UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 20, 2022

KRYSTAL BIOTECH, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-38210**	**82-1080209**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification Number)**

2100 Wharton Street, Suite 701
Pittsburgh, Pennsylvania 15203
(Address of principal executive offices, including Zip Code)

Registrant's telephone number, including area code: (412) 586-5830

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On May 19, 2022, Krystal Biotech, Inc. (the "Company") presented new data entitled "GEM-3: Phase 3 Safety and Immunogenicity Results of beremagene geperpavec (B-VEC), an Investigational, Topical Gene Therapy for Dystrophic Epidermolysis Bullosa (DEB)"at the Society for Investigative Dermatology ("SID") 2022 Annual Meeting in Portland, Oregon. A copy of the poster presented at the SID meeting and the ePoster presentation to be used at the SID meeting are attached hereto as Exhibit 99.1 and Exhibit 99.2, respectively, and are incorporated herein by reference. The poster and ePoster presentation will also be available on the "Investors" section of the Company's website at www.krystalbio.com.

This information in this Item 7.01 of this Current Report on Form 8-K and in Exhibits 99.1 and 99.2 shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, or incorporated by reference in any filing made by the Company pursuant to the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Poster titled "GEM-3: Phase 3 Safety and Immunogenicity Results of beremagene geperpavec (B-VEC), an Investigational, Topical Gene Therapy for Dystrophic Epidermolysis Bullosa (DEB)"
99.2	ePoster presentation titled "GEM-3: Phase 3 Safety and Immunogenicity Results of beremagene geperpavec (B-VEC), an Investigational, Topical Gene Therapy for Dystrophic Epidermolysis Bullosa (DEB)"
104	Cover Page Interactive Data file (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: May 20, 2022

KRYSTAL BIOTECH, INC.

By: /s/ Krish S. Krishnan
Name: Krish S. Krishnan
Title: President and Chief Executive Officer

GEM-3: Phase 3 Safety and Immunogenicity Results of Beremagene Geperpavec (B-VEC), an Investigational, Topical Gene Therapy for Dystrophic Epidermolysis Bullosa (DEB)

Exhibi

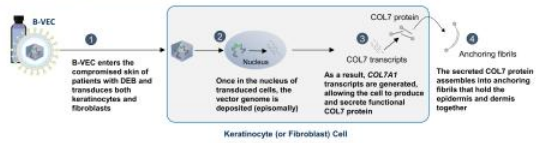
M. Peter Marinkovich,[1] Mercedes E. Gonzalez,[2] Shireen V. Guide,[3] I. Sinem Bagci,[1] Surya Chitra,[4] Brittani Agostini,[5] Hubert Chen,[5] Trevor Parry,[5] Suma Krishnan[5]

[1]Stanford University, Redwood City, CA; [2]University of Miami, Miami, FL; [3]Mission Dermatology Center, Children's Hospital of Orange County, University of California, Irvine, Department of Dermatology, Rancho Santa Margarita, CA; [4]Savio Group Analytics & Statistics, Hockessin, DE; [5]Krystal Biotech, Inc., Pittsburgh, PA

Introduction

- Dystrophic epidermolysis bullosa (DEB) is a serious, ultra-rare genetic blistering disease caused by mutations in the *COL7A1* gene that lead to skin fragility and wounds[1-3]
  - DEB affects ≈9000 people globally, including ≈3000 people in the United States and ≈3000 people in Europe[4]
  - Patients with DEB require proactive management and care due to an increased risk of aggressive squamous cell carcinoma (SCC) and a wide range of other serious secondary complications, regardless of wound size or chronicity[5-7]
  - Current management of DEB is limited to supportive care, such as ameliorating symptoms, palliative wound care, and managing secondary complications[8,9]
- Beremagene geperpavec (B-VEC) is an investigational herpes simplex virus type 1 (HSV-1)–based, topical, redosable gene therapy designed to restore type VII collagen (COL7) protein by delivering the *COL7A1* gene[10] (**Figure 1**)
  - B-VEC utilizes a differentiated HSV-1 vector platform that allows for episomal delivery, high payload capacity, tropism for the skin, and evasion of the immune system, enabling repeat delivery[10]

