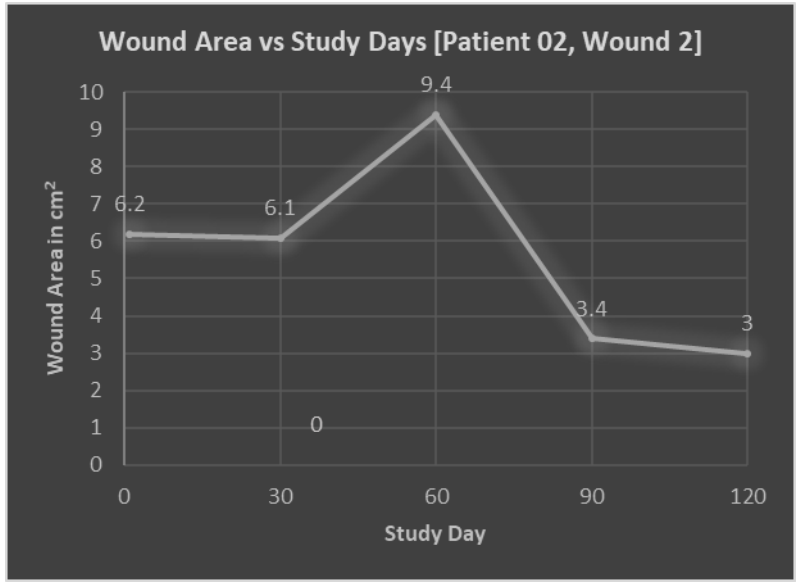
Phase II Study: 120 Day Update: Patients 1, 2, and 3 Placebo Wounds

Placebo administered wounds: (Wound Area over Study Days)

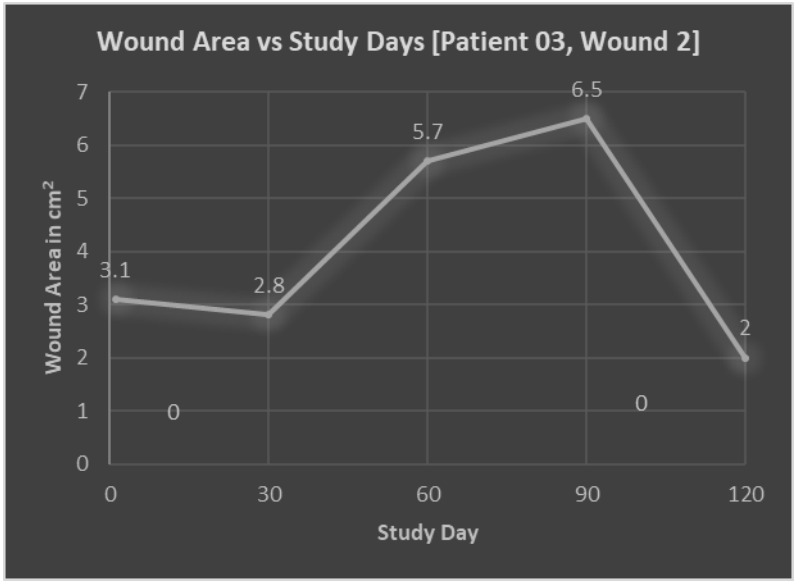
Patient 1, Wound 1, Right knee



Patient 2, Wound 2, Left breast



Patient 3, Wound 2, Left upper arm



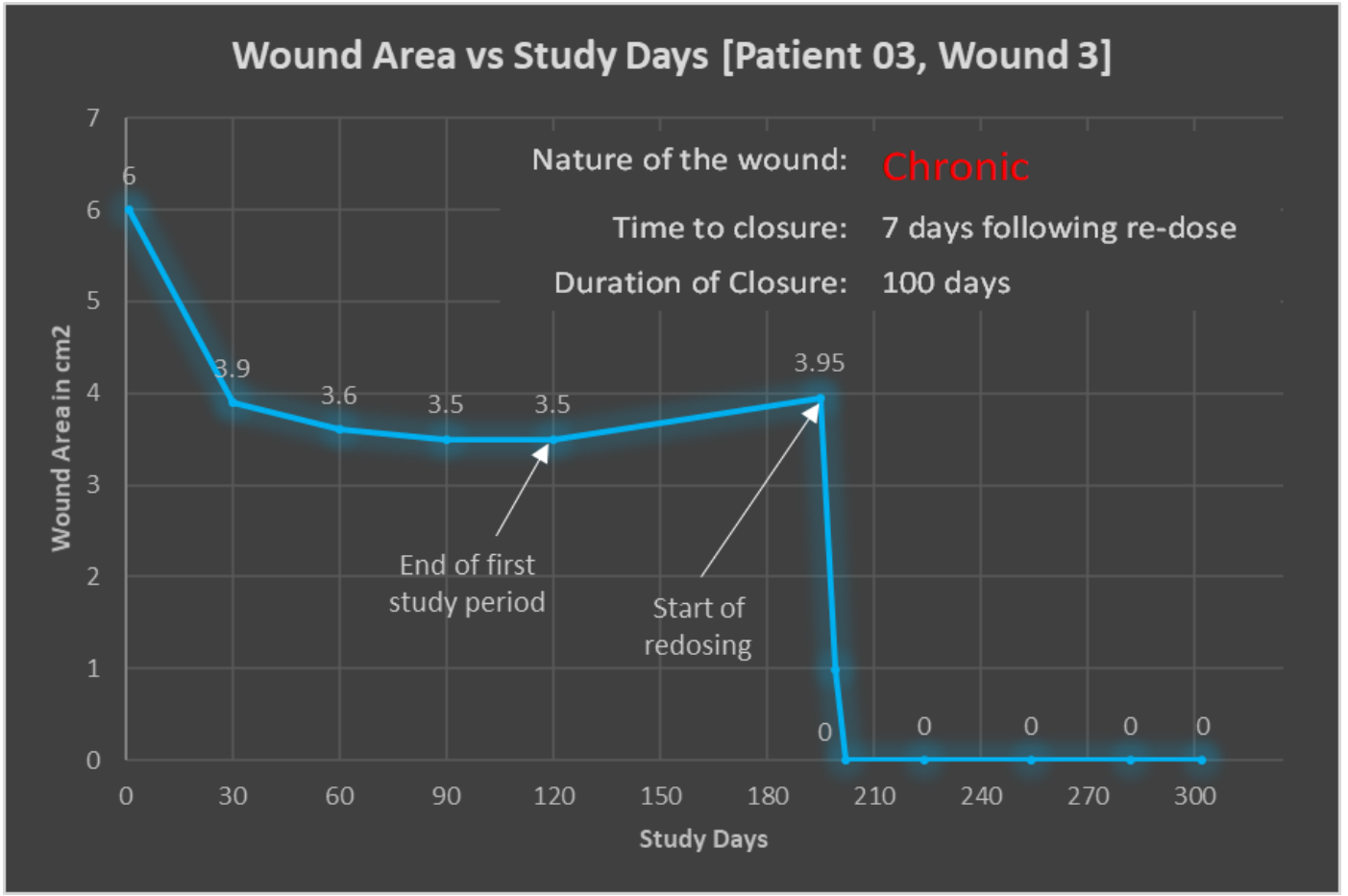
Summary of Phase II Data at Day 120

- B-VEC continued to be well tolerated following initial and repeat dosing.
- 5 out of 6 wounds treated with B-VEC closed completely (100% wound closure) following initial dosing. The remaining wound closed completely following re-dosing.
- The average time to 100% wound closure on 5 out of 6 wounds was 23.4 days. On recurring wounds, the average time to 100% wound closure was 19 days.
- Average duration of wound closure on 5 out of 6 wounds, following complete (100%) wound closure on recurring wounds as measured on Day 120 was 86.4 days (median 89 days).
- Following re-dosing, the duration of wound closure on the second chronic wound as measured on Day 120, was 100 days.

