Clinical Trial Information			
Trial Title	Ph 3 Efficacy and Safety of B-VEC for the Treatment of DEB (GEM-3)		
Drug(s)/Molecule(s)	beremagene geperpavec;	**Trial Identifier**	GDCT0333263
Secondary ID(s)	GDC20021644; GDCT0363915;GDC30021486;NCT04491604;B-VEC-03		
Sponsor (s)	Krystal Biotech Inc	**Indication**	Epidermolysis Bullosa
Trial Status	Completed	**Trial Phase**	Phase III

Clinical Trial Details	
Trial Title	Ph 3 Efficacy and Safety of B-VEC for the Treatment of DEB (GEM-3)
Official Title	A Phase III Efficacy and Safety Study of Beremagene Geperpavec (B-VEC, Previously "KB103") for the Treatment of Dystrophic Epidermolysis Bullosa (DEB)
Acronym	GEM-3
Study Type	Interventional
Therapy Type	Monotherapy
Actual Start Date	17 Aug 2020
Actual End Date	29 Oct 2021
Trial Duration (in Months)	14.60
Study Designs	
Decentralized/Virtual Trials	Yes
Decentralized/Virtual Component	Telemedicine
Purpose	The purpose of the study was to determine whether administration of topical B-VEC improves wound healing as compared to placebo, and to evaluate durability, repeat dosing (Primary Endpoint) and further obtain safety and tolerability data.

Primary Outcome Measure(s)/Objective(s)	• Primary Wound With Complete Wound Healing (100% Wound Closure) on Weeks 22 and 24 or Weeks 24 and 26 - 26 weeks post-baseline
	• The primary wound was defined as a responder wound that met either of the following conditions:
	  ○ Complete wound healing on Week 22 and Week 24, or
	  ○ Complete wound healing on Week 24 and Week 26

<table>
<tr><td></td><td>

For subjects with missing primary wound healing data, a multiple imputation approach (10 repliates) was used. The total numbers of primary wounds with complete healing for B-VEC and Placebo presented below were the average of those from the multiple imputation replicates, and therefore, they would not be whole numbers (integers)

</td></tr>
<tr><td>Secondary Outcome Measure(s)/Objective(s)</td><td>

Primary Wound With Complete Wound Healing (100% Wound Closure) on Weeks 8 and 10 or Weeks 10 and 12 - 12 weeks post-baseline
The primary wound was defined as a responder wound that met either of the following conditions:

Complete wound healing on Week 8 and Week 10, or
Complete wound healing on Week 10 and Week 12
For subjects with missing primary wound healing data, a multiple imputation approach (10 repliates) was used. The total numbers of primary wounds with complete healing for B-VEC and Placebo presented below were the average of those from the multiple imputation replicates, and therefore, they would not be whole numbers (integers)

Primary Wound Pain Severity (Visual Analog Scale (VAS)) Change for Ages 6 and Above Subjects at Weeks 22, 24, and 26. - 26 weeks post-baseline

Changes from baseline at Weeks 22, 24, and 26 in primary wound pain severity (visual analog scale (VAS)) for ages 6 and above subjects. The Visual Analog Scale scores from 0 (no pain) to 10 (the worst possible pain). Negative values in changes from baseline mean improvement in pain severity

</td></tr>
<tr><td>Trial Description</td><td>This was an interventional, phase III, randomized, parallel assignment, quadruple, double-blind, intra subject, pivotal, placebo-controlled, treatment and multi-centered study under paediatric investigation plan for beremagene geperpavec (EMEA-002472-PIP03-22) to determine whether administration of topical B-VEC improves wound healing as compared to placebo, and to evaluate durability, repeat dosing (Primary Endpoint) and further obtain safety and tolerability data. Subjects were randomized into two arms (1:1):
<table>
<tr><th>Arm</th><th>Type</th><th>Intervention</th><th>Description</th></tr>
<tr><td>I</td><td>Placebo</td><td>placebo</td><td>Subjects received matching placebo masked inactive topical gel</td></tr>
<tr><td>II</td><td>Active comparator</td><td>B-VEC</td><td>Subjects received B-VEC-03 topical gel of non-integrating, replication-incompetent HSV-1 expressing the human collagen VII protein</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><td></td><td>Investigator identified wound pairs, up to three in each subject, will be treated once weekly for six months with either B-VEC or placebo. The dose administered to each wound is dependent on the size of the wound and ranges from $4x10^8$ to $1.2x10^9$ PFU per wound. The maximum weekly dose, administered once weekly per subject, is defined by subject age as outlined in the table below. In each subject, a primary wound pair was identified by the investigator; one wound was randomized to receive a weekly topical application of B-VEC and the other a placebo. Primary wound pairs selected in the study included all three wound area segments of <20 cm2, 20-40 cm^2 and 40-60 cm^2 and were assigned the corresponding doses of 4×10^8 PFU/wound, 8×10^8 PFU/wound or 1.2×10^9 PFU/wound, respectively. Weekly application was continued until the investigator determined the wound was completely closed. Re-application occurred at any point throughout the study if the investigator determined the wound was not completely closed. Maximum Weekly Dose Per Subject:

<table>
<tr><th>Age</th><th>Maximum Weekly Dose</th></tr>
<tr><td>≥ 6 months to < 3 years</td><td>$1.6x10^9$ PFU/week</td></tr>
<tr><td>≥ 3 years to < 6 years</td><td>$2.4x10^9$ PFU/week</td></tr>
<tr><td>≥ 6 years</td><td>$3.2x10^9$ PFU/week</td></tr>
</table>
Subjects returned to the clinical site 30 days following the last dosing visit (Week 26) for safety evaluation by the investigator and subsequently had the option to roll into the Open Label Extension (OLE) Study A total of 31 subjects were enrolled in this study.</td></tr>
<tr><td>Trial Notes</td><td>As per the annual report (FORM 10-K) December 2022, study expected to provide an update on the OLE study in 2023. https://www.sec.gov/ix?doc=/Archives/edgar/data/1711279/000171127923000008/krys-20221231.htm (Page No: 07) As of March 2022, study detailed safety results expected at SID (May 08-12) in second quarter of 2022. https://ir.krystalbio.com/static-files/fbe09d1a-d428-4c7e-9ef6-32881968cdc1 (Slide No: 26) As per Fourth Quarter and Full Year 2021 Financial Results, company intends to present more detailed results at upcoming medical congresses.
https://ir.krystalbio.com/node/8446/pdf As per the corporate presentation January 2022, presents more detailed GEM-3 results at medical congress in first half of 2022.
https://ir.krystalbio.com/static-files/5ebb3a7c-4328-4fe3-923f-0c2b511943ed (Slide No: 04) As per third quarter 2021 financial results, top-line results expected in fourth quarter of 2021. https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-reports-third-quarter-2021-financial-results-and As of October 26, 2021, top-line results from the study expected in this quarter of 2021. https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-completion-gem-3-pivotal-phase-3-study As per the corporate presentation October 2021, the study top-line data expected in fourth quarter of 2021.</td></tr>
</table>

	https://ir.krystalbio.com/static-files/3fe442fb-c1cc-43b7-b338-6942a91d881a (Slide No: 29) As per the corporate presentation September 2021, the study top-line data expected in fourth quarter of 2021. https://ir.krystalbio.com/static-files/42934f6f-f225-4bdc-bb03-55dcae00be00 (Slide No: 04) As per the corporate presentation August 2021, the study top-line data expected in fourth quarter of 2021. https://ir.krystalbio.com/static-files/b83cbb82-85f2-428c-9626-bf1ae22985e2 (Slide No: 04) As per the corporate presentation July 2021, the study top-line data expected in fourth quarter of 2021. https://ir.krystalbio.com/static-files/9b7df989-970a-46bf-ab53-ac28ab492c81 (Slide No: 04) As per the corporate presentation June 2021, the study top-line data expected in fourth quarter of 2021. https://ir.krystalbio.com/static-files/d993ec43-6efa-4955-a7c1-282899bfed20 (Slide No: 04) As of April 2021, study remains double blinded until database lock occurs in the fourth quarter of 2021. https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-provides-update-pivotal-gem-3-study-b-vec-deb As per the corporate presentation April 2021, study top-line data expected in fourth quarter of 2021. https://ir.krystalbio.com/index.php/static-files/26fb3e78-e938-4a15-a7bf-ae1d27178e97 (Slide No: 04) As per the corporate presentation March 2021, enrollment completion is expected in first quarter of 2021 and top-line data expected in fourth quarter of 2021. https://ir.krystalbio.com/index.php/static-files/6345b187-aaef-4f32-9b02-0b755c2424e3 (Slide No: 04, 8) As per the corporate presentation January 2021, enrollment completion is expected in first quarter of 2021 and top-line data expected in second half of 2021. https://ir.krystalbio.com/index.php/static-files/34687a98-89a9-4188-8f3c-72e8bd90bd98 (Slide No: 04) As per the annual report FORM 10-K December 2020, enrollment completion is expected in first quarter of 2021 and top-line data expected in fourth quarter of 2021. https://www.sec.gov/ix?doc=/Archives/edgar/data/1711279/000171127921000006/krys-20201231.htm (Page no: 7) As per the corporate presentation November 2020, study pivotal data expected in 2021. https://ir.krystalbio.com/index.php/static-files/34687a98-89a9-4188-8f3c-72e8bd90bd98 (Slide No: 07) As per third quarter 2020 financial results, enrollment completion is expected in early 2021 and Top-line data expected in 2021. https://www.businesswire.com/news/home/20201109005202/en/Krystal-Biotech-Reports-Third-Quarter-2020-Financial-Results-and-Provides-Update-on-Operational-Progress/? As of October 2020, Anticipate completing enrollment early next year. https://ir.krystalbio.com/node/7681/pdf As per the corporate presentation September 2020, study pivotal data expected in 2021. http://ir.krystalbio.com/index.php/static-files/7fed8190-febd-4321-bf91-7917cec96a7b (Slide No: 07) As per corporate facesheet Q3 2020, study top-line