Figure 1. B-VEC mechanism of action

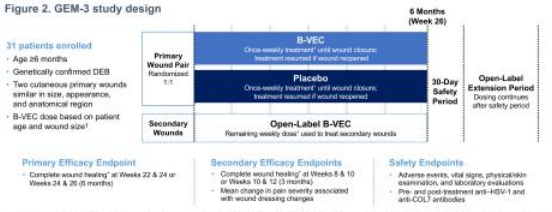


B-VEC, beremagene geperpavec; COL7, type VII collagen; *COL7A1*, collagen type VII alpha 1 chain gene; DEB, dystrophic epidermolysis bullosa.

Methods

- GEM-3 (NCT04491604) is a phase 3, multicenter, double-blind, placebo-controlled intra-patient–randomized study evaluating the efficacy and safety of B-VEC in patients with DEB (**Figure 2**)
- Serum samples before (screening or Week 1) and after (Week 26) B-VEC treatment were collected from patients and evaluated for anti-drug antibodies
  - Anti–HSV-1 specific antibodies were evaluated using a validated plaque reduction neutralization test (PRNT), which determines the percent reduction in B-VEC–mediated plaque formation in the presence of serially diluted patient sera (1:80 to 1:5120) and is reported as PRNT50 (defined as the serum dilution at which a ≈50% reduction in plaques is observed)
  - Immunoglobulin G antibodies against human COL7 were evaluated using a commercially available anti-COL7 enzyme-linked immunosorbent assay (EA 1947-4801 G, EUROIMMUN, Lübeck, Germany), which qualitatively determines anti-COL7 serostatus

Figure 2. GEM-3 study design



†Maximum weekly dose (PFU/week) was based on patient's age and unit dose (PFU/wound) was determined based on wound area at baseline. ‡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; COL7, type VII collagen; DEB, dystrophic epidermolysis bullosa; HSV-1, herpes simplex virus type 1; PFU, plaque-forming unit.

Results

Patient Disposition

- The intent-to-treat (ITT) population, used for all primary and secondary efficacy analyses, included 31 randomized patients, each with a primary wound pair (**Table 1**)
- The safety population, used for all safety analyses, was the same as the ITT population
- Of 31 randomized patients, 3 withdrew from the study for nondrug-related reasons

Table 1. Baseline demographics and clinical characteristics

Patient demographics/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-≤18 years	9 (29.0)
>18 years	12 (38.7)
Male sex, n (%)	20 (64.5)
Race, n (%)	
White	20 (64.5)
Asian	6 (19.4)
American Indian or Alaska native	5 (16.1)
Genotype, n (%)	
Dominant DEB (DDEB)	1 (3.2)
Recessive DEB (RDEB)	30 (96.8)

Primary wound	B-VEC (N=31)	Placebo (N=31)
Wound area by size, cm²		
Mean (SD)	14.4 (12.7)	15.6 (12.1)
Range	2.3-57.3	2.3-51.5
Wound area by size category*, n (%)		
<20 cm²	23 (74.2)	22 (71.0)
20-<40 cm²	6 (19.4)	8 (25.8)
40-60 cm²	2 (6.5)	1 (3.2)

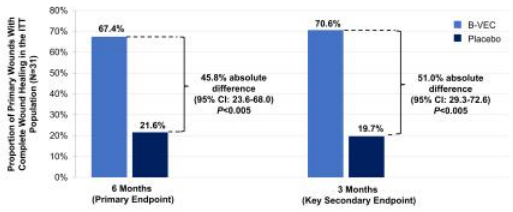
*In a small number of patients, the predefined threshold values for wound area by size category fell in between the size of the 2 wounds. B-VEC, beremagene geperpavec; DEB, dystrophic epidermolysis bullosa; SD, standard deviation.

Results (cont.)