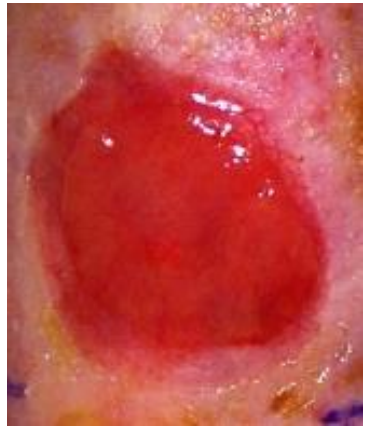
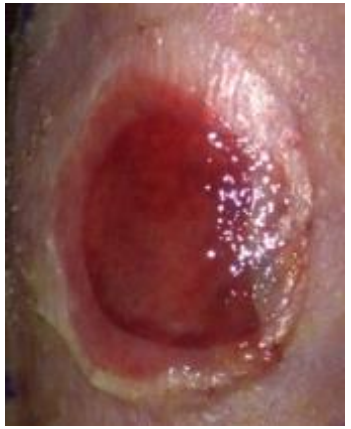
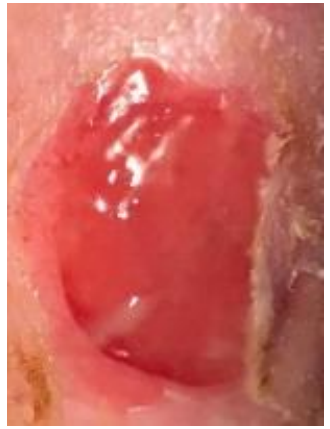
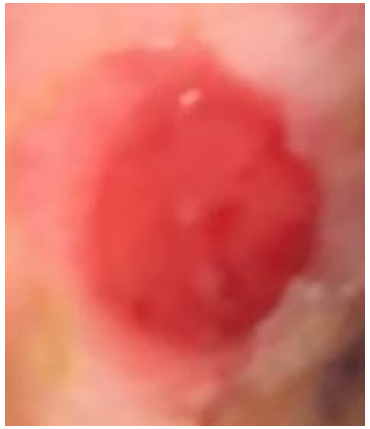
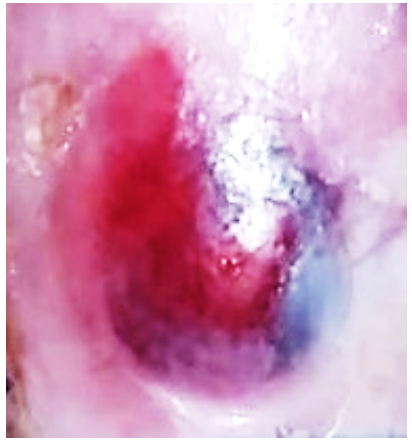
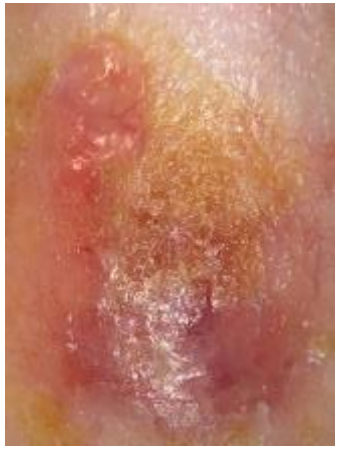
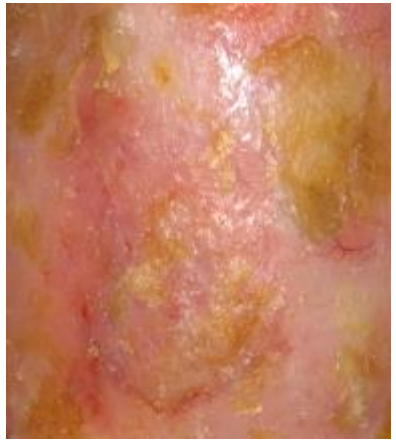
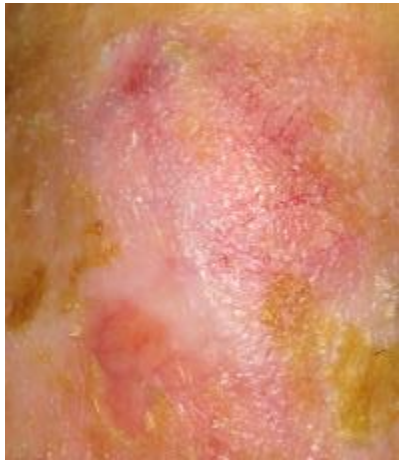
Phase II Chronic Wound Healing Following B-VEC Re-administration

Chronic Wound Healing: Patient 03, Wound 3

- Chronic foot wound with a patient-reported history of being open for more than four years
- Dosing days in Phase II study: Days 1,2,3,4,5 and Day 30 following biopsy
- The wound closed 35% at the 30-day timepoint and 42% at the 90-day timepoint
- The wound was re-administered with B-VEC as shown in the adjacent graph
- Following re-administration, the wound closed rapidly (in 7 days) and remained closed for 100 days (and ongoing)



Gem-2 Study: Patient 3 (Age 22)

	Baseline	Day 30	Day 60	Day 90
Initial Dose				
Re-dose				

Update from 2 Additional Patients Enrolled in the Phase II Study

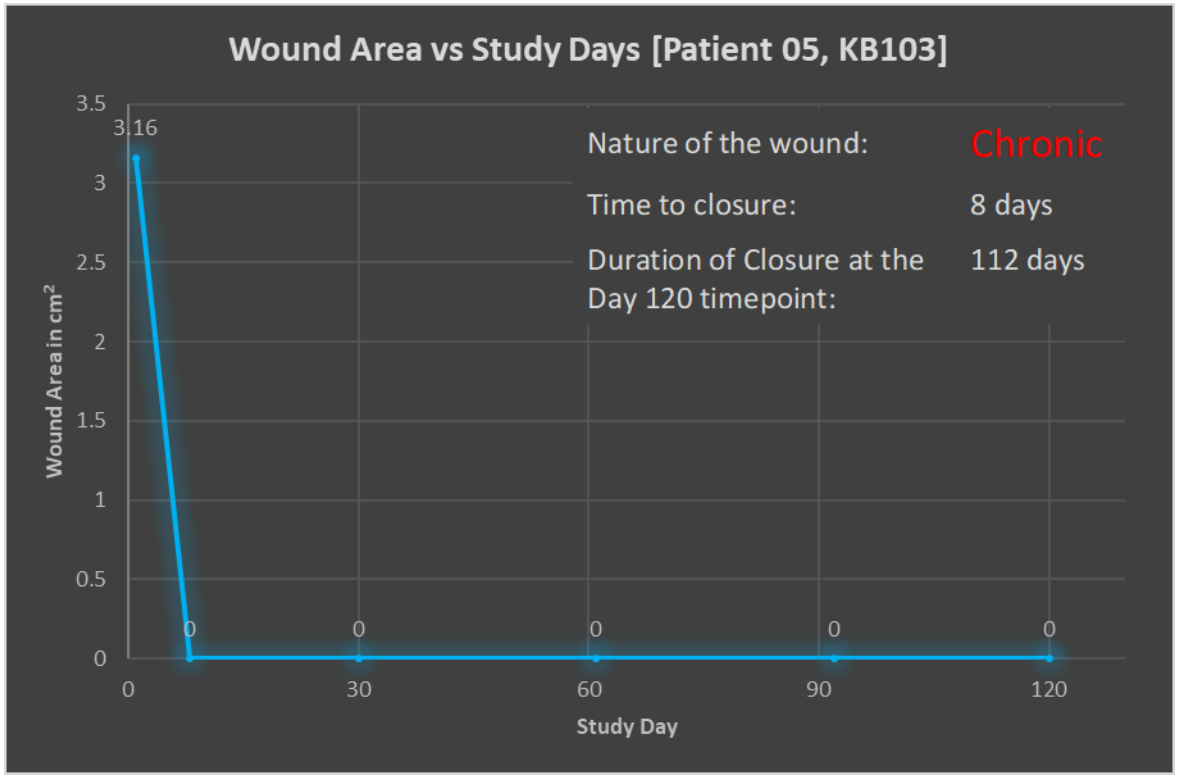
Summary of 2 Additional Phase II Patients

- Two additional adult patients were enrolled in June 2019 to further evaluate wound closure and molecular correction.
    - Patient 05, 21-year-old male
    - Patient 06, 33-year-old female
- Patients were administered B-VEC approximately every other day, for two weeks or till the wound closed completely.
- Patients returned to the clinic for monthly follow-ups, including imaging, biopsies for molecular correction analysis, and safety assessments.