	pivotal data expected in 2021. http://ir.krystalbio.com/index.php/static-files/b32f0709-1eb0-42ec-a825-64efad8a6cd8 (Slide No: 02) As per Corporate Presentation Q3 2020, study top-line pivotal data expected in 2021. http://ir.krystalbio.com/index.php/static-files/01a9092f-d193-468b-87e4-7e95bc095472 (Slide No: 3, 5) As per Corporate Presentation Q2 2020, study initiation expected in first half of 2020. http://ir.krystalbio.com/index.php/static-files/a3b0f424-0974-4306-aab6-afe8d5ba33fd (Slide No: 3,6) As per the first quarter report (FORM 10-Q) March 2020, study initiation expected in first half of 2020. http://ir.krystalbio.com/static-files/35d3e5c1-e09a-44cc-9f59-759272ade377 (Page no: 19, 20) As per the annual report (FORM 10-K) December 2019, study initiation expected in first half of 2020. http://ir.krystalbio.com/static-files/d20ad332-c660-45db-8537-03d85cdacfee (Page No: 05, 51) As per the company presentation at the 40th Cowen and Company Annual Health Care Conference, study initiation expected in first half of 2020. http://wsw.com/webcast/cowen57/krys/?lobby=true&day=2 (Slide 03) As per the second quarter (FORM 10-Q) 2019 report, the study initiation expected in fourth quarter of 2019. http://ir.krystalbio.com/static-files/01e8082a-c5f2-4e38-b43e-c29cdf2094ac (Page No: 17) As of June 2019, study initiation expected before the end of 2019. http://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-positive-results-phase-2-clinical As per the first quarter report (Form 10-Q), the study initiation expected in second half of 2019. http://ir.krystalbio.com/static-files/2e804dac-b448-4850-a78d-aa7ffdd58f23 (Page No:17) As per the company presentation at the 39th Cowen and Company Annual Health Care Conference, study initiation expected in second half of 2019. http://wsw.com/webcast/cowen52/krys/ (Slides 4, 8, 14) As per the Annual Report (Form 10-K) 2018, the study initiation expected in second half of 2019. http://ir.krystalbio.com/static-files/18fa519e-1788-4e30-8598-51ca2d382786 (Page No: 02, 48) As per the corporate presentation Q1 2019, the study initiation expected in second half of 2019. https://krystalbio.gcs-web.com/static-files/b96b7e0c-7692-4a95-b75c-c8ae0b08d487 (Slide No: 14) As per the Cantor Fitzgerald's 4th Annual Healthcare Conference, study initiation expected in second half of 2019. http://wsw.com/webcast/cantor7/krys/?lobby=true&day=1 (Slides 16) As per the Rodman & Renshaw 20th Annual Global Investment Conference, study expected to initiate in second half of 2019. http://wsw.com/webcast/rrshq28/krys/?lobby=true&day=2 (Slides 8, 16)

Sponsor(s)/Collaborator(s)	
Sponsor(s) - Type & Details	
Sponsor	Krystal Biotech Inc

Drug Details

Primary Interventions(s)	**Generic Name** / **Route of Administration** beremagene geperpavec-svdt / Topical
Drug Name	beremagene geperpavec (Marketed Drug)
Drug Description	Beremagene geperpavec (Vyjuvek) is a vector based gene therapy. It is formulated as gel for topical application. Vyjuvek is indicated for the treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene. Beremagene geperpavec is under development for the treatment of dystrophic epidermolysis bullosa (DEB). The drug candidate is a replication-defective, non-integrating viral vector engineered using STAR-D (skin TARgeted delivery) platform to deliver functional human COL7A1 genes. It is administered through a topical route formulated as gel. The STAR-D platform consists of an engineered viral vector based on herpes simplex virus 1.
Mechanism of Action	Bercolagene telserpavec uses a modified HSV-1 vector designed to deliver COL7A1 genes. COL7A1 is responsible for the formation of protein type VII collagen, or COL7, that forms anchoring fibrils that bind the dermis, or inner layer of the skin, to the epidermis for maintaining the integrity of the skin. Upon direct delivery to the skin, KB-103 can efficiently transduce both keratinocytes and fibroblasts. The drug is transported down microtubules to the nucleus, and the viral genome is deposited into the nucleus. Then, it recruits the host cellular machinery to initiate transcription of COL7A1 which allow the production of a precursor protein, procollagen 7.
ATC Classification	D03AX Other cicatrizants
Target	Collagen Alpha 1(VII) Chain (Long Chain Collagen or COL7A1)
Drug Name	beremagene geperpavec (Pipeline Drug)
Mechanism of Action	Bercolagene telserpavec uses a modified HSV-1 vector designed to deliver COL7A1 genes. COL7A1 is responsible for the formation of protein type VII collagen, or COL7, that forms anchoring fibrils that bind the dermis, or inner layer of the skin, to the epidermis for maintaining the integrity of the skin. Upon direct delivery to the skin, KB-103 can efficiently transduce both keratinocytes and fibroblasts. The drug is transported down microtubules to the nucleus, and the viral genome is deposited into the nucleus. Then, it recruits the host cellular machinery to initiate transcription of COL7A1 which allow the production of a precursor protein, procollagen 7.
ATC Classification	D11AX Other dermatologicals
Target	Collagen Alpha 1(VII) Chain (Long Chain Collagen or COL7A1)

Patient Details

Age	**Minimum Age Eligibility**: 6 Months **Maximum Age Eligibility**:
Gender	Both
Healthy Subject(s)	No
Subject(s) Type	Adolescents, Adults, Children, Cutaneous Disease, Elders, Infants, Pediatric, Recessive Dystrophic
Participant Criteria (Inclusion)	• The subject or legally appointed and authorized representative must have read, understood and signed an Institutional Review Board/Ethics Committee (IRB/EC) approved Informed Consent or Assent Form and must be able to and willing to follow study procedures and instructions • Age ≥ 6 months and older at the time of Informed Consent • Clinical diagnosis of the Dystrophic Epidermolysis Bullosa • Confirmation of DEB diagnosis (either DDEB or RDEB) by genetic testing including COL7A1 • Two (2) cutaneous primary wounds meeting the following criteria • Location: similar in size, located in similar anatomical regions, and have similar appearance • Appearance: clean with adequate granulation tissue, excellent vascularization, and do not appear infected • Subjects and caregivers who, in the opinion of the Investigator, are able to understand the study, co-operate with the study procedures and are willing to return to the clinic for all the required follow-up visits • Male or Female of childbearing potential must use a reliable birth control method throughout the duration of the study and for three (3) months post last dose of B-VEC • Negative pregnancy test at Visit 1 (Week 1), if applicable
Participant Criteria (Exclusion)	• Medical instability limiting ability to travel to the Investigative Center • Diseases or conditions that could interfere with the assessment of safety and efficacy of the study treatment and compliance of the subject with study visits/procedures, as determined by the Investigator • Current evidence or a history of squamous cell carcinoma in the area that will undergo treatment • Subject's actively receiving chemotherapy or immunotherapy at Visit 1 (Week 1) • Active drug or alcohol addiction as determined by the Investigator • Hypersensitivity to local anesthesia (lidocaine/prilocaine cream)

	• Participation in an interventional clinical trial within the past three (3) months (not including BVEC administration) • Receipt of a skin graft in the past three (3) months • Pregnant or nursing women

Ethnicity	
Hispanic/Latino	16
Not Hispanic/Latino	15

Race	
American Indian/Alaska Native	5
Asian	6
White	20

Biomarker Details

Biomarker Name	Biomarker Identifier	Biomarker Official Symbol	Biomarker Role
Anti Collagen Type VII Antibody	GDBM0022491		Monitoring Treatment Response
Anti Collagen Type VII Immunoglobulin G Antibody	GDBM0060655		Monitoring Treatment Response
Anti Human Herpesvirus 1 Antibody	GDBM0020190		Monitoring Treatment Response
Collagen Type VII Alpha 1 Chain	GDBM0005900	COL7A1	Inclusion criteria

Trial Results	
No. of Subjects Planned	30
No. of Subjects Enrolled	31
No. of Subjects Analyzed	31
Endpoint	Efficacy, Safety

<table>
<tr><td>Classification</td><td></td></tr>
<tr><td>End Point Status</td><td>Achieved</td></tr>
<tr><td>Efficacy Results</td><td>

February 17, 2023

Ph 3 Efficacy and Safety of B-VEC for the Treatment of DEB (GEM-3) Based on the results published, Globaldata inferred that 31 subjects were analyzed in the study.Primary Wound With Complete Wound Healing (100% Wound Closure) on Weeks 22 and 24 or Weeks 24 and 26

<table>
<tr><th>Arm/Group Title</th><th>B-VEC</th><th>Placebo</th></tr>
<tr><td>Overall Number of Participants Analyzed</td><td>31</td><td>31</td></tr>
<tr><td>Overall Number of Units Analyzed</td><td rowspan="2">31</td><td rowspan="2">31</td></tr>
<tr><td>Type of Units Analyzed: Wounds</td></tr>
<tr><td>Measure Type:Number</td><td rowspan="2"></td><td rowspan="2"></td></tr>
<tr><td>Unit of Measure: number of wounds with complete healing</td></tr>
<tr><td></td><td>20.9</td><td>6.7</td></tr>
</table>

https://clinicaltrials.gov/ct2/show/results/NCT04491604?view=results

December 15, 2022

Trial of Beremagene Geperpavec (B-VEC) for Dystrophic Epidermolysis Bullosa Shireen V. Guide et al The New England Journal of Medicine, Volume:387, Page:2211-2219, 2022 Based on the results reported, GlobalData inferred that 31 subjects were enrolled in this study. At 6 months, complete wound healing occurred in 67% of the wounds exposed to B-VEC as compared with 22% of those exposed to placebo (P=0.002). Complete wound healing at 3 months occurred in 71% of the wounds exposed to B-VEC as compared with 20% of those exposed to placebo (P<0.001). The mean change from baseline to week 22 in pain severity during wound-dressing changes was −0.88 with B-VEC and −0.71 with placebo and similar mean changes were observed at weeks 24 and 26. https://www.nejm.org/doi/full/10.1056/NEJMoa2206663