Efficacy

- The proportion of primary wounds with complete wound healing was significantly greater with B-VEC than placebo at both the 3- and 6-month timepoints (*P*<0.005; **Figure 3**)
  - In the patient with DDEB, the primary endpoint of complete wound healing at 6 months was achieved by the B-VEC–treated wound, but not by the placebo-treated wound
- Pain and health-related quality of life assessments demonstrated improvement consistent with a wound healing response

Figure 3. Proportion of primary wounds with complete healing at 6 and 3 months of B-VEC or placebo treatment



Data as of database lock on November 19, 2021; 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; ITT, intent to treat.

Safety

- The majority of adverse events (AEs) were mild or moderate; no AEs led to treatment discontinuation or death (**Table 2**)
- One AE, mild erythema, was considered possibly related to study drug as assessed by the investigator
- Three patients experienced a total of 5 serious AEs during the study: anemia (2 events) cellulitis, diarrhea, and positive blood culture (1 event each)
  - None were considered related to study drug
- The most frequently reported AEs were pruritus, chills, and SCC (3 patients each)
  - All 3 reports of SCC occurred at sites that were not directly exposed to B-VEC or placebo and were deemed not related to study drug

Table 2. Safety summary

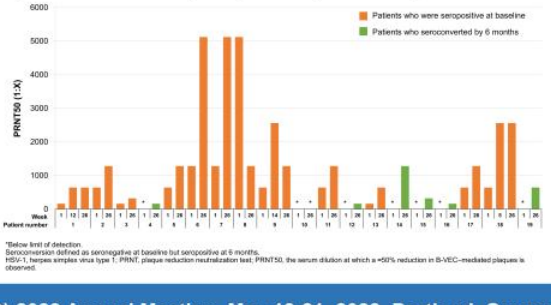
	Total patients (N=31)
Total number of AEs	45
Patients with ≥1 AE, n (%)	18 (58.1)
Mild AE	15 (48.4)
Moderate AE	3 (9.7)
Severe AE	2 (6.5)
Serious AE	3 (9.7)
Drug-related AE	1 (3.2)
AE leading to treatment discontinuation	0 (0)
Death	0 (0)
AEs reported in ≥5% of patients by System Organ Class and Preferred Term*, n (%)	
Skin and subcutaneous disorders	
Pruritus	3 (9.7)
Erythema	2 (6.5)
Rash	2 (6.5)
General disorders and site conditions	
Chills	3 (9.7)
Neoplasms benign, malignant, and unspecified	
Squamous cell carcinoma of the skin	3 (9.7)
Respiratory, thoracic, and mediastinal disorders	
Cough	2 (6.5)
Rhinorrhea	2 (6.5)

*AEs were coded using MedDRA version 24.1. At each level of summarization, a patient was counted once if the patient reported ≥1 event.
AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities.

Antibody Responses

- 22 of 31 patients (71.0%) provided a serum sample at baseline due to the difficulty of blood draws owing to skin fragility; 19 of the 22 patients (86.4%) also had matched serum samples at 6 months
- At baseline, 14 of the 22 patients (63.6%) were anti–HSV-1 antibody seropositive and 8 were seronegative, in agreement with seropositivity rates of the general US population[11]; 6 of 8 (75.0%) baseline seronegative patients seroconverted by 6 months
- For baseline seropositive patients, where quantitative differences at study completion could be calculated, antibody responses were variable (**Figure 4**), and none were determined to be meaningful, as defined by a >4-fold sustained increase in anti–HSV-1 antibody titer

Figure 4. Anti–HSV-1 antibodies in pre- and post-treatment patient serum samples

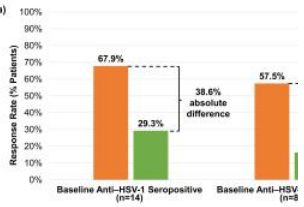


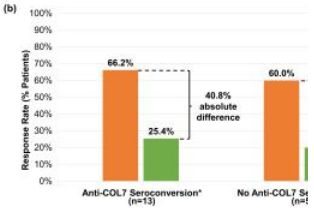
*Below limit of detection.
Seroconversion defined as seronegative at baseline but seropositive at 6 months.
HSV-1, herpes simplex virus type 1; PRNT, plaque reduction neutralization test; PRNT50, the serum dilution at which a ≈50% reduction in B-VEC–mediated plaques is observed.

