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): January 7, 2021

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))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	**KRYS**	**Nasdaq**

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.

Beginning on January 7, 2021, Krystal Biotech, Inc. (the "Company") plans to make a series of presentations to investors and other parties (the "Corporate Presentation") a copy of which is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference. The Company expects to use the Corporate Presentation from time to time thereafter in connection with presentations to potential investors, industry analysts and others. The Corporate Presentation is available under the "Investors" section of the Company's website, located at www.krystalbio.com.

The information presented in Item 7.01 of this Current Report on Form 8-K and Exhibit 99.1 shall not be deemed to be "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, unless the Company specifically states that the information is to be considered "filed" under the Exchange Act or specifically incorporates it by reference into a filing under the Securities Act of 1933, as amended, or the Exchange Act.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Corporate Presentation dated January 2021
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: January 7, 2021

KRYSTAL BIOTECH, INC.

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

Exhibit 99

Krystal

The Leader in Redosable Gene Therapy for Rare Disease

JANUARY 2021

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Forward-looking statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. Any statements in this presentation about future expectations, plans and prospects for Krystal Biotech, Inc. (the "Company"), including but not limited to statements about the development of the Company's product candidates, such as the future development or commercialization of beremagene geperpavec ("B-VEC"), KB105, KB104, KB301 and KB407 and the Company's other product candidates; conduct and timelines of clinical trials, the clinical utility of B-VEC, KB105, KB104, KB301 and KB407 and the Company's other product candidates; plans for and timing of the review of regulatory filings, efforts to bring B-VEC, KB105, KB104, KB301 and KB407 and the Company's other product candidates to market; the market opportunity for and the potential market acceptance of B-VEC", KB105, KB104, KB301 and KB407 and the Company's other product candidates, the development of B-VEC, KB105, KB104, KB301 and KB407 and the Company's other product candidates for additional indications; the development of additional formulations of B-VEC, KB105, KB104, KB301 and KB407 and the Company's other product candidates; plans to pursue research and development of other product candidates, the sufficiency of the Company's existing cash resources; and other statements containing the words "anticipate", "believe", "estimate", "expect", "intend", "may", "plan", "predict", "project", "target", "potential", "likely", "will", "would", "could", "should", "continue" and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the content and timing of decisions made by the U.S. Food and Drug Administration, European Medicines Agency and other regulatory authorities; the uncertainties inherent in the initiation and conduct of clinical trials, availability and timing of data from clinical trials; whether results of early clinical trials or studies in different disease indications will be indicative of the results of ongoing or future trials; uncertainties associated with regulatory review of clinical trials and applications for marketing approvals; the availability or commercial potential of product candidates; the ability to retain and hire key personnel; the sufficiency of cash resources and need for additional financing; and such other important factors as are set forth in the Company's annual and quarterly reports and other filings on file with the U.S. Securities and Exchange Commission. In addition, the forward-looking statements included in this presentation represent the Company's views as of the date of this presentation. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this presentation.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Krystal overview

A fully integrated, clinical stage gene therapy company powered by proprietary HSV-1 vector technology

Differentiated viral vector platform enables *in vivo*, repeat dose gene therapies

- Proprietary, engineered *replication incompetent* HSV-1 based platform
- Clinical data shows maintenance of safety and transgene expression after repeat dosing
- Positive external clinical and regulatory precedent with *in vivo* HSV-1 based therapy

Initial focus on rare, dermatologic indications led to rapid clinical proof of concept and pipeline

- Lead program, B-VEC (formerly KB103) went from IND to Phase 3 in less than 3 years; pivotal data anticipated in 2021
- Two lead dermatologic pipeline programs, KB104 and KB105, leverage the same vector

Broadening focus to address larger indications and new tissue types

- Ongoing Phase 1 trial in acne scars and wrinkles with KB301, under our wholly owned subsidiary Jeune, Inc.
- Positive pre-clinical data from KB407 for cystic fibrosis demonstrates potential to target lung tissue; pre-IND studies underway
- Continue to drive innovation by investing in next-gen platform capabilities

In-house GMP manufacturing to support clinical and commercial needs

- Stable producer cell lines developed for each program have cost, scale, and regulatory benefits
- Current ~7,500 sqft GMP facility near company headquarters in Pittsburgh is producing pivotal material at commercial scale, and BLA readiness is underway
- Investing in additional capacity via construction of an ~150,000 sqft facility which is expected to be operational in 2022

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Key 2021 Milestones

Progress across pipeline will yield pivotal data for B-VEC, a 4th clinical stage program and a new respiratory candidate in 2021

Timing	Program	Event
1Q21	B-VEC for DEB	Complete enrollment in pivotal GEM-3 study in DEB
1Q21	KB301 for aesthetic indications	Announce Initial safety data from cohort 1 of Phase 1 study in facial wrinkles and acne scars
1Q21	KB301 for aesthetic indications	Provide update on strategy for KB301 and aesthetic pipeline (under Jeune Inc.)
1H21	KB105 for TGM1-ARCI	Announce initial Phase 2 data and update on next Phase 2 cohorts
1H21	KB407 for CF	Announce data from IND enabling toxicology study in nonhuman primates
1H21	KB407 for CF	Initiate Phase 1/2 study
1H21	Respiratory pipeline	Announce development candidate for new genetic lung disease
2H21	**B-VEC for DEB**	**Announce top line data from the pivotal GEM-3 study**
2H21	KB104 for Netherton	File IND

All pipeline compounds are investigational, being evaluated in clinical or pre-clinical studies.