May 20, 2022

Presented at the 21st Hybrid European Society for Pediatric Dermatology (ESPD 2022) Annual Meeting, May 20 - 22, 2022, Munich, Germany EM-3: Phase 3 study of beremagene geperpavec, aninvestigational, topical gene therapy, for the treatment of dystrophicEpidermolysis Bullosa
Session: ORAL PRESENTATIONS
Abstract No.: O013 Hubert Chen et al.Based on the results presented, GlobalData inferred that 31 subjects were enrolled in this study. At month 6, beremagene geperpavec resulted in 67.4% wound closure as compared to21.6% for placebo

</td></tr>
</table>

	(absolute difference (95% confidence interval): 45.8% (23.6%–68.0%);P< 0.005). At month 3, 70.6% beremagene geperpavec-treated wounds closed versus 19.7% placebo-treated wounds (absolute difference (95% confidence interval):51.0% (29.3%-72.6%);P< 0.005). Of wounds closed at month3, 66.7% of beremagene geperpavec-treated wounds were also closed at month 6, as compared to 33.3% for placebo (P is 0.02).https://onlinelibrary.wiley.com/doi/epdf/10.1111/pde.14998 **May 18, 2022** Presented at the 80th Hybrid Annual Meeting of the Society for Investigative Dermatology (SID 2022), May 18 - 21, 2022, Portland, Oregon, USA GEM-3: Phase 3 Safety and Immunogenicity Results of Beremagene Geperpavec (B-VEC), an Investigational, Topical Gene Therapy for Dystrophic Epidermolysis Bullosa (DEB) Session: Clinical Research - Sociobehavioral and Health Services Research Abstract No.: 465 Marinkovich M et al.Based on the results presented, GlobalData inferred that a total of 31 subjects were analyzed in the study. At M6, B-VEC resulted in 67.4% wound closure compared to 21.6% for placebo (absolute difference (95% CI): 45.8% (23.6%-68.0%); p<0.005). Due to the difficulty of blood draws for DEB subjects owing to skin fragility, 22/31 subjects (71.0%) were able to provide a serum sample at baseline, and matched serum samples were obtained at M6 for 19 of these subjects. 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). In the subject 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 resulted in 70.6% wound closure compared to 19.7% for placebo (absolute difference (95% CI): 51.0% (29.3%-72.6%); p<0.005) at 3 months. 19 of the 22 subjects (86.4%) also had matched serum samples at 6 months. At baseline, 14 of the 22 subjects (63.6%) were anti-HSV-1 seropositive and 8 were seronegative, in agreement with seropositivity rates of the general US population. 6 of 8 (75.0%) baseline seronegative subjects seroconverted at 6 months. For baseline seropositive subjects, where quantitative differences at study completion could be calculated, antibody responses were not determined to be meaningful. At baseline, 1 of 22 subjects (4.5%) was positive for anti-COL7 antibodies, 13 of 18 subjects (72.2%) with matched serum samples seroconverted by 6 months; no clinically significant immunologic reactions or differences in treatment response were seen. 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.

B-VEC treatment demonstrated a durable and statistically significant improvement in complete wound healing at 3 and 6 months compared with placebo. 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.
https://ir.krystalbio.com/static-files/52bf3182-9694-43c1-9e6b-0af5d4952a91
https://ir.krystalbio.com/static-files/0523aa7c-11e5-444e-9f90-9603bb67f02chttps://www.sidannualmeeting.org/wp-content/uploads/2022/05/SID_Abstracts-Booklet_r6.pdf

March 28, 2022

Krystal Biotech Inc.,Based on the results presented, GlobalData inferred that a total of 31 subjects were randomized in the study. The proportion of primary wounds with complete wound healing was significantly greater with B-VEC than placebo at both 3- and 6-month timepoints (p <0.005). In the subjects with DDEB, primary endpoint of complete wound healing at 6 months was achieved by the B-VEC treated wound, but not by the placebo treated wound. At 6 months, 15 of 17 discordant pairs showed response to B-VEC but not placebo.

Parameter	B-VEC	Placebo	95%CI
Primary end point (6 months)	67.4%	21.6%	23.6-68.0
Secondary end points (3 months)	70.3%	20.0%	28.7-72

49.7% of B-VEC treated wounds compared to 7.1% of placebo treated wounds demonstrated durability of response, defined as wounds that met complete wound healing at both 3 months (key secondary endpoint) and 6 months (primary endpoint). Nearly half of all B-VEC treated wounds demonstrated complete wound healing for three consecutive visits. Of the total B-VEC wounds closed at 3 months, 66.7% (14/21) of B-VEC-treated wounds were also closed at 6 months, as compared to 33.3% (2/6) for placebo treated wounds (p=0.02).

Parameter	B-VEC	Placebo	95%CI
Durability of response†	15.4 (49.7)	2.2(7.1)	42.6 (22.6, 62.6)
Complete wound healing			
Weeks 8, 10, and 12	14.8 (47.7)	5.1 (16.5)	31.3 (10.6, 51.9)
Weeks 22, 24, and 26	13.4 (43.2)	2.0 (6.5)	36.8 (19.8, 53.7)

Treatment response was in favor of B-VEC for all gender, age, and wound area/size subgroups, however the individual subgroups were not powered to demonstrate statistical significance. **Complete Wound Healing at 6 Months by**

Baseline Primary Wound Area/Size Category

Baseline primary wound area/size category	B-VEC n	Complete wound healing at 6 months, n (%)	Placebo	Complete wound healing at 6 months, n (%)
<20 cm	23	14 (60.9)	22	5(22.7)
20 - <40	6	4 (66.7)	8	1(12.5)
40 - 60	2	1(50.0)	1	0

PRO measures (EQ-5D-5L and Skindex-29) assessed before and after treatment with B-VEC demonstrated improvement across multiple domains directionally, consistent with a wound healing response.

Change from baseline in pain following B-VEC treatment	Observation
Week 22	-0.61
Week 24	-0.88
Week 26	-0.56

https://ir.krystalbio.com/static-files/fbe09d1a-d428-4c7e-9ef6-32881968cdc1

November 29, 2021

Krystal Biotech Announces Positive Topline Results from GEM-3 Pivotal Trial of VYJUVEK in Patients with Dystrophic Epidermolysis BullosaBased on the top-line results announced in the press release, GlobalData inferred that 31 subjects were analyzed. VYJUVEK achieved the primary endpoint of investigator assessed complete wound healing 67% of wounds treated at the six-month timepoints as compared to 22% of wounds treated with placebo (absolute difference (95% CI): 45.8% (23.6%-68.0%); p<0.005) VYJUVEK achieved the secondary endpoint of investigator assessed complete wound healing in 71% of subjects compared to 20% of wounds treated with placebo (absolute difference (95% CI): 51.0% (29.3%-72.6%); p<0.005) In an ad-hoc analysis, study 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). The immunogenicity profile of VYJUVEK (as measured by anti-HSV-1 and anti-COL7 antibodies) was consistent with the previous study.https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-positive-topline-results-gem-3-pivotal

Based on the results reported, Geperpavec had complete wound healing, overall efficacy was preserved in subjects with dystrophic epidermolysis bullosa.

Safety Result	**February 17, 2023**

Ph 3 Efficacy and Safety of B-VEC for the Treatment of DEB (GEM-3) Based on the results published, Globaldata inferred that 31 subjects were analyzed in the study.Serious Adverse Events

Frequency Threshold for Reporting Other Adverse Events	**5%**	
	All Participants ("Topical Beremagene Geperpavec (B-VEC)", and "Placebo")	
	Affected / at Risk (%)	**# Events**
Total	17/31(54.84%)	
General disorders		
Chills	3/31(9.68%)	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Squamous cell carcinoma	3/31(9.68%)	4

https://clinicaltrials.gov/ct2/show/results/NCT04491604?view=results

December 15, 2022

Trial of Beremagene Geperpavec (B-VEC) for Dystrophic Epidermolysis Bullosa Shireen V. Guide et al The New England Journal of Medicine, Volume:387, Page:2211-2219, 2022 Based on the results reported, GlobalData inferred that adverse events observed with B-VEC and placebo included pruritus and chills.https://www.nejm.org/doi/full/10.1056/NEJMoa2206663

May 20, 2022

Presented at the 21st Hybrid European Society for Pediatric Dermatology (ESPD 2022) Annual Meeting, May 20 - 22, 2022, Munich, Germany EM-3: Phase 3 study of beremagene geperpavec, aninvestigational, topical gene therapy, for the treatment of dystrophicEpidermolysis Bullosa
Session: ORAL PRESENTATIONS
Abstract No.: O013 Hubert Chen et al.Based on the results presented, GlobalData inferred that 31 subjects were enrolled in this study. The B-VEC was well-tolerated with no drug-related serious adverse events or discontinuations due to treatment.https://onlinelibrary.wiley.com/doi/epdf/10.1111/pde.14998

May 18, 2022

Presented at the 80th Hybrid Annual Meeting of the Society for Investigative Dermatology (SID 2022), May 18 - 21, 2022, Portland, Oregon, USA GEM-3: Phase 3 Safety and Immunogenicity Results of Beremagene Geperpavec (B-VEC), an Investigational, Topical Gene Therapy for Dystrophic Epidermolysis Bullosa (DEB)
Session: Clinical Research - Sociobehavioral and Health Services Research
Abstract No.: 465 Marinkovich M et al.Based on the results presented, GlobalData inferred that fourteen of 22 (63.6%) tested subjects had anti-HSV-1 antibodies at baseline; 6 subjects seroconverted by M6. 1/22 (4.5%) subjects were positive for anti-COL7 antibodies at baseline; 13 subjects seroconverted by M6. B-VEC was well-tolerated with no drug-related serious AEs or discontinuations due to treatment.

