# Long-Term Safety and Efficacy of Beremagene Geperpavec (B-VEC) in an Open-Label Extension Study of Patients with Dystrophic Epidermolysis Bullosa (DEB)

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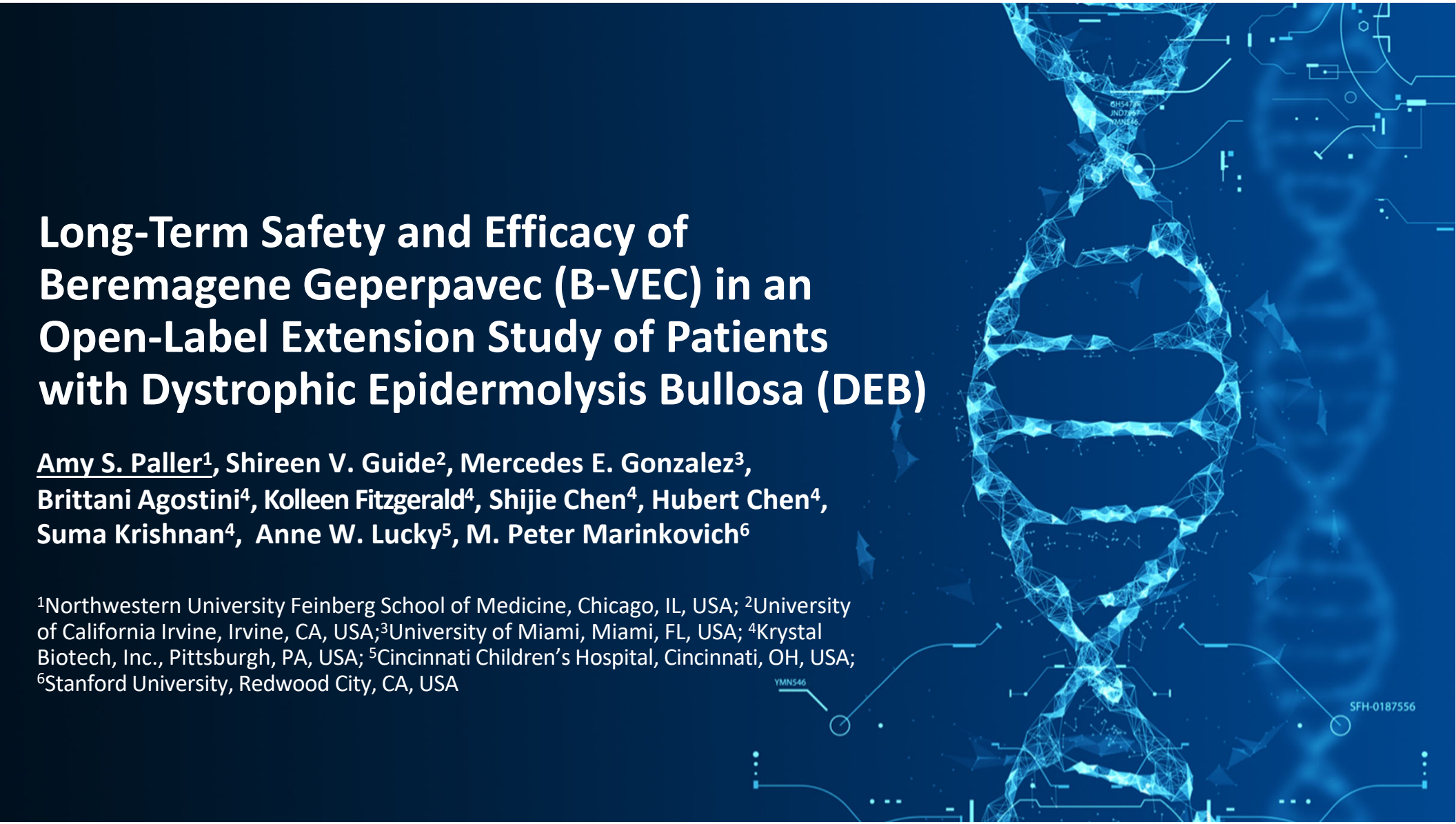