Results (cont.)

- At baseline, 1 of 22 patients (4.5%) was positive for anti-COL7 antib
- 13 of 18 patients (72.2%) with matched serum samples seroconvert
  - no clinically significant immunologic reactions or differences in treat
  - were seen
- Post hoc analysis of response rates in primary wound pairs at 6 mo
  - equivalent efficacy regardless of baseline anti–HSV-1 antibody stat
- At 6 months, post hoc analysis of treatment response to B-VEC was
  - regardless of anti-COL7 seroconversion (**Figure 5b**)
    - A responder was defined as meeting the primary endpoint of com
    - at 6 months

Figure 5. B-VEC response rate at 6 months according to (a) anti–HSV-1 serostatus and (b) anti-COL7 seroconversion





*Seroconversion defined as seronegative at baseline but seropositive when tested at 6 months. Data
analysis using imputation.
B-VEC, beremagene geperpavec; COL7, type VII collagen; HSV-1, herpes simplex virus type 1.

Conclusions

- **B-VEC treatment demonstrated a durable and statis significant improvement in complete wound healing 6 months compared with placebo**
- **B-VEC was generally well tolerated, with no treatme discontinuations**
- **No clinically significant immunologic reactions wer during the study**
- **Treatment response to B-VEC was not associated v serostatus at baseline or with anti-COL7 seroconve**
- **An ongoing open-label extension study (NCT049178 investigating the long-term efficacy and safety of B patients with DEB, regardless of prior enrollment in**

References

1. Harari S. *Eur Respir Rev*. 2016;25(140):101-103.
2. Fine J-D. *JAMA Dermatol*. 2016;152(11):1231-1238.
3. Has C, et al. *Br J Dermatol*. 2020;182(3):574-592.
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11. Xu F, et al. *J Infect Dis*. 2002;185(8):1019-1024.

Acknowledgments

This study was funded by Krystal Biotech, Inc.

Disclosures

MPM: Krystal Biotech (investigator), Abeona Therapeutics (investigator), CastleCreek
Tissue Repair (investigator), WINGS Therapeutics (investigator). MEG: Dove/Unilever
Lehrman Group (consultant), Galderma USA (speaker), Krystal Biotech (investigator),
AbbVie (investigator), Primus Pharmaceuticals (speaker), Verrica Pharmaceuticals Inc
Pharmaceuticals Inc (investigator), National Eczema Association (consultant), Dermira
(investigator), Innovaderm Research Inc (investigator), Pierre Fabre Dermatologie (cor
Biotech (investigator), Innovaderm Research Inc (investigator), Arcutis Inc (investigato
(investigator), Pardion (investigator), Castle Biosciences (investigator). ISB: Krystal Bio
Creek Biosciences (investigator). SC: Krystal Biotech (consultant), Paratek Pharmace
BA, HC, TP, SK: Krystal Biotech (employees and stockholders).

Presented at the Society for Investigative Dermatology (SID) 2022 Annual Meeting, May 18-21, 2022, Portland, Oregon

Exhibit 99.2

GEM-3: Phase 3 Safety and Immunogenicity Results of Beremagene Geperpavec (B-VEC), an Investigational, Topical Gene Therapy for Dystrophic Epidermolysis Bullosa (DEB)