The majority of AEs were mild or moderate. 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 subjects 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. **Findings:**

Safety summary	**Total subjects (N=31)**
Total number of AEs	45
Subjects with 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 subjects 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)

	<table><tr><td colspan="2">Respiratory, thoracic, and mediastinal disorders</td></tr><tr><td>Cough</td><td>2 (6.5)</td></tr><tr><td>Rhinorrhea</td><td>2 (6.5)</td></tr></table> https://ir.krystalbio.com/static-files/52bf3182-9694-43c1-9e6b-0af5d4952a91 https://ir.krystalbio.com/static-files/0523aa7c-11e5-444e-9f90-9603bb67f02c https://www.sidannualmeeting.org/wp-content/uploads/2022/05/SID_Abstracts-Booklet_r6.pdf **March 28, 2022** Krystal Biotech Inc.,Based on the results presented, GlobalData inferred that B-VEC was generally well tolerated in subjects. The majority of AEs were mild; there were no AEs leading to treatment discontinuation or death, one AE, mild erythema, was considered possibly related to study drug as assessed by the investigator. Three subjects experienced a total of 5 SAEs during the study: cellulitis, anemia (2 events), diarrhea and positive blood culture. None were considered related to study drug, no clinically significant immunologic reactions were reported during the study. <table><tr><th>Event</th><th>Total subjects (n=31)</th></tr><tr><td>Total number of adverse events (AEs)</td><td>45</td></tr><tr><td>Patients with ≥ 1 AE, n (%)</td><td>18(58.1)</td></tr><tr><td>Serious AEs</td><td>3(9.7)</td></tr><tr><td>Severe AEs</td><td>2(6.5)</td></tr><tr><td>Drug-related AEs</td><td>1(3.2)</td></tr><tr><td>AE leading to treatment discontinuation</td><td>0</td></tr><tr><td>Death</td><td>0</td></tr></table> https://ir.krystalbio.com/static-files/fbe09d1a-d428-4c7e-9ef6-32881968cdc1 **November 29, 2021** Krystal Biotech Announces Positive Topline Results from GEM-3 Pivotal Trial of VYJUVEK in Patients with Dystrophic Epidermolysis BullosaBased on the top-line results announced in the press release, GlobalData inferred that VYJUVEK was well tolerated. Drug-related serious adverse events or discontinuations due to treatment were not reported. One mild drug-related adverse event was reported. https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-positive-topline-results-gem-3-pivotal
Pharmacokinetic Evaluation	

Statistical Method (if any)	**February 17, 2023** Ph 3 Efficacy and Safety of B-VEC for the Treatment of DEB (GEM-3) Based on the results published, Globaldata inferred that 31 subjects were analyzed in the study.McNemar method was used in this study.https://clinicaltrials.gov/ct2/show/results/NCT04491604?view=results
Conclusion	The trial was completed. Based on the results reported, GlobalData concluded that Geperpavec has complete wound healing and is well tolerated in subjects with Dystrophic Epidermolysis Bullosa.

Enrollment Data	
Trial Start Date (Actual):	17 Aug 2020
No. of Subjects Planned:	30
Trial Enrollment Completion Date (Actual):	30 Mar 2021
No. of Subjects Enrolled:	31
Enrollment Period (in Months) (Actual):	7.50
Enrollment Efficiency (%):	31
Trial End Date (Actual):	29 Oct 2021
No. of Sites:	4
Treatment Period (in Months)	7.10

(Actual):	
Trial Duration (in Months) (Actual):	14.60

Enrollment Rate Parameters:	
Subjects/Site:	7.75
Subjects/Month:	4.13
Subjects/Site/Month:	1.03

Trial Cost Overview	
Trial Cost Parameters	**Cost ($ Millions)**
Trial Cost	11.78
Trial Cost/Month	0.81
Trial Cost/Site	2.94
Trial Cost/Subject	0.38

Trial Cost By Year	
Year	**Trial Cost ($ Millions)**
2020	3.57
2021	7.84

Trial Cost By Components	
Cost Components	**Cost ($ Millions)**
Admin Costs	1.18
Central Lab	1.41
Subject Costs	1.30
Personnel Costs	3.06
Site Costs	4.83

Investigators Information			
Name	Amy S Paller	Role	Contact Person; Principal Investigator
Specialty	Dermatology; Pediatric	Board Certification	

	dermatology; Pediatric Medicine		
Primary Designation	Professor	Associated Organization	Northwestern University
Contact Number	1-312-2276060; 1-312-6953721; 1-800-5437362	Email	apaller@northwestern.edu
State	Illinois	Country	United States

Similar studies done by Investigator

Investigators Information			
Name	Matt P Marinkovich	Role	Principal Investigator
Specialty	Dermatology; Internal Medicine	Board Certification	
Primary Designation	Associate Professor	Associated Organization	Stanford University School of Medicine
Contact Number	1-650-7234000; 1-650-4985425; 1-650-7236028	Email	mpm@stanford.edu
State	California	Country	United States

Similar studies done by Investigator

Investigators Information			
Name	Kunju J Sridhar	Role	Co-Author
Specialty	Clinical Investigation	Board Certification	
Primary Designation		Associated Organization	Stanford Health Care
Contact Number	1-650-7214902; 1-650-7235721	Email	kunjusridhar@yahoo.com; kunju@stanford.edu
State	California	Country	United States

Similar studies done by Investigator

Investigators Information			
Name	Mercedes E Gonzalez	Role	Principal Investigator
Specialty	Dermatology; Pediatric dermatology; Pain Medicine; Pediatric Medicine	Board Certification	
Primary Designation	Clinical Assistant Professor	Associated Organization	Herbert Wertheim College of Medicine
Contact Number	1-305-6673152; 1-305-2436704	Email	mercedes.e.gonzalez@gmail.com
State	Florida	Country	United States

Similar studies done by Investigator

Investigators Information			
Name	Lyndsey O'Hara	Role	Contact Person
Specialty	Nursing	Board Certification	
Primary Designation		Associated Organization	Northwestern University
Contact Number	1-586-6347131; 1-847-5038649	Email	lyndsey.dombrowski@northwestern.edu
State	Illinois	Country	United States

Location(s) (6)

Region	Country	State	Trial Site	Address	Status
North America	United States	California	Mission Dermatology Center	Mission Dermatology Center, Rancho Santa Margarita, California, United States, 92688	Completed
North America	United States	California	Stanford University	Stanford University, Stanford, California, United States,	Completed

				94305	
North America	United States	Florida	Children’s Skin Center Coral Gables	Pediatric Skin Research, LLC, Coral Gables, Florida, United States, 33146	Completed
North America	United States	Illinois	Northwestern University	Northwestern University, Chicago, Illinois, United States, 60611	Completed
North America	United States	Ohio	Cincinnati Children's Hospital Medical Center	Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, United States, 45229	Withdrawn
North America	United States	Texas	Ascension	Ascension Seton, Austin, Texas, United States, 78723	Withdrawn

Investigator Affiliated Site(s)(16)					
Region	**Country**	**State**	**Trial Site**	**Address**	**Status**
North America	United States	Illinois	Ann & Robert H Lurie Children’s Hospital of Chicago	225 E. Chicago Ave. Chicago, Illinois 60611	
North America	United States	Illinois	Ann & Robert H Lurie Children’s Hospital of Chicago	467 W. Deming, Suite 600, Chicago, Illinois 60614	
North America	United States	Illinois	Feinberg School of Medicine	Arthur J. Rubloff Building420 East Superior StreetChicago, IL 60611	

North America	United States	Florida	Nicklaus Children's Hospital	3100 S.W. 62nd Ave Miami, Florida 33155	
North America	United States	Illinois	Northwestern Memorial HealthCare	259 E. Erie St. Chicago, IL 60611	
North America	United States	Illinois	Northwestern Memorial Hospital	251 E. Huron St. Chicago, IL, 60611	
North America	United States	California	Palo Alto Medical Foundation	795 El Camino Real, 1st Floor, Main Building, Palo Alto, CA 94301	
North America	United States	Oregon	Providence Health & Services	4400 NE Halsey St.Portland, OR 97213	
North America	United States	California	Stanford Health Care	300 Pasteur Drive, Stanford, CA 94305	
North America	United States	California	Stanford University School of Medicine	291 Campus Drive Li Ka Shing Building Stanford, CA 94305	
North America	United States	Florida	University of Miami Health System	Miami, Florida, 33136, United States	
North America	United States	Florida	University of Miami Miller School of Medicine	1400 N.W. 10th Avenue, Suite 206 (M-815) Miami, Florida 33136	
North America	United States	Florida	Skin Associates of South Florida	4425 Ponce de Leon Blvd, Suite 200, Coral Gables, FL, 33146	

Asia-Pacific	China	Beijing	Beijing Cancer Hospital	No.52 Fucheng Road, Haidian District, Beijing (Dinghui Temple), 100142	
North America	United States	Florida	Herbert Wertheim College of Medicine	11200 SW 8th Street, AHC2, Miami, FL 33199	
North America	United States	Florida	Pediatric Skin Research	4425 Ponce De Leon Blvd, Coral Gables, Florida 33146, United States	

Contact Detail(s)

Contact Person Name	Phone Number	Email ID	Address	State	Country	Region
Krish S Krishnan	No references available	No references available	Krystal Biotech Inc., suite 701, 2100 Wharton Street, Pittsburgh, Pennsylvania, 15203, USA	Pennsylvania	United States	North America

Key Trial Events (46)

Event Date	Event Brief	Event Type	Source
19 May 2023	Krystal Biotech receives FDA Approval for the First-Ever Redosable Gene Therapy, VYJUVEK for the treatment of dystrophic epidermolysis bullosa	Trial Update	https://www.globenewswire.com/news-release/2023/05/19/2672756/0/en/Krystal-Biotech-Receives-FDA-Approval-for-the-First-Ever-Redosable-Gene-Therapy-VYJUVEK-beremagene-geperpavec-svdt-for-the-Treatment-of-Dystrophic-Epidermolysis-Bullosa.html