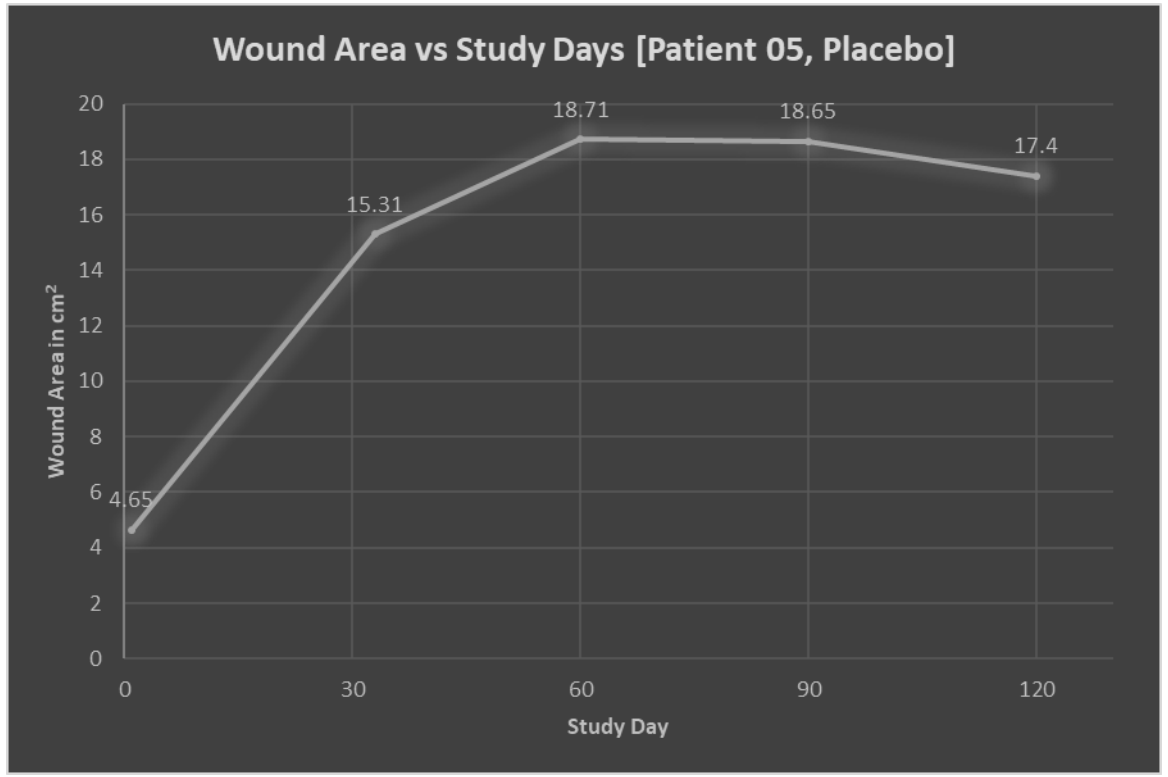
Phase II Study, Day 120 Update: Patient 05 (Age 21)

B-VEC and Placebo-Administered wounds: Wound Area over Study Days

B-VEC-administered, Right upper thigh



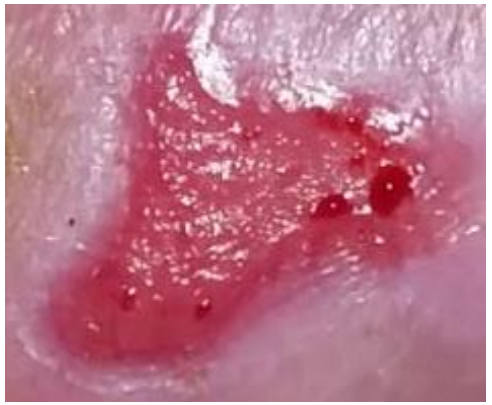
Placebo-administered, Right lower thigh



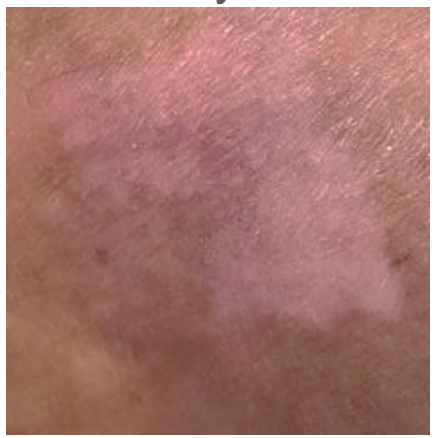
Phase II Study, Day 120 Update: Patient 05 (Age 21)