# Disclosures

- AP has been an Investigator (funds to institution) for AbbVie, Arcutis, Dermavant, Eli Lilly, Incyte, Janssen, Krystal Biotech, and UCB; a consultant for BioCryst, Boehringer-Ingelheim, Bristol Myers Squibb, Dermavant, Johnson & Johnson, Krystal Biotech, LEO Pharma, Mitsubishi Tanabe Pharma, Novartis, Primus Pharmaceuticals, Procter and Gamble, Regeneron, Sanofi/Genzyme, TWI Biotechnology, and UCB; and on the data safety monitoring board for AbbVie, Abeona, Catawba, and Galderma.
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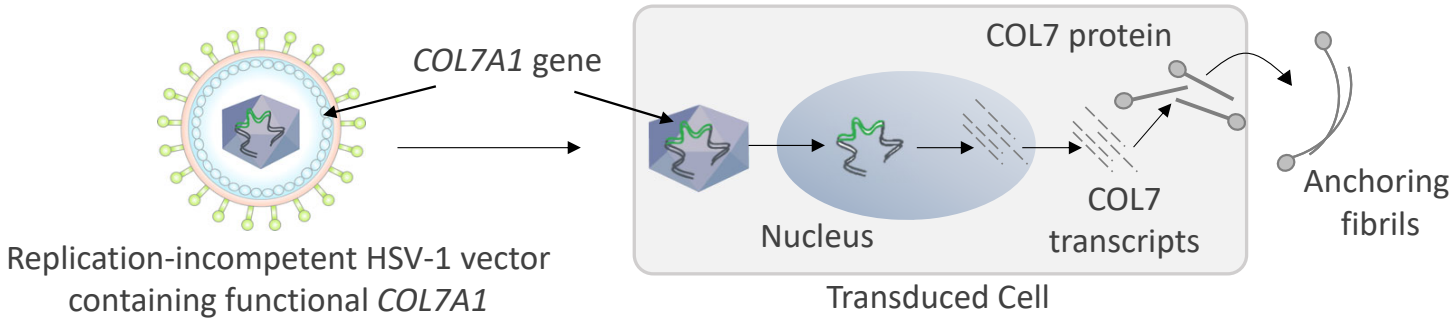
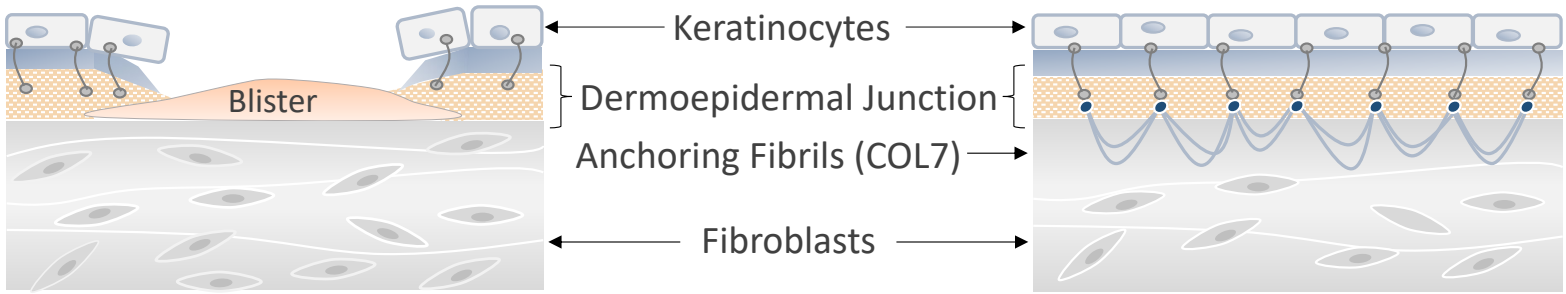
# B-VEC: HSV–1–Based, Topical, Redosable Gene Therapy