13 Apr 2023	Krystal Biotech to present at Association for Research in Vision and Ophthalmology Annual Meeting	Trial Update	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-present-association-research-vision-and
27 Feb 2023	Krystal Biotech Announces Fourth Quarter and Full Year 2022 Financial Results and Operational Progress	Trial Update	https://www.globenewswire.com/news-release/2023/02/27/2615924/0/en/Krystal-Biotech-Announces-Fourth-Quarter-and-Full-Year-2022-Financial-Results-and-Operational-Progress.html
17 Feb 2023	Clinical trial registry update Trial results updated	Results	https://clinicaltrials.gov/ct2/history/NCT04491604?A=4&B=7&C=Side-by-Side#StudyPageTop
14 Dec 2022	New England Journal of Medicine publishes phase 3 data on B-VEC in patients with dystrophic epidermolysis bullosa	Trial Update	https://ir.krystalbio.com/news-releases/news-release-details/new-england-journal-medicine-publishes-phase-3-data-b-vec
21 Sep 2022	Krystal Biotech receives positive opinion from EMA Pediatric Committee on the Pediatric Investigation Plan for B-VEC for the treatment of Dystrophic Epidermolysis Bullosa	Trial Update	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-receives-positive-opinion-ema-pediatric
18 Aug 2022	FDA Accepts Krystal Biotech's Biologics License Application for Dystrophic Epidermolysis Bullosa	Trial Update	https://ir.krystalbio.com/news-releases/news-release-details/fda-accepts-krystal-biotechs-biologics-license-application
08 Aug 2022	Krystal Biotech Announces Second Quarter 2022 Financial Results and Reports Updates on Operational Progress	Trial Update	https://www.globenewswire.com/news-release/2022/08/08/2493723/0/en/Krystal-Biotech-Announces-Second-Quarter-2022-Financial-Results-and-Reports-Updates-on-Operational-Progress.html
30 Jun 2022	Corporate presentation January 2022,	Results	https://ir.krystalbio.com/static

	presents more detailed GEM-3 results at medical congress in first half of 2022.		-files/5ebb3a7c-4328-4fe3-923f-0c2b511943ed (Slide No: 04)
22 Jun 2022	Krystal Biotech submits biologics license application to U.S. FDA seeking approval of B-VEC for the treatment of patients with dystrophic epidermolysis bullosa	Trial Update	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-submits-biologics-license-application-us-fda
20 May 2022	EM-3: Phase 3 study of beremagene geperpavec, aninvestigational, topical gene therapy, for the treatment of dystrophicEpidermolysis Bullosa Trial results updated	Results	https://onlinelibrary.wiley.com/doi/epdf/10.1111/pde.14998
19 May 2022	Krystal Biotech to present additional data on B-VEC from the GEM-3 Phase 3 study at the Society for Investigative Dermatology Annual Meeting	Trial Update	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-present-additional-data-b-vec-gem-3-phase-3
18 May 2022	GEM-3: Phase 3 Safety and Immunogenicity Results of Beremagene Geperpavec (B-VEC), an Investigational, Topical Gene Therapy for Dystrophic Epidermolysis Bullosa (DEB) Results updated	Results	https://www.sidannualmeeting.org/wp-content/uploads/2022/05/SID_Abstracts-Booklet_r6.pdf (Abstract No.: 465); https://ir.krystalbio.com/static-files/52bf3182-9694-43c1-9e6b-0af5d4952a919; https://ir.krystalbio.com/static-files/0523aa7c-11e5-444e-9f90-9603bb67f02c
09 May 2022	Krystal Biotech Announces First Quarter 2022 Financial Results and Reports Updates on Operational Progress	Trial Update	https://www.globenewswire.com/news-release/2022/05/09/2439098/0/en/Krystal-Biotech-Announces-First-Quarter-2022-Financial-Results-and-Reports-Updates-on-Operational-Progress.html
26 Mar 2022	New GEM-3 phase 3 results for B-VEC presented at 2022 American Academy	Trial Update	https://ir.krystalbio.com/news-releases/news-release-

	of Dermatology Annual Meeting		details/new-gem-3-phase-3-results-b-vec-presented-2022-american-academy
18 Mar 2022	Krystal Biotech to present at 2022 American Academy of Dermatology annual meeting	Trial Update	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-present-2022-american-academy-dermatology-annual
18 Mar 2022	Krystal Biotech to Present at 2022 American Academy of Dermatology Annual Meeting	Trial Update	https://www.globenewswire.com/news-release/2022/03/18/2405916/0/en/Krystal-Biotech-to-Present-at-2022-American-Academy-of-Dermatology-Annual-Meeting.html
28 Feb 2022	Krystal Biotech Reports Fourth Quarter and Full Year 2021 Financial Results and Provides Update on Operational Progress	Trial Update	https://www.globenewswire.com/news-release/2022/02/28/2392964/0/en/Krystal-Biotech-Reports-Fourth-Quarter-and-Full-Year-2021-Financial-Results-and-Provides-Update-on-Operational-Progress.html
31 Dec 2021	Corporate Presentation March 2021 Topline data expected in fourth quarter of 2021.	Results	https://ir.krystalbio.com/index.php/static-files/6345b187-aaef-4f32-9b02-0b755c2424e3 (Slide No: 8)
31 Dec 2021	Corporate Presentation march 2021 study topline pivotal data expected in fourth quarter of 2021.	Top-line Results	https://ir.krystalbio.com/index.php/static-files/6345b187-aaef-4f32-9b02-0b755c2424e3 (Slide No: 8)
01 Dec 2021	Corporate Presentation Q3 2020 study topline pivotal data expected in 2021.	Top-line Results	http://ir.krystalbio.com/index.php/static-files/01a9092f-d193-468b-87e4-7e95bc095472
30 Nov 2021	Krystal's dystrophic EB gene therapy trial meets primary goal Top-line results added	Top-line Results	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-positive-topline-results-gem-3-pivotal,https://pixabay.com/p

			hotos/cream-lotion-hands-sunscreen-spa-4713579/
08 Nov 2021	Krystal Biotech Reports Third Quarter 2021 Financial Results and Provides Update on Operational Progress	Trial Update	http://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-reports-third-quarter-2021-financial-results-and
26 Oct 2021	Krystal Biotech announces completion of the GEM-3 pivotal phase 3 study evaluating B-VEC for the treatment of dystrophic epidermolysis bullosa Trial Status Changed from "Ongoing, not recruiting" to "Completed"	Trial Status	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-completion-gem-3-pivotal-phase-3-study
09 Aug 2021	Krystal Biotech Reports Second Quarter 2021 Financial Results and Provides Update on Operational Progress	Trial Update	https://www.globenewswire.com/news-release/2021/08/09/2277080/0/en/Krystal-Biotech-Reports-Second-Quarter-2021-Financial-Results-and-Provides-Update-on-Operational-Progress.html
26 Apr 2021	Krystal Biotech provides update on pivotal GEM-3 study of B-VEC for DEB	Trial Update	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-provides-update-pivotal-gem-3-study-b-vec-deb
30 Mar 2021	Krystal Biotech announces completion of patient enrollment in the GEM-3 pivotal trial of B-VEC for the treatment of dystrophic epidermolysis bullosa	Enrollment Status;Trial Status	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-completion-patient-enrollment-gem-3
01 Mar 2021	Krystal Biotech Provides Update on Operational Progress and Reports Fourth Quarter and Full Year 2020 Financial Results	Trial Update	http://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-provides-update-operational-progress-and-reports
09 Nov 2020	Krystal Biotech reports third quarter 2020 financial results and provides update on operational progress	Trial Update	https://www.businesswire.com/news/home/20201109005202/en/Krystal-Biotech-Reports-Third-Quarter-2020-Financial-Results-and-Provides-Update-on-

			Operational-Progress/?
16 Oct 2020	Krystal Biotech announces departure of Chief Commercial Officer	Trial Update	https://www.businesswire.com/news/home/20201016005404/en/Krystal-Biotech-Announces-Departure-of-Chief-Commercial-Officer/?feedref=JjAwJuNHiystnCoBq_hl-RLXHJgazfQJNuOVHefdHP-D8R-QU5o2AvY8bhI9uvWSD8DYIYv4TIC1g1u0AKcacnnViVjtb72bOP4-4nHK5ieT3WxPE8m_kWI77F87CseT
01 Oct 2020	Krystal Biotech to present on beremagene geperpavec to the 2020 Virtual debra Care Conference	Trial Update	https://www.sec.gov/Archives/edgar/data/1711279/000119312520261297/d60899d8k.htm
10 Aug 2020	Krystal Biotech reports second quarter 2020 financial results and provides update on operational progress	Trial Update	https://www.globenewswire.com/news-release/2020/08/10/2075601/0/en/Krystal-Biotech-Reports-Second-Quarter-2020-Financial-Results-and-Provides-Update-on-Operational-Progress.html
28 Jul 2020	Krystal Biotech announces initiation of pivotal phase 3 study of Beremagene Geperpavec in patients with Dystrophic Epidermolysis Bullosa Trial initiation reported	Trial Initiation	http://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-initiation-pivotal-phase-3-study
04 May 2020	Krystal Biotech reports first quarter 2020 financial results and provides update on operational progress	Trial Update	http://www.globenewswire.com/news-release/2020/05/04/2026680/0/en/Krystal-Biotech-Reports-First-Quarter-2020-Financial-Results-and-Provides-Update-on-Operational-Progress.html
10 Mar 2020	Krystal Biotech reports 2019 financial results and business progress	Trial Update	http://www.globenewswire.com/news-release/2020/03/10/1997934/

			0/en/Krystal-Biotech-Reports-2019-Financial-Results-and-Business-Progress.html
31 Dec 2019	Krystal Biotech reports second quarter 2019 financial and operating results Study expected to be initiated in the fourth quarter of 2019	Trial Initiation	https://www.globenewswire.com/news-release/2019/08/05/1896834/0/en/Krystal-Biotech-Reports-Second-Quarter-2019-Financial-and-Operating-Results.html
04 Nov 2019	Krystal Biotech reports third quarter 2019 financial and operating results	Trial Update	http://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-reports-third-quarter-2019-financial-and
24 Jun 2019	Krystal Biotech announces positive results from phase 2 clinical trial (“GEM-2 study”) of KB103 and receives regenerative medicine advanced therapy designation from FDA for KB103	Trial Update	http://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-positive-results-phase-2-clinical
14 Jun 2019	Krystal submits investigational new drug (IND) application for KB105, topical gene therapy candidate for transglutaminase-1 deficient autosomal recessive congenital ichthyosis	Trial Update	http://ir.krystalbio.com/news-releases/news-release-details/krystal-submits-investigational-new-drug-ind-application-kb105
06 May 2019	Krystal Biotech reports first quarter 2019 financial results and provides corporate update	Trial Update	http://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-reports-first-quarter-2019-financial-results-and
29 Mar 2019	EMA grants PRIME eligibility for KB103 to treat Dystrophic Epidermolysis Bullosa	Trial Update	http://ir.krystalbio.com/news-releases/news-release-details/ema-grants-prime-eligibility-kb103-treat-dystrophic
12 Mar 2019	Krystal Biotech reports 2018 financial results and business progress	Trial Update	https://www.globenewswire.com/news-release/2019/03/12/1751728/0/en/Krystal-Biotech-Reports-2018-Financial-