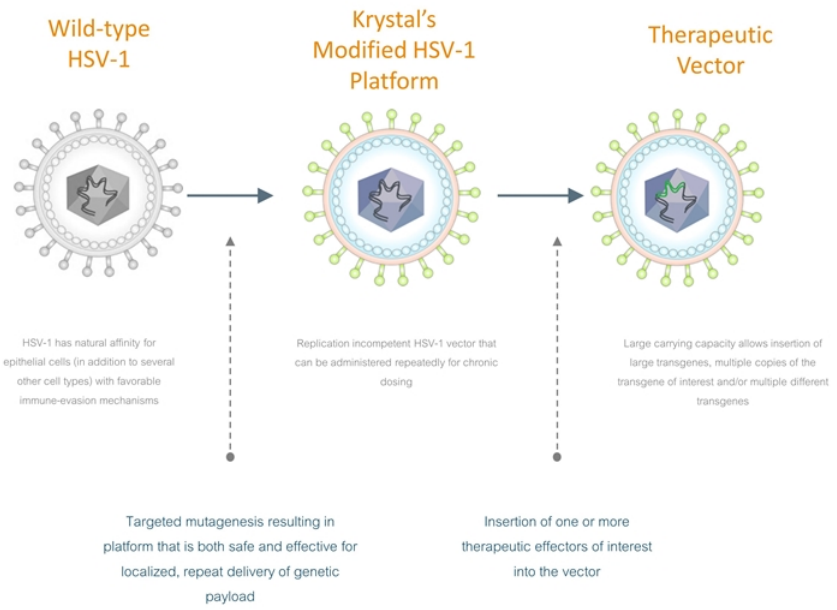
© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Krystal

Our technology platform enables noninvasive, redosable gene therapy

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

HSV-1 is positively differentiated vs. other gene therapy technologies



Vector Platform Comparison

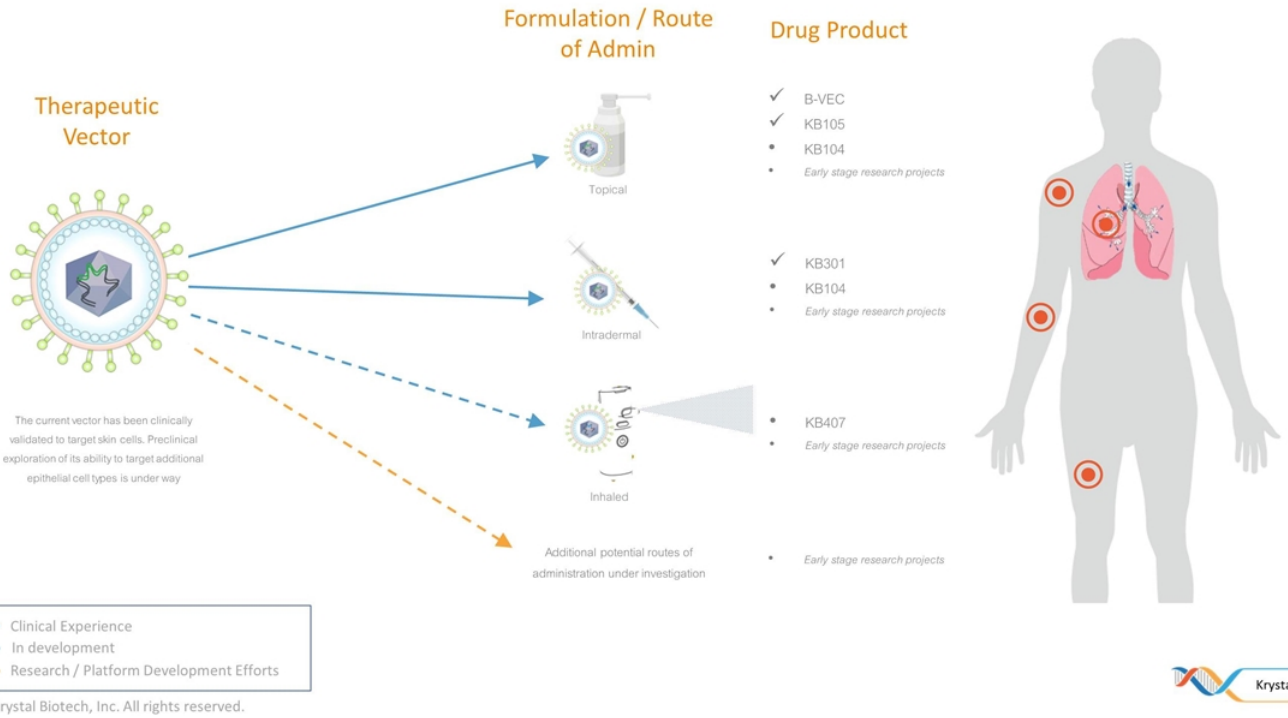
	LV	AAV	HSV-1	LNP
In vivo dosing?	No	Yes	**Yes**	Yes
Baseline antibody exclusion criteria?	No (if *ex vivo*)	Yes	**No**	No
Repeat-dose capabilities?	Yes (if *ex vivo*)	No	**Yes**	Yes
Carrying capacity?	8 kb[1]	<4 kb[1]	**>30 kb**	~12 kb[2]
Integrates payload into host cell DNA?	Yes	No	**No**	No
Regulatory precedent?	Yes	Yes	**Yes**	Yes