## Dystrophic Epidermolysis Bullosa (DEB)

- Rare genetic blistering disease caused by variants in the *COL7A1* gene, leading to skin fragility and wounds[1-3]
- *COL7A1* encodes COL7, which forms anchoring fibrils, responsible for epidermal-dermal adhesion

### B-VEC Mechanism of Action : Molecular Correction

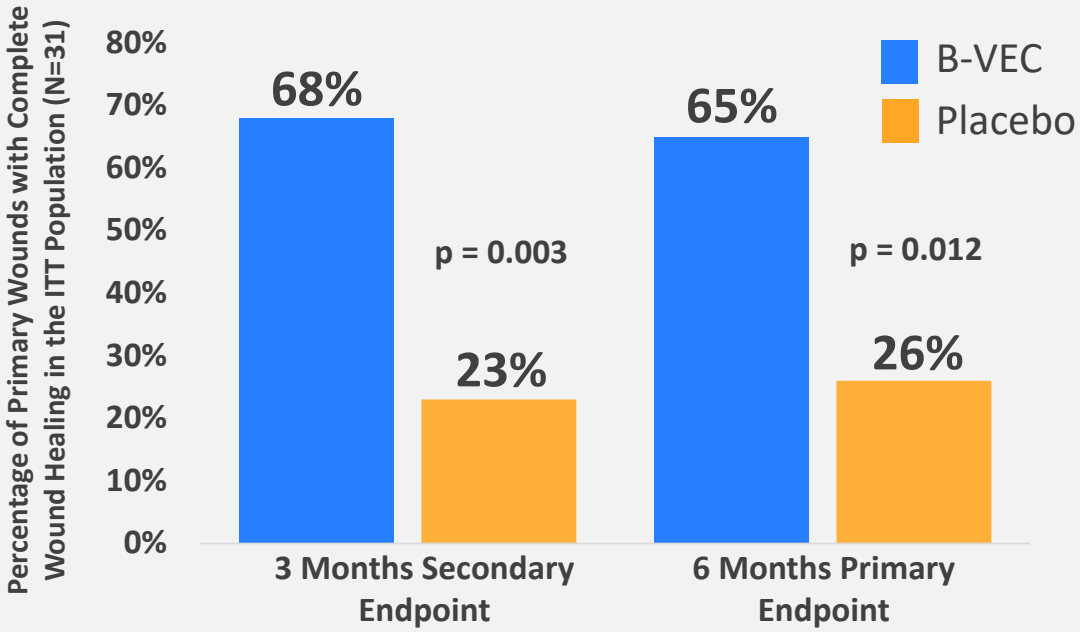



B-VEC, beremagene geperpavec; COL7, type VII collagen; 1. Fine JD, et al. *J Am Acad Dermatol.* 2009;61(3):367-384; 2. DEBRA of America. Accessed February 20, 2024. https://www.debra.org/about-eb/eb-depth; 3. Has C, et al. *Br J Dermatol.* 2020;182(3):574-592.

# GEM-3 Pivotal Study: 26-Week, Double-Blind, Intrapatient Randomized, Placebo-Controlled Phase 3 Study of B-VEC in Patients with DEB

## Significantly Greater Wound Healing with B-VEC*




*Complete wound healing defined as 100% wound closure from exact wound area at baseline at 2 study visits, 2 weeks apart

## Safety/Adverse Events (AEs)

- No AEs led to treatment discontinuation
- One AE, mild erythema (3.2%), was considered possibly related to study drug
- No SAEs related to study drug
- Despite seroconversion for COL7 antibodies there was no difference in treatment response[1]

B-VEC was approved by the FDA in May 2023 and is indicated for the treatment of wounds in patients 6 months of age and older with DEB with mutation(s) in the *COL7A1* gene.

AE, adverse event; B-VEC, beremagene geperpavec; COL7, type VII collagen; DEB, dystrophic epidermolysis bullosa; FDA, US Food and Drug Administration; ITT, intent-to-treat; SAE, serious adverse event. 1. Guide SV, et al. *N Engl J Med.* 2022;387(24):2211-9.