			Results-and-Business-Progress.html
15 Jan 2019	Krystal Biotech completes construction of Ancoris - a new GMP facility for commercial manufacturing of a viral vector-based gene therapy to treat dystrophic epidermolysis bullosa	Trial Update	http://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-completes-construction-ancoris-new-gmp-facility
05 Nov 2018	Krystal Biotech reports third quarter 2018 financial results and provides corporate update	Trial Update	http://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-reports-third-quarter-2018-financial-results-and
01 Nov 2018	GlobalData Primary Research from Insights	Trial Update	
15 Oct 2018	Krystal biotech announces positive interim results from placebo-controlled phase 1/2 clinical trial of KB103	Trial Update	http://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-positive-interim-results-placebo

Insights (4)

Published Date	Headline
01-Nov-2018	Krystal to recruit two more adult patients on four-patient Phase I/II DEB trial of topical gene therapy, considers eye and fused hand clinical studies in 2019, sources say
07-Nov-2018	Krystal’s KB103 splits experts' thoughts on potential for HSV-1 risk in dystrophic epidermolysis bullosa patients, but final Phase I/II efficacy assured
02-Nov-2021	LoA Update: Krystal’s topical gene therapy approval shot in epidermolysis bullosa bolstered by Phase III follow-up completion
10-Mar-2023	Krystal’s Topical Gene Therapy for DEB Likely to Confront Access Challenges After Probable FDA Approval

History of changes

Modified Date	Update Type	Description	From Data	To Data	Source Date	Source Type	Source
07-Nov-2023	Study Design/ Trial Descripti	Trial Description Updated			17-Feb-2023	Clinical Trial Registry	https://clinicaltrials.gov/study/NCT04491604

	on						
13-Oct-2023	Study Design/ Trial Description	Trial Description Updated			28-Oct-2022	Regulatory Website	https://www.ema.europa.eu/en/documents/pip-decision/p/0464/2022-ema-decision-28-october-2022-agreement-paediatric-investigation-plan-beremagene-geperpavec-emea_en.pdf
13-Oct-2023	Study Design/ Trial Description	Study Design Updated	Randomized, Placebo-controlled, Parallel Assignment, Double Blind, Treatment, Multi-centered, Pivotal/ Registration	Randomized, Placebo-controlled, Parallel Assignment, Double Blind, Treatment, Multi-centered, Pivotal/ Registration, Pediatric Investigation Plan (PIP)	28-Oct-2022	Regulatory Website	https://www.ema.europa.eu/en/documents/pip-decision/p/0464/2022-ema-decision-28-october-2022-agreement-paediatric-investigation-plan-beremagene-geperpavec-emea_en.pdf
05-Mar-2023	Study Design/ Trial Description	Virtual Component Added	N/A	Telemedicine	21-Feb-2023	Clinical Trial Registry	https://clinicaltrials.gov/ProvidedDocs/04/NCT04491604/Prot_000.pdf
02-Mar-2023	Study Design/ Trial	Trial Notes Updated			20-Feb-2023	Company SEC Filings	https://www.sec.gov/ix?doc=/Archives/edgar/data/1711279/0001711

	Description						27923000008/krys-20221231.htm
20-Feb-2023	Acronym/Secondary ID	Trial Secondary ID Updated	GDC30021486, GDCT0363915, NCT04491604	B-VEC-03, GDC30021486, GDCT0363915, NCT04491604	17-Feb-2023	Clinical Trial Registry	https://clinicaltrials.gov/ct2/history/NCT04491604?A=4&B=7&C=Side-by-Side#StudyPageTop
20-Feb-2023	Endpoint Classification	Endpoint Classification Updated	Efficacy,Quality of Life,Safety	Efficacy,Safety	17-Feb-2023	Clinical Trial Registry	https://clinicaltrials.gov/ct2/history/NCT04491604?A=4&B=7&C=Side-by-Side#StudyPageTop
20-Feb-2023	Primary/ Secondary outcomes	Primary Outcome Measures Updated			17-Feb-2023	Clinical Trial Registry	https://clinicaltrials.gov/ct2/history/NCT04491604?A=4&B=7&C=Side-by-Side#StudyPageTop
20-Feb-2023	Primary/ Secondary outcomes	Secondary Outcome Measures Updated			17-Feb-2023	Clinical Trial Registry	https://clinicaltrials.gov/ct2/history/NCT04491604?A=4&B=7&C=Side-by-Side#StudyPageTop
20-Feb-2023	Study Design/ Trial Description	Trial Description Updated			17-Feb-2023	Clinical Trial Registry	https://clinicaltrials.gov/ct2/history/NCT04491604?A=4&B=7&C=Side-by-Side#StudyPageTop
20-Feb-2023	Trial Result	Trial Results Updated			17-Feb-2023	Clinical Trial Registry	https://clinicaltrials.gov/ct2/show/results/NCT04491604?view=results
19-Dec-2022	Trial Result	Trial Results Updated			15-Dec-2022	Journals	https://www.nejm.org/doi/full/10.1056/NEJMoa2206663
19-Dec-2022	Trial Result	Trial Conclusion Updated			15-Dec-2022	Journals	https://www.nejm.org/doi/full/10.1056/NEJMoa2206663
19-Dec-	Study	Trial			15-Dec-	Journals	https://www.nejm.org/doi/full/10.

2022	Design/ Trial Description	Description Updated			2022		1056/NEJMoa2206663
04-Aug-2022	Trial Date	Trial Actual End Date Changed from **"26 Oct 2021"** to **"29 Oct 2021"**	26 Oct 2021	29 Oct 2021	03-Aug-2022	Clinical Trial Registry	https://clinicaltrials.gov/ct2/history/NCT04491604?A=3&B=4&C=Side-by-Side#StudyPageTop
04-Aug-2022	Age Eligibility	Maximum Age Eligibility Removed	44 Years	N/A	03-Aug-2022	Clinical Trial Registry	https://clinicaltrials.gov/ct2/history/NCT04491604?A=3&B=4&C=Side-by-Side#StudyPageTop
04-Aug-2022	Age Eligibility	Minimum Age Eligibility Updated from **"1 Years"** to **"6 Months"**	1 Years	6 Months	03-Aug-2022	Clinical Trial Registry	https://clinicaltrials.gov/ct2/history/NCT04491604?A=3&B=4&C=Side-by-Side#StudyPageTop
04-Aug-2022	Primary/ Secondary outcomes	Secondary Outcome Measures Updated			03-Aug-2022	Clinical Trial Registry	https://clinicaltrials.gov/ct2/history/NCT04491604?A=3&B=4&C=Side-by-Side#StudyPageTop
04-Aug-2022	Subjects	Trial Subjects Updated	Cutaneous Disease, Recessive Dystrophic, Adolescents, Adults, Children,	Cutaneous Disease, Recessive Dystrophic, Adolescents, Adults, Children,	03-Aug-2022	Clinical Trial Registry	https://clinicaltrials.gov/ct2/history/NCT04491604?A=3&B=4&C=Side-by-Side#StudyPageTop

			Infants, Pediatric	Elders, Infants, Pediatric			
27-May-2022	Biomarkers	Biomarkers Updated	Anti Collagen Type VII Antibody; Anti Human Herpesvirus 1 Antibody; Collagen Type VII Alpha 1 Chain	Anti Collagen Type VII Antibody; Anti Collagen Type VII Immunoglobulin G Antibody; Anti Human Herpesvirus 1 Antibody; Collagen Type VII Alpha 1 Chain	18-May-2022	Conferences	https://ir.krystalbio.com/static-files/0523aa7c-11e5-444e-9f90-9603bb67f02c
26-May-2022	Biomarkers	Biomarkers Updated	N/A	Collagen Type VII Alpha 1 Chain	20-May-2022	Conferences	https://onlinelibrary.wiley.com/doi/epdf/10.1111/pde.14998
26-May-2022	Biomarkers	Biomarkers Updated	Collagen Type VII Alpha 1 Chain	Anti Collagen Type VII Antibody; Collagen Type VII	18-May-2022	Conferences	https://ir.krystalbio.com/static-files/52bf3182-9694-43c1-9e6b-0af5d4952a91