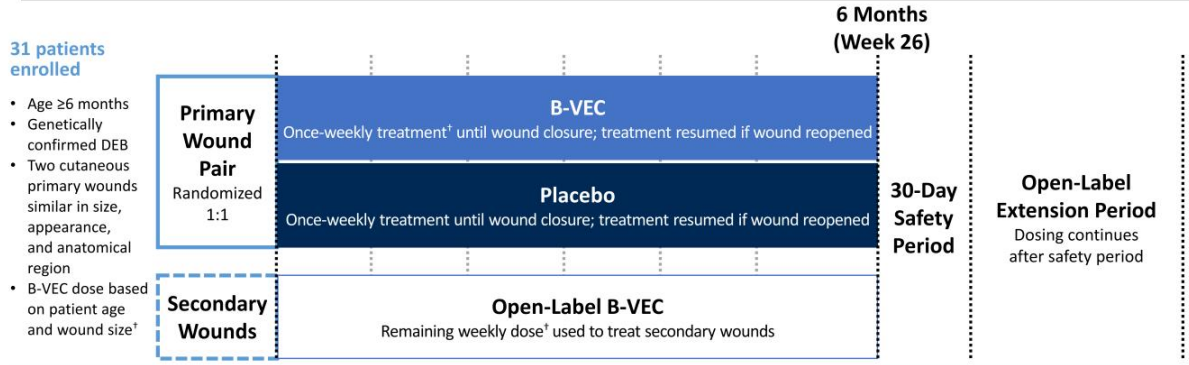
M. Peter Marinkovich,[1] Mercedes E. Gonzalez,[2] Shireen V. Guide,[3] I. Sinem Bagci,[1] Surya Chitra,[4] Brittani Agostini,[5] Hubert Chen,[5] Trevor Parry,[5] Suma Krishnan[5]

[1]Stanford University, Redwood City, CA, USA; [2]University of Miami, Miami, FL, USA; [3]Mission Dermatology Center, Children's Hospital of Orange County, University of California, Irvine, Department of Dermatology, Rancho Santa Margarita, CA, USA; [4]Savio Group Analytics & Statistics, Hockessin, DE, USA; [5]Krystal Biotech, Inc., Pittsburgh, PA, USA

Disclosures

- M. Peter Marinkovich reports the following disclosures:
  - Krystal Biotech (Investigator), Abeona Therapeutics (Investigator), CastleCreek (Investigator), Phoenix Tissue Repair (Investigator), WINGS Therapeutics (Investigator)
- This study was funded by Krystal Biotech, Inc.

GEM-3: Phase 3 Study Evaluating the Efficacy and Safety of B-VEC in Patients with DEB



Primary Efficacy Endpoint

- Complete wound healing* at Weeks 22 & 24 or Weeks 24 & 26 (6 months)

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

Secondary Efficacy Endpoints

- Complete wound healing* at Weeks 8 & 10 or Weeks 10 & 12 (3 months)
- Mean change in pain severity associated with wound dressing changes

Safety Endpoints

- Adverse events, vital signs, physical/skin examination, and laboratory evaluations
- Pre- and post-treatment anti-HSV-1 and anti-COL7 antibodies

NCT04491604; †Maximum weekly dose (PFU/week) was based on patient's age and unit dose (PFU/wound) was determined based on wound area at baseline.
B-VEC, beremagene geperpavec; COL7, type VII collagen; DEB, dystrophic epidermolysis bullosa; HSV-1, herpes simplex virus type 1; PFU, plaque-forming unit.

B-VEC was Generally Well Tolerated

- The majority of AEs were mild or moderate; no AEs led to treatment discontinuation or death
- One AE, mild erythema, was considered possibly related to study drug as assessed by the investigator
- The most frequently reported AEs were pruritus, chills, and squamous cell carcinoma (3 patients each)
  - All 3 reports of squamous cell carcinoma occurred at sites that were not directly exposed to B-VEC or placebo and were deemed not related to study drug

	Total patients (n=31)
Total number of AEs	45
Patients with ≥1 AE, n (%)	18 (58.1)
Mild AE	15 (48.4)
Moderate AE	3 (9.7)
Severe AE	2 (6.5)
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Death	0 (0)

AEs reported in ≥5% of patients by System Organ Class and Preferred Term*, n (%)	Total patients (n=31)
Skin and subcutaneous disorders	
Pruritus	3 (9.7)
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*AEs were coded using MedDRA version 24.1. At each level of summarization, a patient was counted once if the patient reported ≥1 event.
AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities.