# Open Label Extension (OLE) Study Design

Prospective, open-label, uncontrolled cohort study at 5 US sites

## Study Population

- Genetic confirmation of DDEB/RDEB
  - Rollover – From the Phase 3 study
  - Treatment-Naïve – No previous B-VEC

## Dosing

- Maximum weekly dose determined by age
  - <3 years old: 0.8 mL
  - ≥3 years old: 1.6 mL

## Treatment Duration

- Up to 112 weeks

## Key Objectives

- Collect safety and tolerability outcomes on B-VEC
- Provide continued access for Phase 3 study subjects
- Provide B-VEC to patients with DEB who had not participated in Phase 3 study

## Exploratory Objectives

- Evaluate mean change in treatment satisfaction (TSQM-9) and quality-of-life (Skindex-29 and EQ-5D)
- Describe durability of closure for wounds previously treated with B-VEC in Phase 3

OLE study was initiated in May 2021 and terminated in July 2023 once subjects could be transitioned to commercially available product.

B-VEC, beremagene geperpavec; DDEB, dominant dystrophic epidermolysis bullosa; DEB, dystrophic epidermolysis bullosa; RDEB, recessive dystrophic epidermolysis bullosa; TSQM-9, Treatment Satisfaction Questionnaire for Medication 9

# Study Demographics

- 47 subjects were enrolled
  - 24 rollover subjects
  - 23 naïve subjects
- Mean age ~16 years old
  - 2 naïve subjects were <1 year old
  - 2 naïve subjects were Black
  - 45% Hispanic

| | Rollover Subjects (N=24) n (%) | Naïve Subjects (N=23) n (%) | All Subjects (N=47) n (%) |
|---|---|---|---|
| **Age (years)** | | | |
| Mean (SD) | 16.7 (10.1) | 16.3 (11.5) | 16.5 (10.7) |
| Range | 2.0 – 35.0 | 0.5 – 45.9 | 0.5 – 45.9 |
| **Sex, n (%)** | | | |
| Male | 18 (75.0) | 12 (52.2) | 30 (63.8) |
| Female | 6 (25.0) | 11 (47.8) | 17 (36.2) |
| **Race, n (%)** | | | |
| White | 17 (70.8) | 15 (65.2) | 32 (68.1) |
| Black or African American | 0 | 2 (8.7) | 2 (4.3) |
| Asian | 2 (8.3) | 2 (8.7) | 4 (8.5) |
| American Indian or Alaska Native | 5 (20.8) | 3 (13.0) | 8 (17.0) |
| Unknown | 0 | 1 (4.3) | 1 (2.1) |
| **Ethnicity, n (%)** | | | |
| Hispanic or Latino | 13 (54.2) | 8 (34.8) | 21 (44.7) |

DEB, dystrophic epidermolysis bullosa; SD, standard deviation

# OLE Duration of Exposure and Adverse Events

## Duration

- 5 subjects withdrew for reasons unrelated to treatment
- Mean duration of study treatment in the OLE: 475 days
- 62% (29 of 47 subjects) had >1 year of exposure
- Longest duration ~2.2 years

## Adverse Events

| Subjects with at least 1 | Rollover Subjects (N = 24) | | Naive Subjects (N = 23) | | All Subjects (N =47) | |
|---|---|---|---|---|---|---|
| | n (%) | Events | n (%) | Events | n (%) | Events |
| Any AE | 17 (70.8) | 102 | 18 (78.3) | 72 | 35 (74.5) | 174 |
| Drug-related AE | 0 | 0 | 1 (4.3) | 2 | 1 (2.1) | 2 |
| Severe AE | 8 (33.3) | 12 | 2 (8.7) | 2 | 10 (21.3) | 14 |
| Serious AE | 9 (37.5) | 11 | 5 (21.7) | 6 | 14 (29.8) | 17 |

- Two AEs (wound hemorrhage) in 1 patient: possibly related to treatment
- No drug-related AEs
- No deaths or discontinuations due to AE
- No SAE was considered related to treatment

- AE types resembled those observed in Phase 3 and consistent with those expected in patients with DEB

AE, adverse event; DEB, dystrophic epidermolysis bullosa; OLE, open-label extension; SAE, serious adverse event.