				Alpha 1 Chain			
26-May-2022	Biomarkers	Biomarkers Updated	Anti Collagen Type VII Antibody; Collagen Type VII Alpha 1 Chain	Anti Collagen Type VII Antibody; Anti Human Herpesvirus 1 Antibody; Collagen Type VII Alpha 1 Chain	18-May-2022	Conferences	https://ir.krystalbio.com/static-files/52bf3182-9694-43c1-9e6b-0af5d4952a91
25-May-2022	Study Design/ Trial Description	Trial Description Updated			20-May-2022	Conferences	https://onlinelibrary.wiley.com/doi/epdf/10.1111/pde.14998
25-May-2022	Trial Result	Trial Results Updated			20-May-2022	Conferences	https://onlinelibrary.wiley.com/doi/epdf/10.1111/pde.14998
24-May-2022	Primary/ Secondary outcomes	Primary Outcome Measures Updated			18-May-2022	Conferences	https://www.sidannualmeeting.org/wp-content/uploads/2022/05/SID_Abstracts-Booklet_r6.pdf (Abstract No.: 465); https://ir.krystalbio.com/static-files/52bf3182-9694-43c1-9e6b-0af5d4952a919; https://ir.krystalbio.com/static-files/0523aa7c-11e5-444e-9f90-9603bb67f02c
24-May-2022	Primary/ Secondary	Secondary Outcome Measures			18-May-2022	Conferences	https://www.sidannualmeeting.org/wp-content/uploads/2

	outcomes	Updated					022/05/SID_Abstracts-Booklet_r6.pdf (Abstract No.: 465); https://ir.krystalbio.com/static-files/52bf3182-9694-43c1-9e6b-0af5d4952a919; https://ir.krystalbio.com/static-files/0523aa7c-11e5-444e-9f90-9603bb67f02c
24-May-2022	Study Design/ Trial Description	Trial Description Updated			18-May-2022	Conferences	https://www.sidannualmeeting.org/wp-content/uploads/2022/05/SID_Abstracts-Booklet_r6.pdf (Abstract No.: 465); https://ir.krystalbio.com/static-files/52bf3182-9694-43c1-9e6b-0af5d4952a919; https://ir.krystalbio.com/static-files/0523aa7c-11e5-444e-9f90-9603bb67f02c
24-May-2022	Subjects	Inclusion Criteria Updated			18-May-2022	Conferences	https://www.sidannualmeeting.org/wp-content/uploads/2022/05/SID_Abstracts-Booklet_r6.pdf (Abstract No.: 465); https://ir.krystalbio.com/static-files/52bf3182-9694-43c1-9e6b-0af5d4952a919; https://ir.krystalbio.com/static-files/0523aa7c-11e5-444e-9f90-9603bb67f02c
23-May-2022	Trial Result	Trial Results Updated			18-May-2022	Conferences	https://www.sidannualmeeting.org/wp-content/uploads/2022/05/SID_Abstracts-Booklet_r6.pdf (Abstract No.: 465); https://ir.krystalb

							io.com/static-files/52bf3182-9694-43c1-9e6b-0af5d4952a919; https://ir.krystalbio.com/static-files/0523aa7c-11e5-444e-9f90-9603bb67f02c
23-May-2022	Trial Result	Trial Conclusion Updated			18-May-2022	Conferences	https://www.sidannualmeeting.org/wp-content/uploads/2022/05/SID_Abstracts-Booklet_r6.pdf (Abstract No.: 465); https://ir.krystalbio.com/static-files/52bf3182-9694-43c1-9e6b-0af5d4952a919; https://ir.krystalbio.com/static-files/0523aa7c-11e5-444e-9f90-9603bb67f02c
30-Mar-2022	Study Design/ Trial Description	Trial Notes Updated			28-Mar-2022	Conferences	https://ir.krystalbio.com/static-files/fbe09d1a-d428-4c7e-9ef6-32881968cdc1
30-Mar-2022	Trial Result	Trial Results Updated			28-Mar-2022	Conferences	https://ir.krystalbio.com/static-files/fbe09d1a-d428-4c7e-9ef6-32881968cdc1
01-Mar-2022	Study Design/ Trial Description	Trial Notes Updated			28-Feb-2022	Company Press Release	https://ir.krystalbio.com/node/8446/pdf
11-Jan-2022	Study Design/ Trial Description	Trial Notes Updated			01-Jan-2022	Company Presentation	https://ir.krystalbio.com/static-files/5ebb3a7c-4328-4fe3-923f-0c2b511943ed
02-Dec-2021	Trial Result	Top-line Results Updated			29-Nov-2021	Company Press Release	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-

							positive-topline-results-gem-3-pivotal
02-Dec-2021	Endpoint Status	Endpoint Status Updated to **"Achieved "**	N/A	Achieved	29-Nov-2021	Company Press Release	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-positive-topline-results-gem-3-pivotal
02-Dec-2021	Enrollment	Number of Subjects Analyzed Updated to **"31"**	N/A	31	29-Nov-2021	Company Press Release	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-positive-topline-results-gem-3-pivotal
02-Dec-2021	Trial Result	Trial Conclusion Updated					
09-Nov-2021	Study Design/ Trial Description	Trial Notes Updated			08-Nov-2021	Company Press Release	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-reports-third-quarter-2021-financial-results-and
27-Oct-2021	Age Eligibility	Maximum Age Eligibility Updated to **"44 Years"**	N/A	44 Years	26-Oct-2021	Company Press Release	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-completion-gem-3-pivotal-phase-3-study
27-Oct-2021	Age Eligibility	Minimum Age Eligibility Updated from **"6 Months"** to **"1 Years"**	6 Months	1 Years	26-Oct-2021	Company Press Release	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-completion-gem-3-pivotal-phase-3-study
27-Oct-2021	Study Design/	Trial Descriptio			26-Oct-2021	Company Press	https://ir.krystalbio.com/news-

	Trial Description	n Updated				Release	releases/news-release-details/krystal-biotech-announces-completion-gem-3-pivotal-phase-3-study
27-Oct-2021	Subjects	Trial Subjects Updated	Cutaneous Disease, Recessive Dystrophic, Adolescents, Adults, Children, Elders, Infants	Cutaneous Disease, Recessive Dystrophic, Adolescents, Adults, Children, Elders, Infants, Pediatric	26-Oct-2021	Company Press Release	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-completion-gem-3-pivotal-phase-3-study
27-Oct-2021	Trial Date	Trial Actual End Date Added **"26 Oct 2021"**	N/A	26 Oct 2021	26-Oct-2021	Company Press Release	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-completion-gem-3-pivotal-phase-3-study
27-Oct-2021	Trial Status	Trial Status Changed from **"Ongoing, not recruiting"** to **"Completed"**	Ongoing, not recruiting	Completed	26-Oct-2021	Company Press Release	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-completion-gem-3-pivotal-phase-3-study
27-Oct-2021	Trial Result	Trial Conclusion Updated			26-Oct-2021	Company Press Release	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-

							announces-completion-gem-3-pivotal-phase-3-study
27-Oct-2021	Study Design/ Trial Description	Trial Notes Updated			26-Oct-2021	Company Press Release	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-completion-gem-3-pivotal-phase-3-study
27-Oct-2021	Subjects	Trial Subjects Updated	Cutaneous Disease, Recessive Dystrophic, Adolescents, Adults, Children, Elders, Infants, Pediatric	Cutaneous Disease, Recessive Dystrophic, Adolescents, Adults, Children, Infants, Pediatric	26-Oct-2021	Company Press Release	https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-completion-gem-3-pivotal-phase-3-study
13-Oct-2021	Study Design/ Trial Description	Trial Notes Updated			01-Oct-2021	Company Presentation	https://ir.krystalbio.com/static-files/3fe442fb-c1cc-43b7-b338-6942a91d881a
24-Sep-2021	Study Design/ Trial Description	Trial Notes Updated			01-Sep-2021	Company Presentation	https://ir.krystalbio.com/static-files/42934f6f-f225-4bdc-bb03-55dcae00be00
20-Sep-2021	Trial Date	Trial Estimated End Date Changed from **"01 Aug**	01 Aug 2021	01 Sep 2021	17-Sep-2021	Clinical Trial Registry	https://clinicaltrials.gov/ct2/history/NCT04491604?A=2&B=3&C=Side-by-Side#StudyPageTop

		2021" to **"01 Sep 2021"**					
03-Sep-2021	Study Design/ Trial Description	Trial Notes Updated			01-Aug-2021	Company Presentation	https://ir.krystalbio.com/static-files/b83cbb82-85f2-428c-9626-bf1ae22985e2
14-Jul-2021	Study Design/ Trial Description	Trial Notes Updated					https://ir.krystalbio.com/static-files/9b7df989-970a-46bf-ab53-ac28ab492c81
06-Jul-2021	Study Design/ Trial Description	Trial Notes Updated					https://ir.krystalbio.com/static-files/d993ec43-6efa-4955-a7c1-282899bfed20
30-Apr-2021	Primary/ Secondary outcomes	Primary Outcome Measure Updated					https://clinicaltrials.gov/ct2/history/NCT04491604?A=1&B=2&C=Side-by-Side#StudyPageTop
30-Apr-2021	Primary/ Secondary outcomes	Secondary Outcome Measure Updated					https://clinicaltrials.gov/ct2/history/NCT04491604?A=1&B=2&C=Side-by-Side#StudyPageTop
30-Apr-2021	Subjects	Inclusion Criteria Updated					https://clinicaltrials.gov/ct2/history/NCT04491604?A=1&B=2&C=Side-by-Side#StudyPageTop
30-Apr-2021	Trial Date	Trial Actual Start Date Changed from **"28 Jul 2020"** to **"17 Aug 2020"**	28 Jul 2020	17 Aug 2020			https://clinicaltrials.gov/ct2/history/NCT04491604?A=1&B=2&C=Side-by-Side#StudyPageTop

28-Apr-2021	Study Design/ Trial Description	Trial Notes Updated					https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-provides-update-pivotal-gem-3-study-b-vec-deb
27-Apr-2021	Study Design/ Trial Description	Trial Notes Updated					https://ir.krystalbio.com/index.php/static-files/26fb3e78-e938-4a15-a7bf-ae1d27178e97
01-Apr-2021	Enrollment	Number of Subjects Enrolled Changed from "N/A" to "31"	N/A	31			https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-completion-patient-enrollment-gem-3
01-Apr-2021	Trial Status	Trial Status Changed from **"Ongoing, recruiting"** to **"Ongoing, not recruiting"**	Ongoing, recruiting	Ongoing, not recruiting			https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-completion-patient-enrollment-gem-3
01-Apr-2021	Study Design/ Trial Description	Trial Description Updated					
01-Apr-2021	Trial Result	Trial Conclusion Updated					
23-Mar-2021	Study Design/ Trial Description	Trial Notes Updated					https://www.sec.gov/ix?doc=/Archives/edgar/data/1711279/000171127921000006/krys-20201231.htm