B-VEC

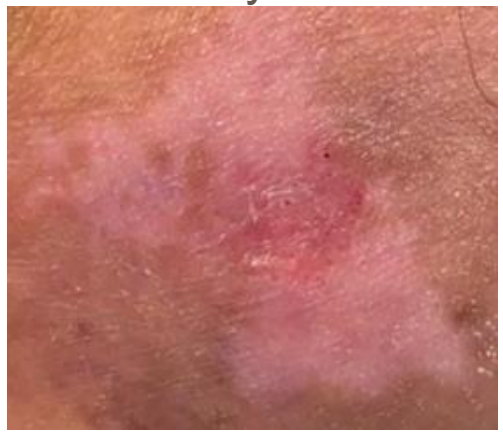
Baseline



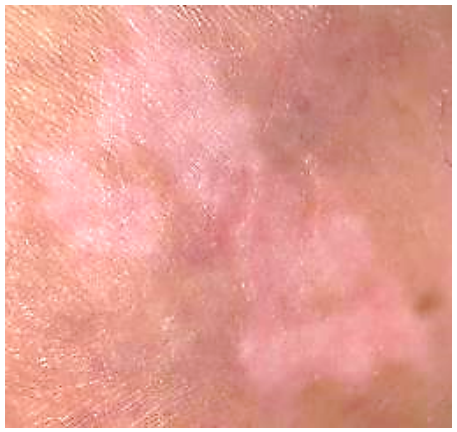
Day 30



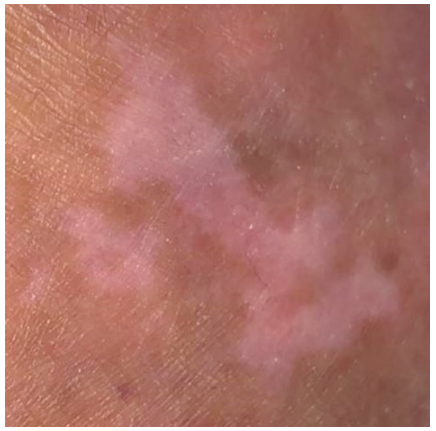
Day 60



Day 90

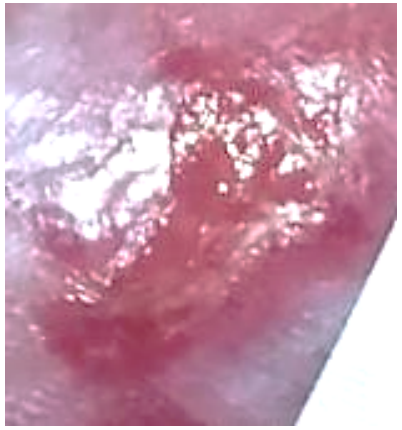


Day 120

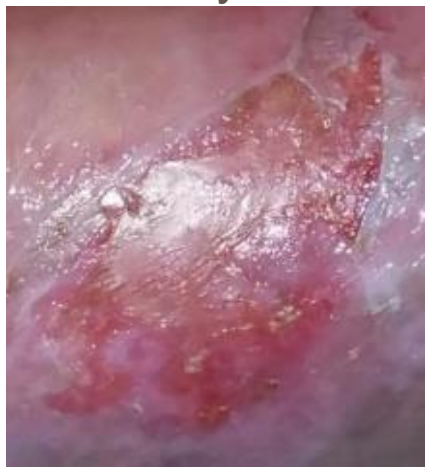


Placebo

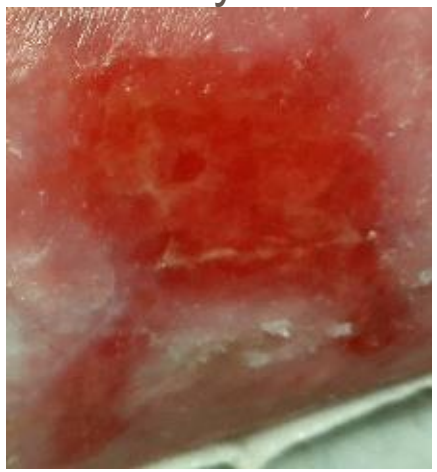
Baseline



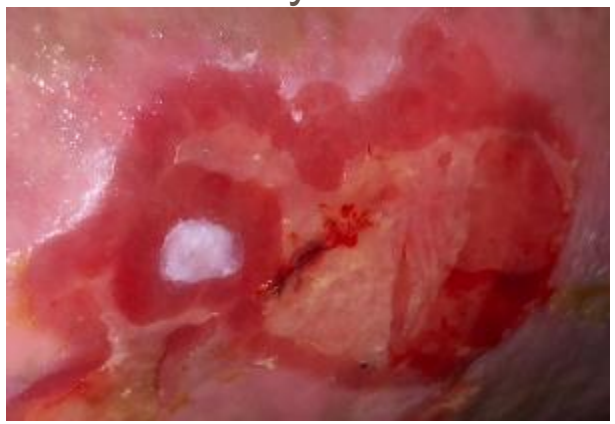
Day 30



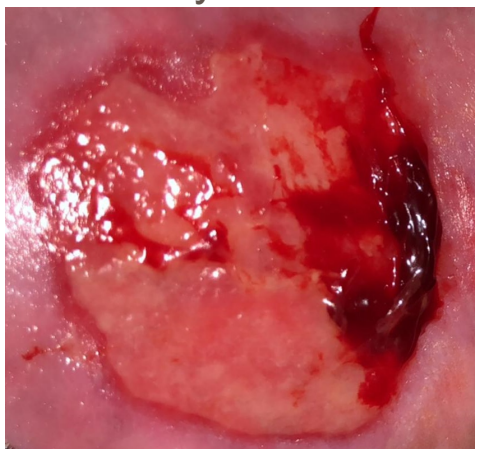
Day 60



Day 90



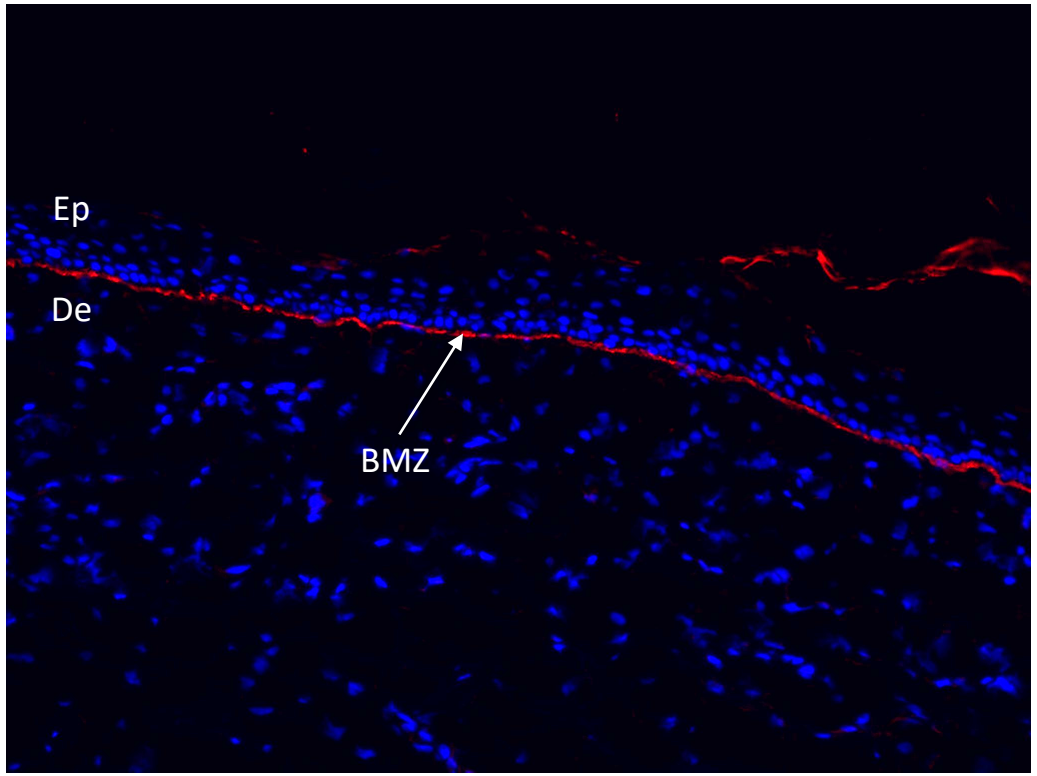
Day 120



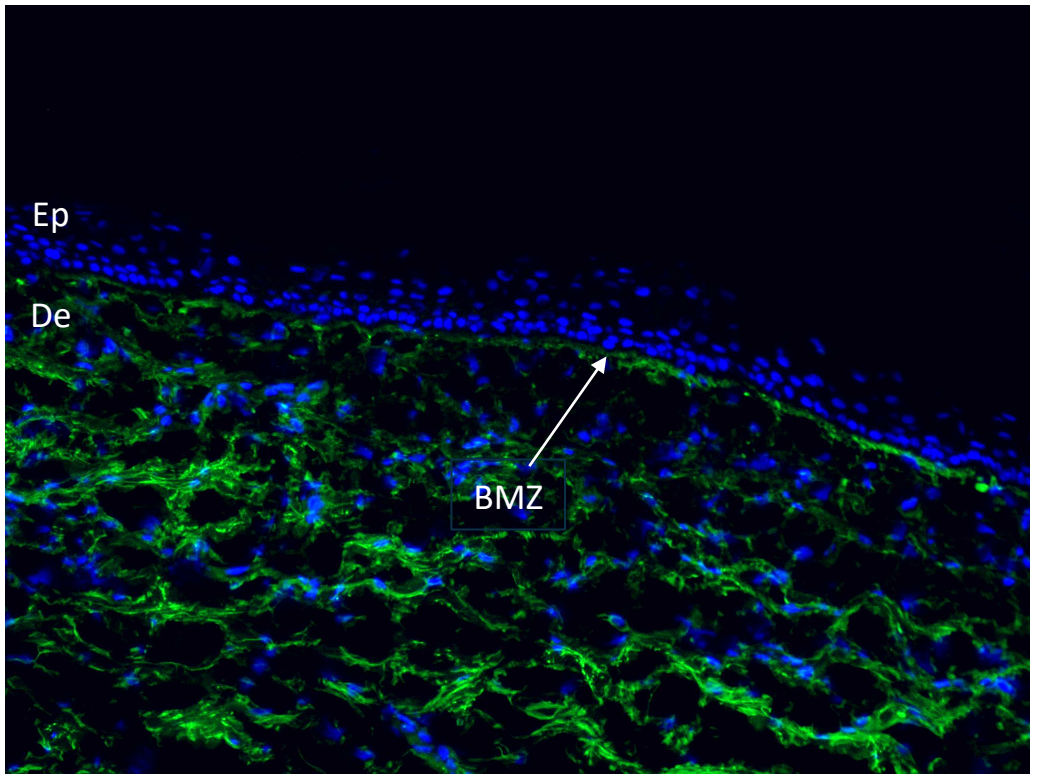
Phase II Study, Day 120 Update: Patient 05 (Age 21)