# Durable Closure of Wounds Treated in Phase 3 Study

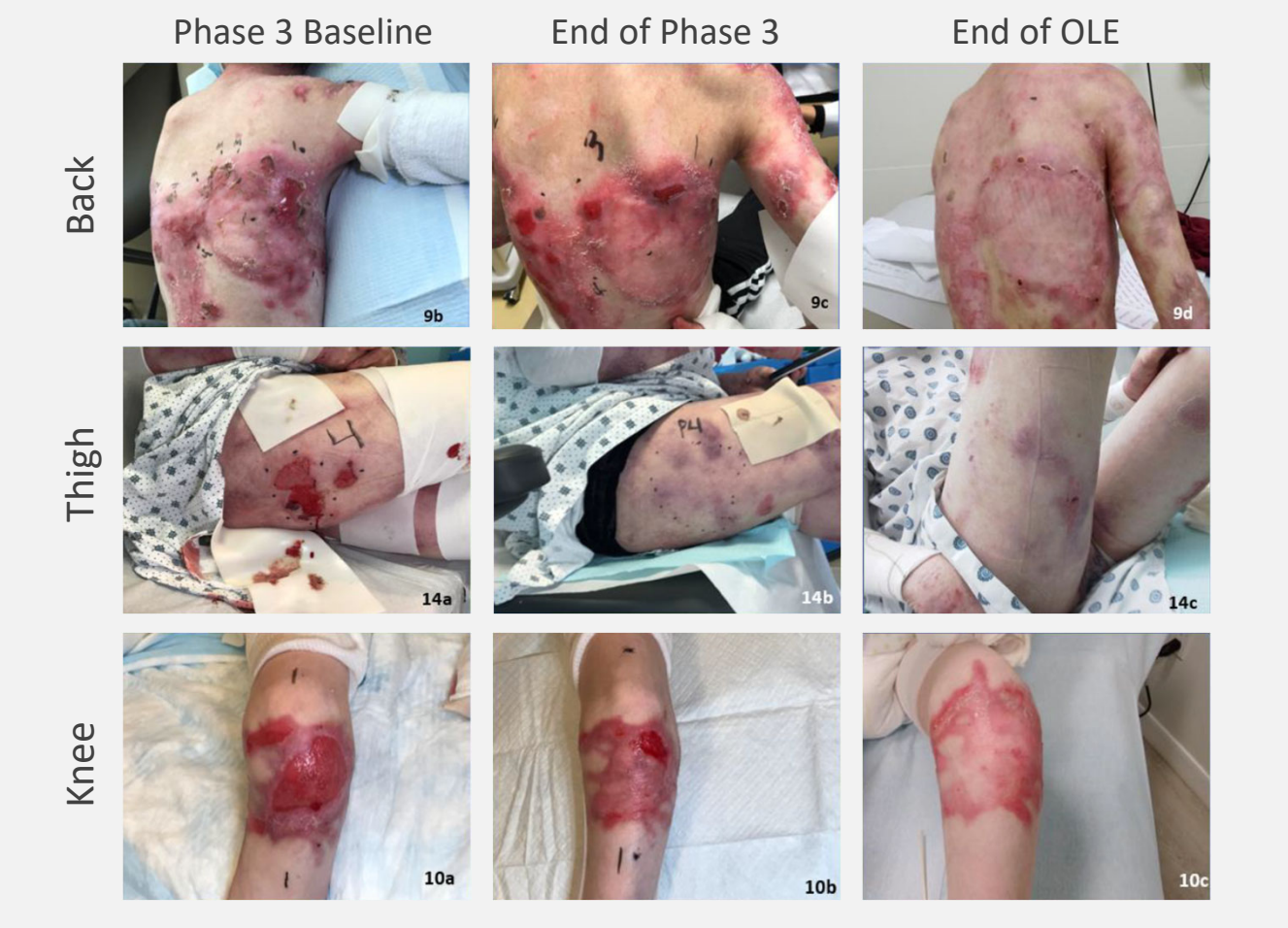
- Sufficient data on 19 of 24 rollover subjects to serially assess closure
- Closure rates were 61.1% to 89.5% in the OLE study
- Comparable to rates observed at Months 3 and 6 in the Phase 3 study.