23-Mar-2021	Subjects	Trial Subjects Updated					
04-Mar-2021	Study Design/ Trial Description	Trial Notes Updated					https://ir.krystalbio.com/index.php/static-files/6345b187-aaef-4f32-9b02-0b755c2424e3
12-Jan-2021	Study Design/ Trial Description	Trial Notes Updated					https://ir.krystalbio.com/index.php/static-files/34687a98-89a9-4188-8f3c-72e8bd90bd98
08-Dec-2020	Study Design/ Trial Description	Trial Notes Updated					
30-Nov-2020	Study Design/ Trial Description	Trial Notes Updated					https://www.businesswire.com/news/home/20201109005202/en/Krystal-Biotech-Reports-Third-Quarter-2020-Financial-Results-and-Provides-Update-on-Operational-Progress/?
06-Nov-2020	Primary/ Secondary outcomes	Primary Outcome Measure Updated					https://www.sec.gov/Archives/edgar/data/1711279/000119312520261297/d60899dex991.htm
26-Oct-2020	Study Design/ Trial Description	Trial Notes Updated					https://ir.krystalbio.com/node/7681/pdf
23-Sep-2020	Study Design/ Trial Description	Trial Notes Updated					http://ir.krystalbio.com/index.php/static-files/7fed8190-febd-4321-bf91-7917cec96a7b

09-Sep-2020	Study Design/ Trial Description	Trial Notes Updated					http://ir.krystalbio.com/index.php/static-files/b32f0709-1eb0-42ec-a825-64efad8a6cd8
02-Sep-2020	Study Design/ Trial Description	Trial Notes Updated					http://ir.krystalbio.com/index.php/static-files/01a9092f-d193-468b-87e4-7e95bc095472
19-Aug-2020	Trial Locations	Trial Locations Updated					https://clinicaltrials.gov/ct2/show/NCT04491604
18-Aug-2020	Acronym/Secondary ID	Trial Secondary ID Updated					https://clinicaltrials.gov/ct2/show/NCT04491604
18-Aug-2020	Study Design/ Trial Description	Study Design Updated					https://clinicaltrials.gov/ct2/show/NCT04491604
18-Aug-2020	Trial Date	Trial Estimated End Date Updated					https://clinicaltrials.gov/ct2/show/NCT04491604
18-Aug-2020	Trial Date	Trial Estimated Start Date Changed from **"01 Jun 2020"** to **"01 Aug 2020"**	01 Jun 2020	01 Aug 2020			https://clinicaltrials.gov/ct2/show/NCT04491604
29-Jul-2020	Acronym/Secondary ID	Trial Acronym Updated					http://www.globenewswire.com/news-release/2020/07/28/2069060/0/en/Krystal-Biotech-Announces-Initiation-of-Pivotal-Phase-3-Study-of-

							Beremagene-Geperpavec-in-Patients-with-Dystrophic-Epidermolysis-Bullosa.html
29-Jul-2020	Enrollment	Number of Subjects Planned Changed from "N/A" to "30"	N/A	30			http://www.globenewswire.com/news-release/2020/07/28/2069060/0/en/Krystal-Biotech-Announces-Initiation-of-Pivotal-Phase-3-Study-of-Beremagene-Geperpavec-in-Patients-with-Dystrophic-Epidermolysis-Bullosa.html
29-Jul-2020	Primary/ Secondary outcomes	Primary Outcome Measure Updated					http://www.globenewswire.com/news-release/2020/07/28/2069060/0/en/Krystal-Biotech-Announces-Initiation-of-Pivotal-Phase-3-Study-of-Beremagene-Geperpavec-in-Patients-with-Dystrophic-Epidermolysis-Bullosa.html
29-Jul-2020	Primary/ Secondary outcomes	Secondary Outcome Measure Updated					http://www.globenewswire.com/news-release/2020/07/28/2069060/0/en/Krystal-Biotech-Announces-Initiation-of-Pivotal-Phase-3-Study-of-Beremagene-Geperpavec-in-Patients-with-Dystrophic-Epidermolysis-Bullosa.html
29-Jul-2020	Study Design/ Trial Description	Study Design Updated					http://www.globenewswire.com/news-release/2020/07/28/2069060/0/en/Krystal-Biotech-Announces-Initiation-of-

							Pivotal-Phase-3-Study-of-Beremagene-Geperpavec-in-Patients-with-Dystrophic-Epidermolysis-Bullosa.html
29-Jul-2020	Study Design/ Trial Description	Trial Description Updated					http://www.globenewswire.com/news-release/2020/07/28/2069060/0/en/Krystal-Biotech-Announces-Initiation-of-Pivotal-Phase-3-Study-of-Beremagene-Geperpavec-in-Patients-with-Dystrophic-Epidermolysis-Bullosa.html
29-Jul-2020	Subjects	Inclusion Criteria Updated					http://www.globenewswire.com/news-release/2020/07/28/2069060/0/en/Krystal-Biotech-Announces-Initiation-of-Pivotal-Phase-3-Study-of-Beremagene-Geperpavec-in-Patients-with-Dystrophic-Epidermolysis-Bullosa.html
29-Jul-2020	Trial Date	Trial Actual Start Date Updated					http://www.globenewswire.com/news-release/2020/07/28/2069060/0/en/Krystal-Biotech-Announces-Initiation-of-Pivotal-Phase-3-Study-of-Beremagene-Geperpavec-in-Patients-with-Dystrophic-Epidermolysis-Bullosa.html
29-Jul-2020	Trial Status	Trial Status Changed from	Planned	Ongoing, recruiting			http://www.globenewswire.com/news-release/2020/07/28/2069060/0/en/Krystal-Biotech-

		"Planned " to **"Ongoing, recruiting "**					Announces-Initiation-of-Pivotal-Phase-3-Study-of-Beremagene-Geperpavec-in-Patients-with-Dystrophic-Epidermolysis-Bullosa.html
29-Jul-2020	Trial Result	Trial Conclusion Updated					
10-Jul-2020	Study Design/ Trial Description	Trial Notes Updated					http://ir.krystalbio.com/index.php/static-files/a3b0f424-0974-4306-aab6-afe8d5ba33fd
10-Jul-2020	Acronym/Secondary ID	Trial Secondary ID Updated					
10-Jul-2020	Trial Contacts	Trial Contacts Updated					
10-Jul-2020	Trial Contacts	Trial Contacts Updated					
10-Jul-2020	Trial Contacts	Trial Contacts Updated					
08-May-2020	Study Design/ Trial Description	Trial Notes Updated					http://ir.krystalbio.com/static-files/35d3e5c1-e09a-44cc-9f59-759272ade377
02-Apr-2020	Study Design/ Trial Description	Trial Notes Updated					http://ir.krystalbio.com/static-files/d20ad332-c660-45db-8537-03d85cdacfee
06-Mar-2020	Study Design/ Trial	Trial Notes Updated					http://wsw.com/webcast/cowen57/krys/?lobby=true&day=2

	Description						
06-Mar-2020	Trial Date	Trial Estimated Start Date Changed from **"01 Dec 2019"** to **"01 Jun 2020"**	01 Dec 2019	01 Jun 2020			http://wsw.com/webcast/cowen57/krys/?lobby=true&day=2
12-Sep-2019	Study Design/ Trial Description	Trial Notes Updated					http://ir.krystalbio.com/static-files/01e8082a-c5f2-4e38-b43e-c29cdf2094ac
07-Aug-2019	Trial Locations	Trial Locations Updated					http://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-reports-second-quarter-2019-financial-and
26-Jun-2019	Study Design/ Trial Description	Trial Notes Updated					http://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-positive-results-phase-2-clinical
15-May-2019	Study Design/ Trial Description	Trial Notes Updated					http://ir.krystalbio.com/static-files/2e804dac-b448-4850-a78d-aa7ffdd58f23
15-May-2019	Subjects	Inclusion Criteria Updated					
15-May-2019	Subjects	Inclusion Criteria Updated					
26-Mar-2019	Study Design/ Trial	Trial Notes Updated					http://wsw.com/webcast/cowen52/krys/

	Description						
21-Mar-2019	Study Design/ Trial Description	Trial Notes Updated					http://ir.krystalbio.com/static-files/18fa519e-1788-4e30-8598-51ca2d382786
16-Jan-2019	Study Design/ Trial Description	Trial Notes Updated					https://krystalbio.gcs-web.com/static-files/b96b7e0c-7692-4a95-b75c-c8ae0b08d487
08-Nov-2018	Primary/ Secondary outcomes	Primary Outcome Measure Updated					
17-Oct-2018	Study Design/ Trial Description	Trial Notes Updated					http://wsw.com/webcast/cantor7/krys/?lobby=true&day=1

Sources

- GlobeNewswire, Corporate News Providers, "Krystal Biotech Announces Initiation of Pivotal Phase 3 Study of Beremagene Geperpavec in Patients with Dystrophic Epidermolysis Bullosa", 28 Jul 2020 (Trial status, actual start date, study design, acronym, end points, outcome)\ The Cantor Fitzgerald's 4th Annual Healthcare Conference, "Krystal Biotech Inc., Company Update Presentation (Slides 8, 16)", 01 Oct 2018 (Trial notes)
- GlobalData Primary Research from Insights (Primary outcome)
- Krystal Biotech Inc, "Krystal Biotech Reports Third Quarter 2018 Financial Results and Provides Corporate Update", 05 Nov 2018
- Krystal Biotech Inc, "Corporate Presentation Q1 2019 (Slide No: 03, 08, 14)", Jan 2019 (Trial notes)
- U. S. Securities and Exchange Commission (SEC), Krystal Biotech Inc., FORM 10-K, 31 Dec 2018 (Page No: 02, 08, 22, 48, 54) (Trial Notes)
- The 39th Cowen and Company Annual Health Care Conference, "Krystal Biotech Inc., Company Update Presentation (Slides 4, 8, 14)", 13 Mar 2019 (Trial notes)
- U. S. Securities and Exchange Commission (SEC), Krystal Biotech Inc., FORM 10-Q, 31 Mar 2019 (Page No: 17) (Trail notes)
- Krystal Biotech, Inc., "Krystal Biotech Announces Positive Results from Phase 2 Clinical Trial (“GEM-2 study”) of KB103 and Receives Regenerative Medicine Advanced Therapy

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