Collagen VII Staining by Immunofluorescence, Day 15

NC1



NC2

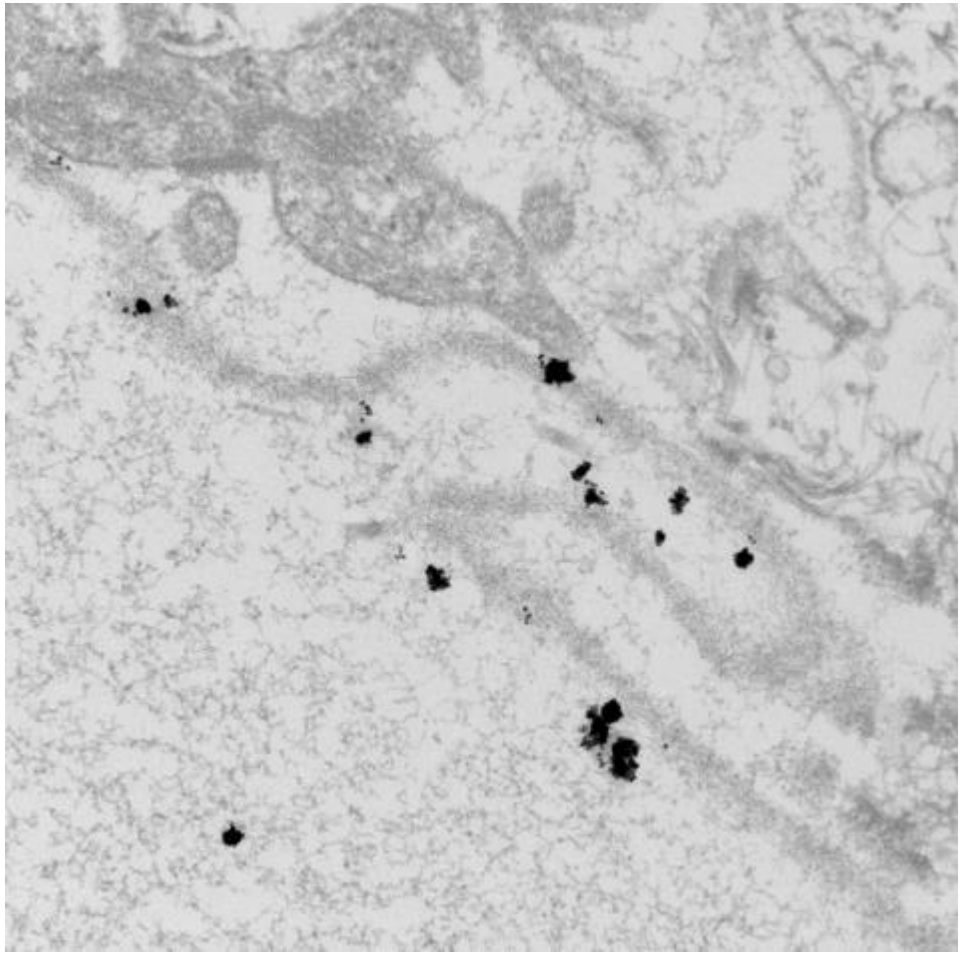


Ep: epidermis, De: dermis, BMZ: basement membrane zone

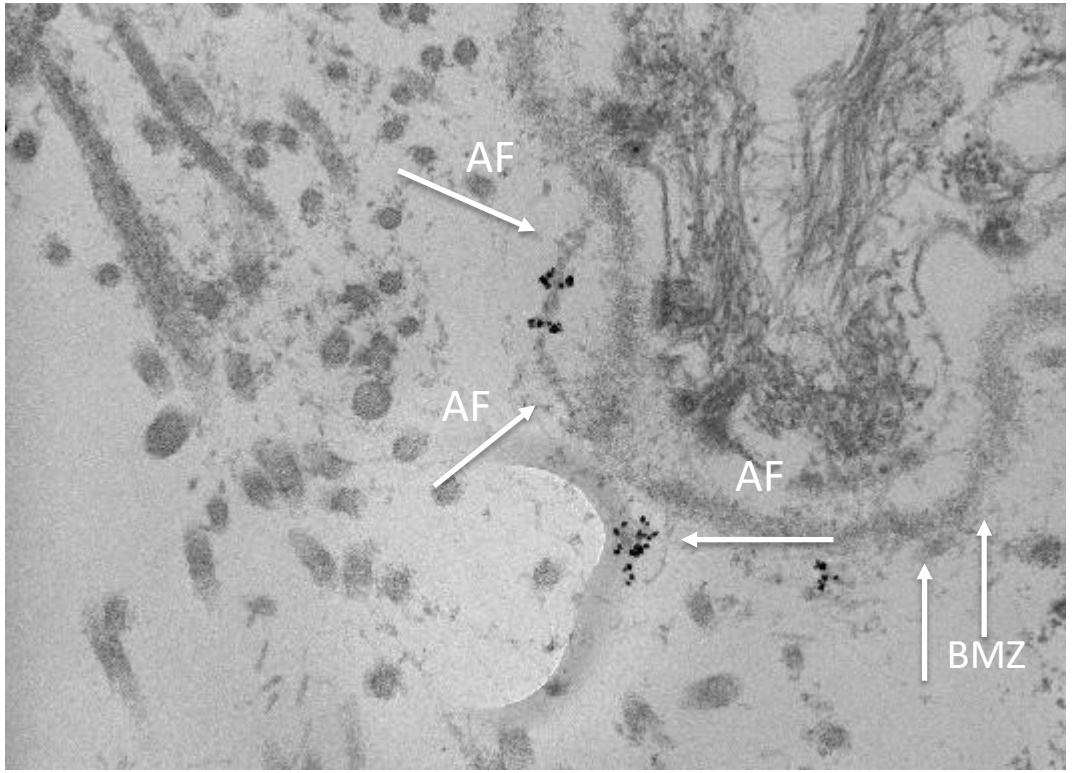
Phase II Study, Day 120 Update: Patient 05 (Age 21)