| Visit | Percentage of subjects with wound closure (proportion)[†] |
|---|---|
| Month 3 (Phase 3) | 68.4 (13/19) |
| Month 6 (Phase 3) | 73.7 (14/19) |
| Baseline OLE | 89.5 (17/19) |
| 3 Months | 84.2 (16/19) |
| 6 Months | 61.1 (11/18) |
| 9 Months | 82.4 (14/17) |
| 12 Months | 62.5 (10/16) |

[†]The proportion of subjects with wound closure was defined as those with complete wound closure based on comparison to the exact wound area selected at baseline at initiation of the Phase 3 study.

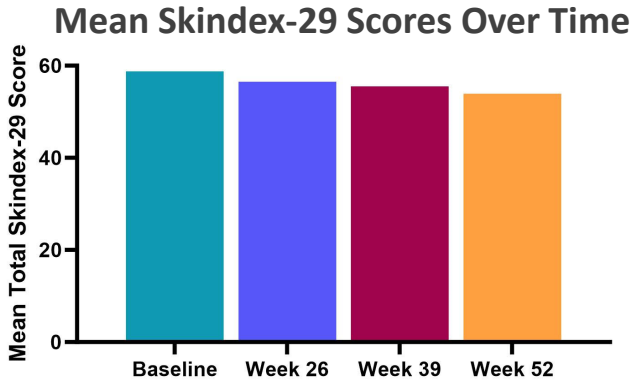
B-VEC, beremagene geperpavec; OLE, open-label extension