Anti-HSV-1 and Anti-COL7 Antibody Results

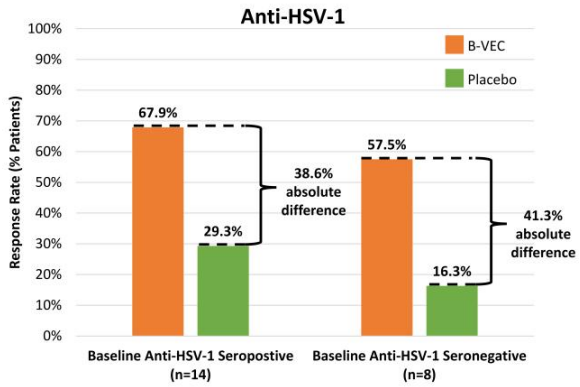
- 22 of 31 patients (71.0%) provided a serum sample at baseline due to the difficulty of blood draws owing to skin fragility
  - 19 of the 22 patients (86.4%) also had matched serum samples at 6 months

- At baseline, 14 of the 22 patients (63.6%) were anti-HSV-1 seropositive and 8 were seronegative, in agreement with seropositivity rates of the general US population[1]
  - 6 of 8 (75.0%) baseline seronegative patients seroconverted at 6 months
  - For baseline seropositive patients, where quantitative differences at study completion could be calculated, antibody responses were not determined to be meaningful

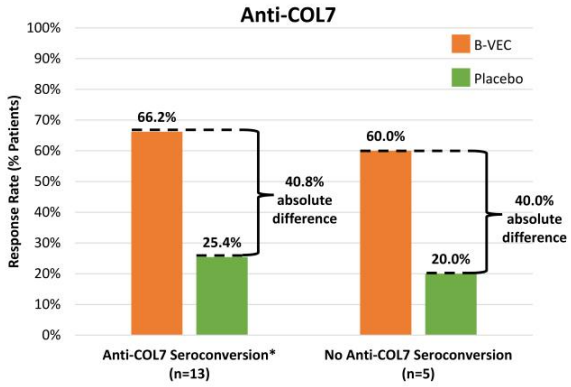
- At baseline, 1 of 22 patients (4.5%) was positive for anti-COL7 antibodies
  - 13 of 18 patients (72.2%) with matched serum samples seroconverted by 6 months; no clinically significant immunologic reactions or differences in treatment response were seen

1. Xu F, et al. *J Infect Dis*. 2002;185(8):1019-1024.
COL7; type VII collagen; HSV-1, herpes simplex virus type 1.

Treatment Response to B-VEC was Not Associated with Anti-HSV-1 Serostatus at Baseline or with Anti-COL7 Seroconversion



- Response rates in primary wound pairs at 6 months suggested equivalent efficacy regardless of baseline anti–HSV-1 antibody status



- At 6 months, treatment response to B-VEC was consistent regardless of anti-COL7 seroconversion

Data in figures based on post hoc analyses using imputation; a responder was defined as meeting the primary endpoint of complete wound healing at 6 months.
*Seroconversion defined as seronegative at baseline but seropositive when tested at 6 months.
B-VEC, beremagene geperpavec; COL7, type VII collagen; HSV-1, herpes simplex virus type 1.

Conclusions

- B-VEC treatment demonstrated a durable and statistically significant improvement in complete wound healing at 3 and 6 months compared with placebo
- B-VEC was generally well tolerated, with no treatment-related discontinuations
- No clinically significant immunologic reactions were reported during the study
- Treatment response to B-VEC was not associated with anti-HSV-1 serostatus at baseline or with anti-COL7 seroconversion
- An ongoing open-label extension study is investigating the long-term efficacy and safety of B-VEC in patients with DEB, regardless of prior enrollment in GEM-3

Open-label extension study: NCT04917874
B-VEC, beremagene geperpavec; COL7, type VII collagen; DEB, dystrophic epidermolysis bullosa; HSV-1, herpes simplex virus type 1.