Anchoring Fibril Formation by Immunoelectron Microscopy

NC1



NC2

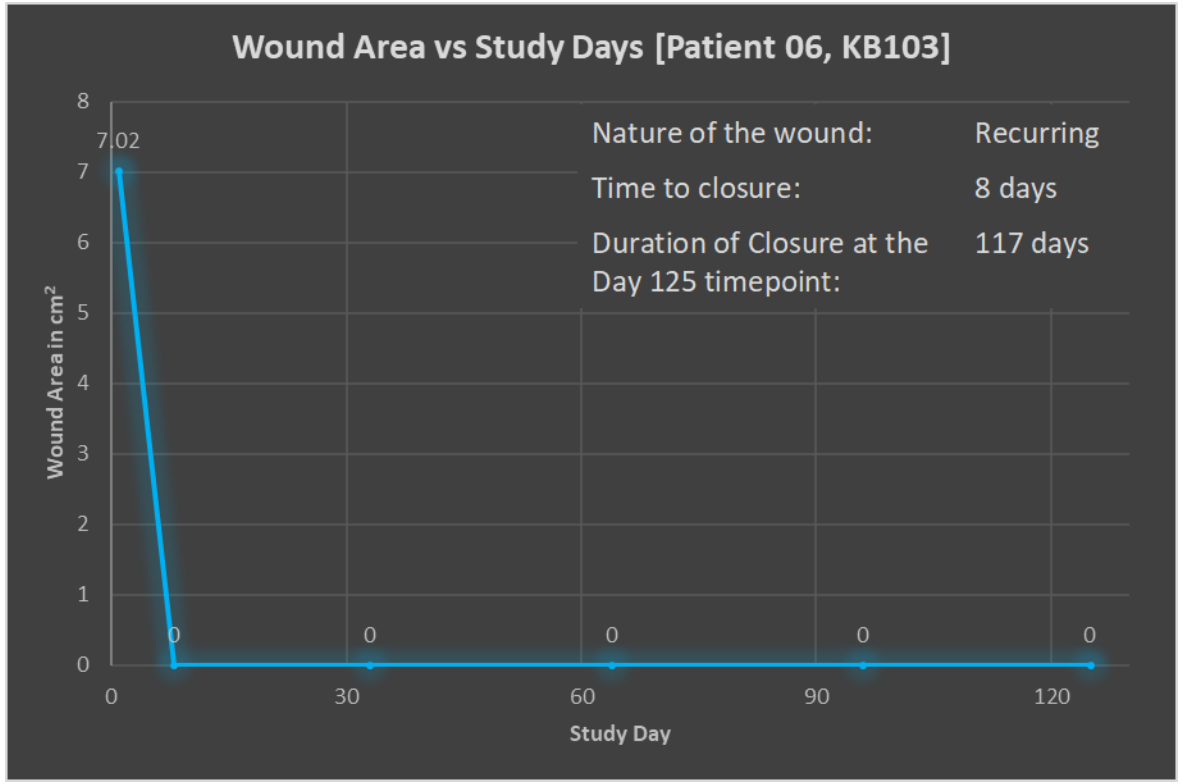


AF: Anchoring Fibrils
BMZ: Basement Membrane Zone

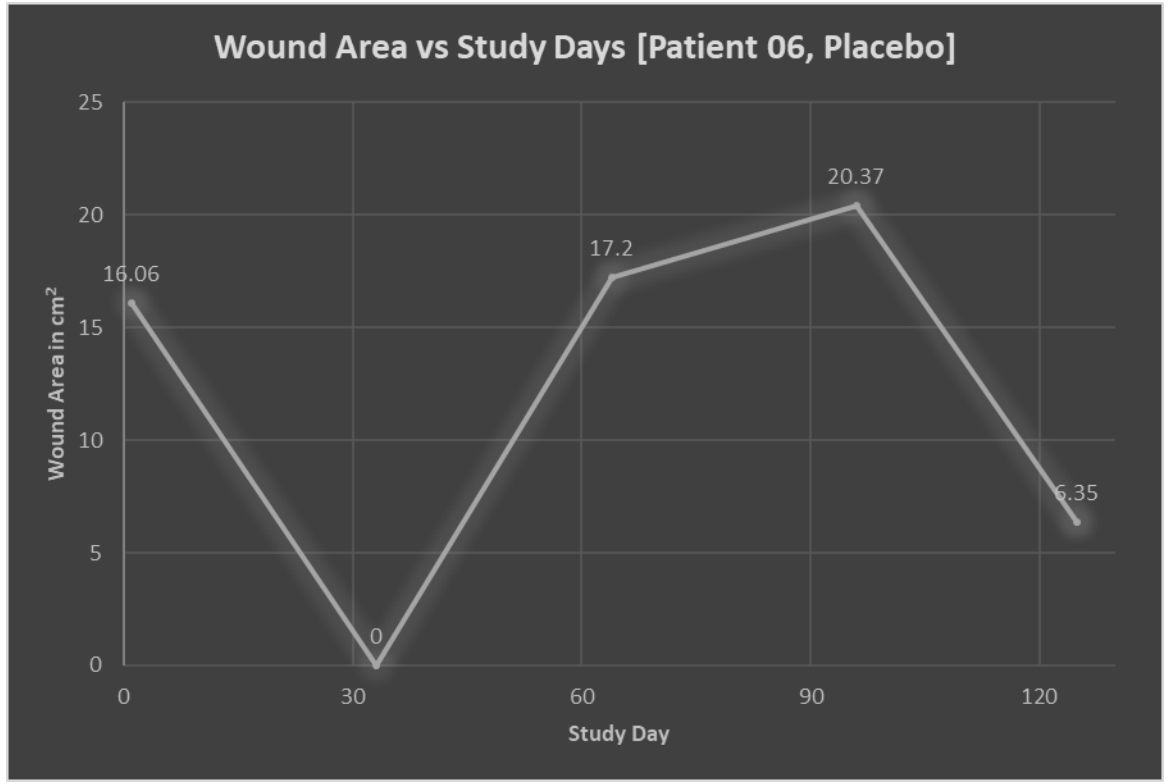
Phase II Study, Day 120 Update: Patient 06 (Age 33)