# Examples of Wound Healing from Baseline of Phase 3 to End of OLE

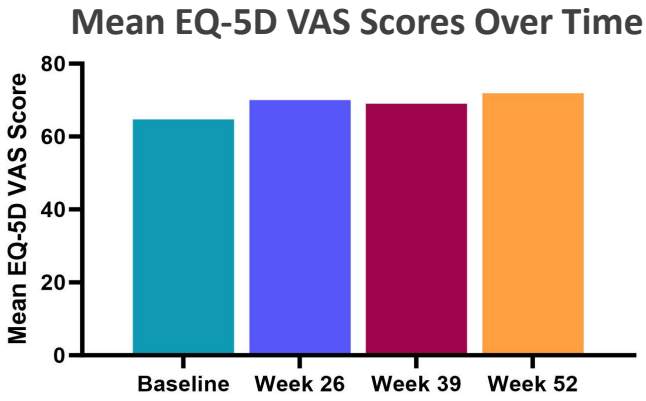


# Patient-Reported Outcomes

## *Quality-of-life (QoL) and treatment satisfaction preserved with continued treatment*

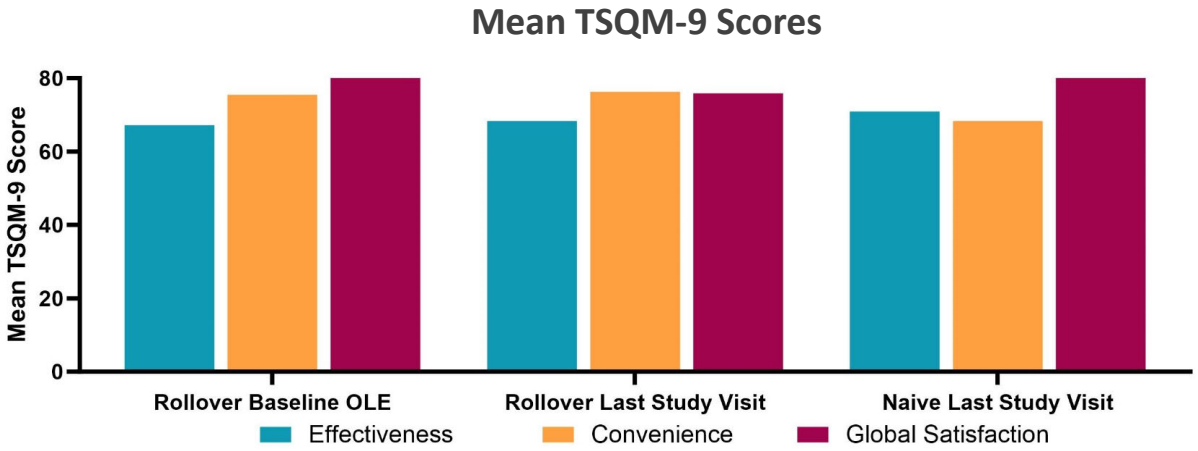



Lower score on Skindex-29 indicates less impairment




Higher VAS score on EQ-5D indicates better health status

- QoL assessed among subjects ≥12 years old at baseline (n=28), Week 26 (n=21), Week 39 (n=22), and Week 52 (n=18)
- TSQM-9 measured at baseline and last study visit for rollover subjects (n=24) and last study visit for naïve subjects (n=23)

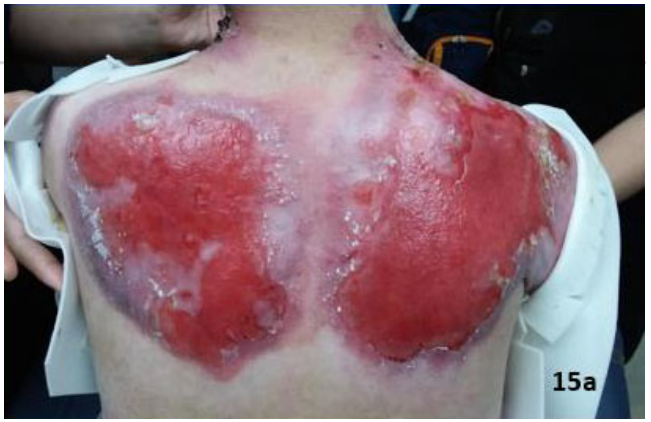



Higher score on TSQM-9 indicates higher treatment satisfaction

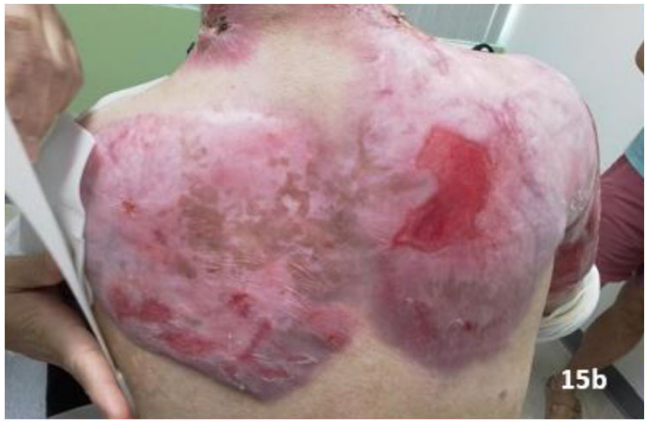
TSQM-9, Treatment Satisfaction Questionnaire for Medication 9; VAS, visual analogue scale

# Conclusions

- The OLE study provides additional safety data in a broader population with longer duration of exposure.
- The majority of the AEs reported were mild or moderate in severity.
- AEs reported were similar to those observed in the Phase 3 study.
- No new safety signals were identified during the OLE.
- Patient-reported outcomes show high treatment satisfaction and trend toward improved quality of life.
- Wounds from Phase 3 show high durability of closure with continued treatment.



Beginning of OLE



End of OLE

***Thank you to the patients, families, investigators, and study staff for their participation in the OLE study***