B-VEC and Placebo-Administered wounds: Wound Area over Study Days

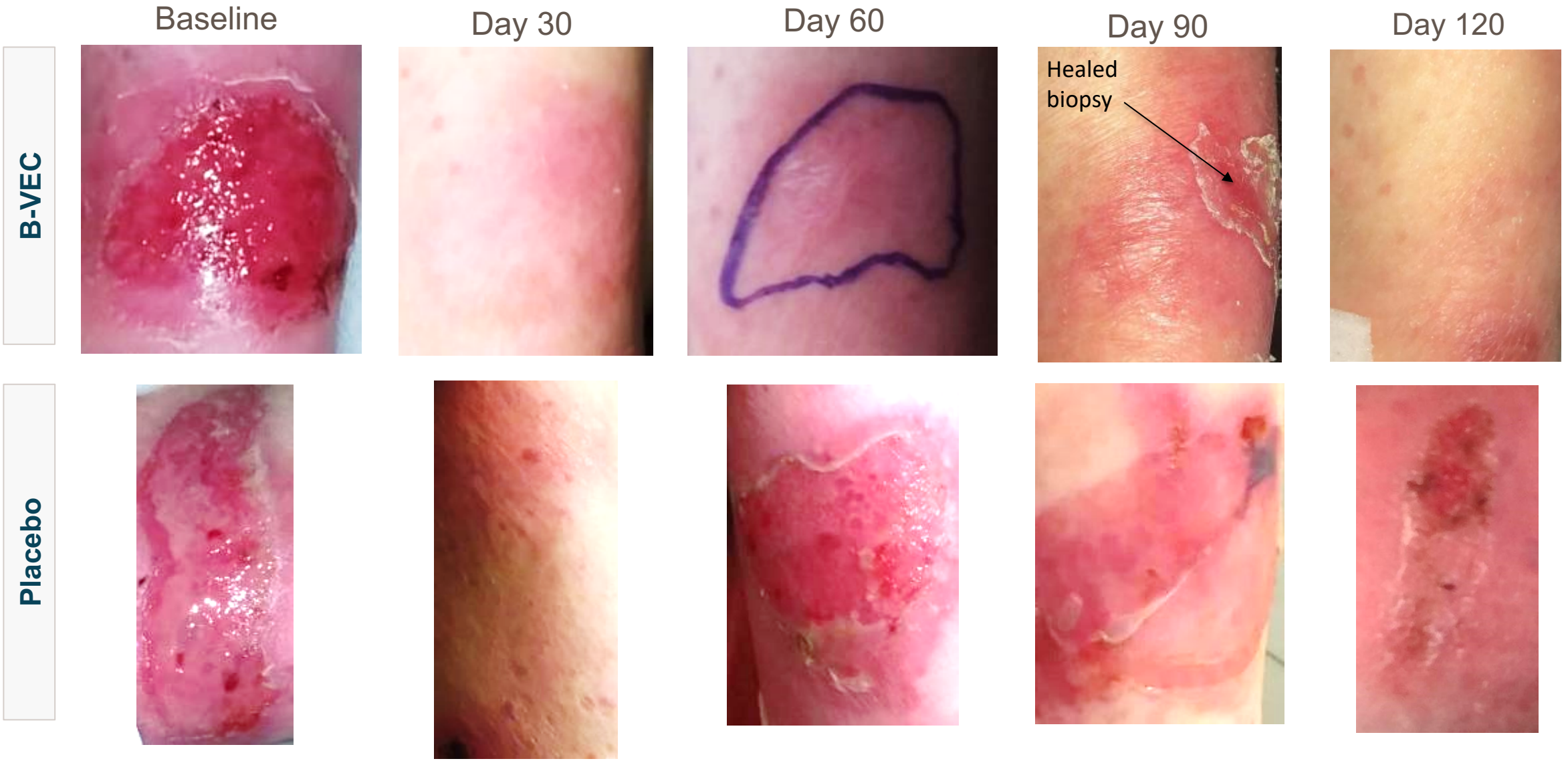
B-VEC-administered, Right wrist



Placebo-administered, Left under arm



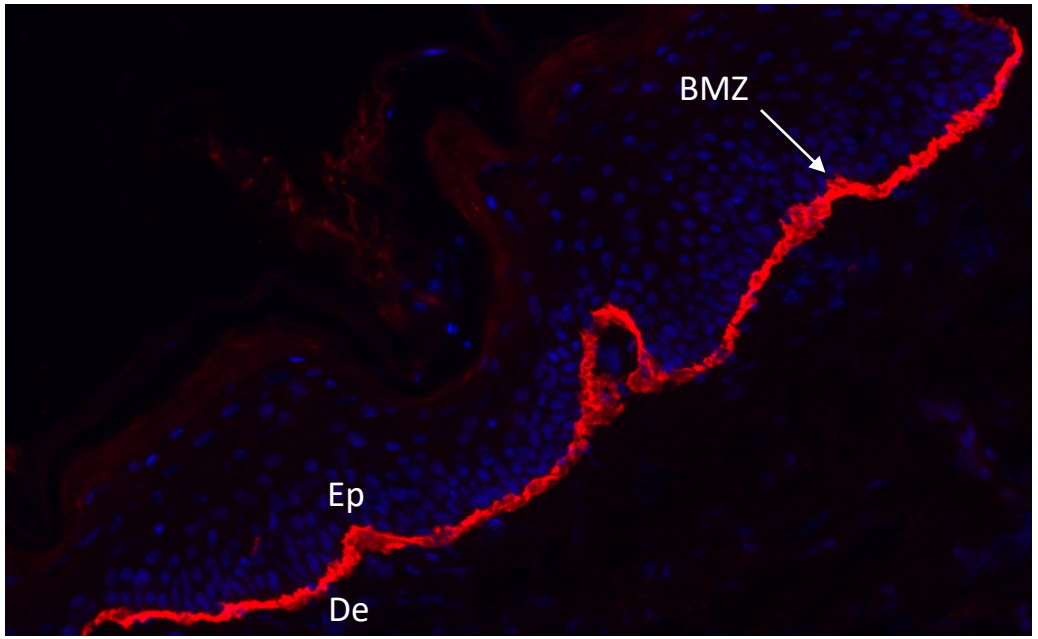
Phase II Study, Day 120 Update: Patient 06 (Age 33)



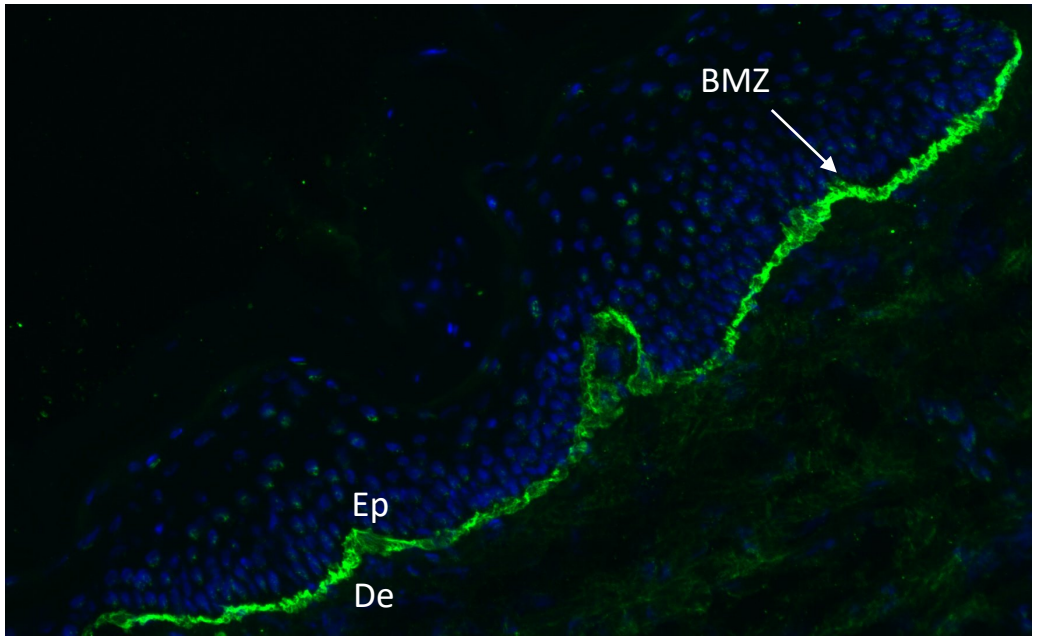
Phase II Study, Day 120 Update: Patient 06 (Age 33)

Collagen VII Staining by Immunofluorescence, Day 8

NC1



NC2

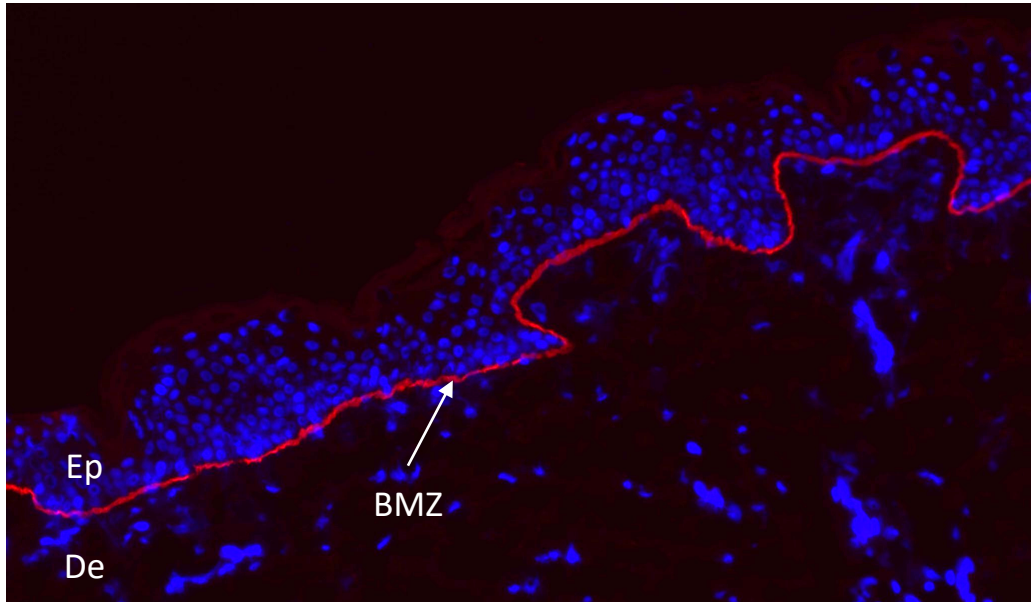


Ep: epidermis, De: dermis, BMZ: basement membrane zone

Phase II Study, Day 120 Update: Patient 06 (Age 33)

Collagen VII Staining by Immunofluorescence, Day 90

NC1



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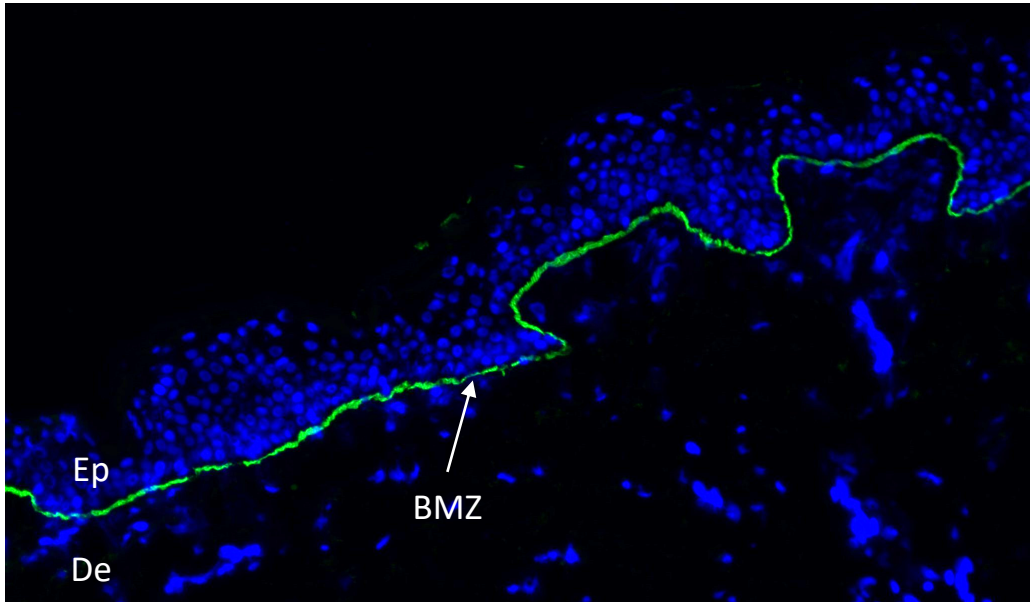

Ep: epidermis, De: dermis, BMZ: basement membrane zone

Phase II Study, Day 120 Update: Patient 06 (Age 33)

Anchoring Fibril Formation by Immunoelectron Microscopy

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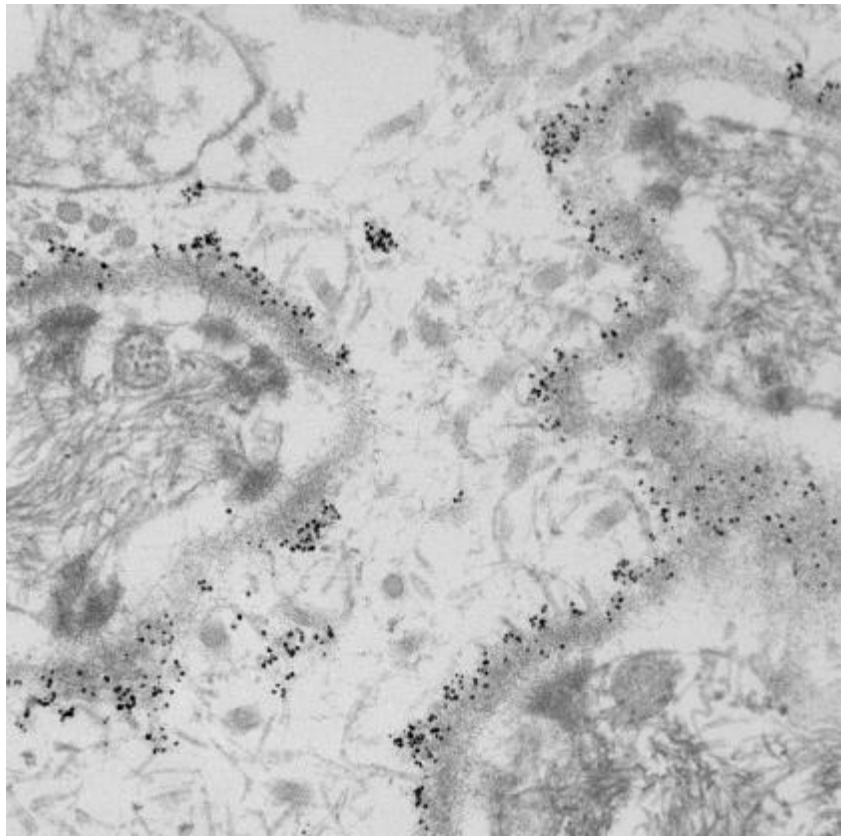
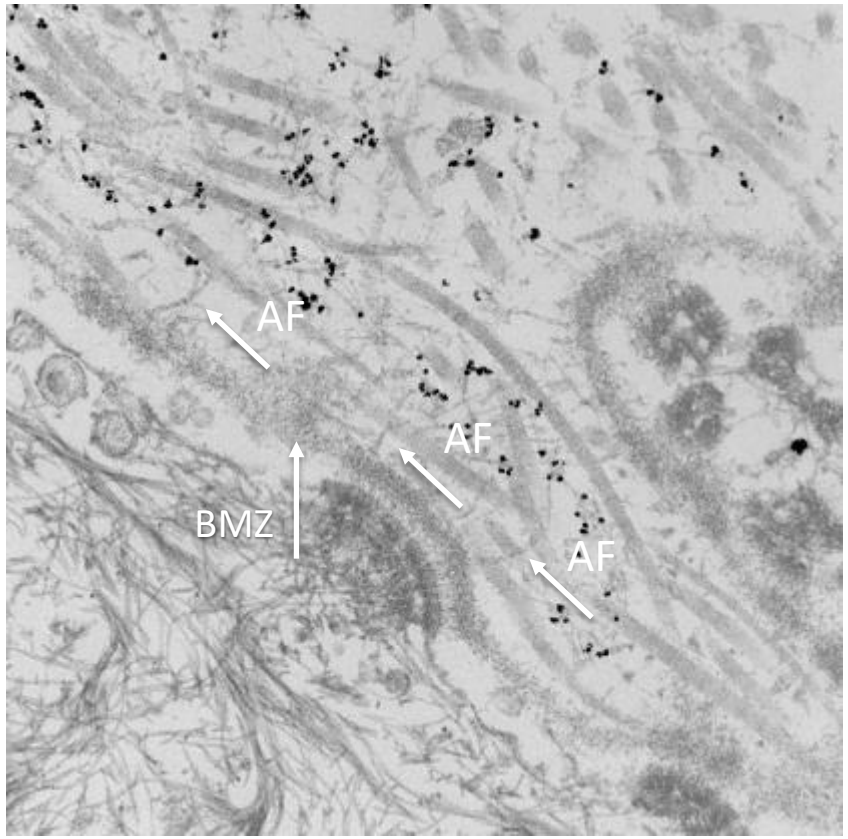


NC2



AF: Anchoring Fibrils
BMZ: Basement Membrane Zone

Summary of 2 Additional Phase II Patients

- Consistent with previous wound data, the data from Patients 05 and 06 strongly correlate molecular correction with clinical wound healing.
- **Immunofluorescence staining for collagen VII:** the presence of NC1 and NC2 domains demonstrates functional collagen VII linearly deposited in the basement membrane zone.
- **Immunoelectron microscopy:** IEM shows the formation of mature anchoring fibrils in the basement membrane zone.
- **Wound imaging**
  - The time to closure for both wounds was 8 days
  - The average duration of closure at the 4-month timepoint for the two wounds was 114.5 days

Overall Summary of Data from the Phase I/II Study

B-VEC Combined Summary Efficacy Update

- 9 out of 10 wounds closed completely (100% closure) following initial administrations of B-VEC.
- The average time to 100% wound closure on the 9 B-VEC treated wounds was 17.4 days (median 14 days).
- The average duration of wound closure on the 9 B-VEC treated wounds at last measured timepoint was 113 days (median 110 days).
- The wound that did not close was re-administered B-VEC and closed completely within 7 days following re-administration
  - The wound was originally reported to be open for over 4 years
  - The wound has remained closed for over 100 days (and ongoing)
- B-VEC continued to be well tolerated following initial and repeat dosing.