1. Lundstrom, K. Viral Vectors in Gene Therapy. *Diseases* 2018, 6, 42.
2. Generation Bio (GBIO) Prospectus. (2020, June 11). Retrieved September 4, 202020, https://www.sec.gov/Archives/edgar/data/1733294/000119312520167812/d924849d424b4.htm

LV = lentivirus
AAV = adeno-associated virus
LNP = lipid nanoparticle

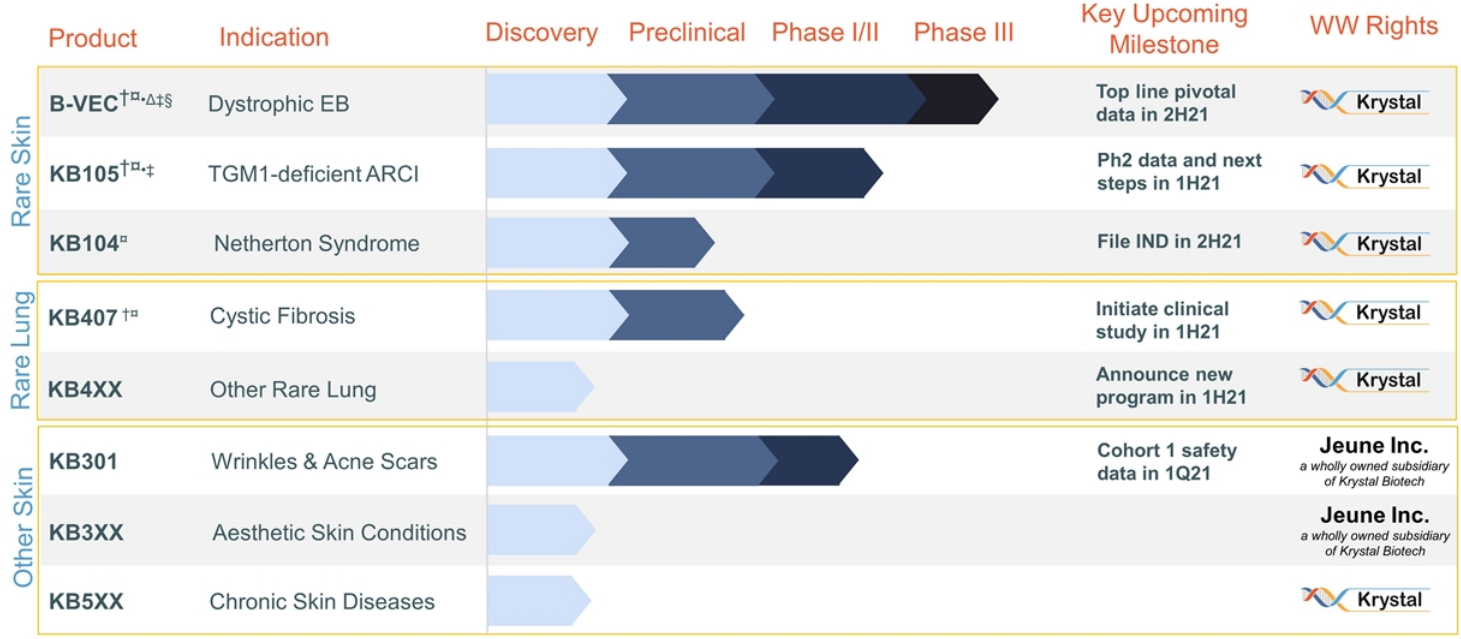
© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Clinically validated platform targeting skin; broad tropism of HSV-1 could unlock additional target tissues



© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Current pipeline



All pipeline compounds are investigational, being evaluated in clinical or pre-clinical studies.

†: FDA Orphan Drug Designation;
¤: FDA Rare Pediatric Disease Designation;
•: Fast-track Designation;
Δ: FDA RMAT designation;
‡: EMA Orphan Drug Designation;
§: EMA PRIME Designation.

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Krystal

Initial focus on rare skin diseases led to rapid clinical POC and pipeline

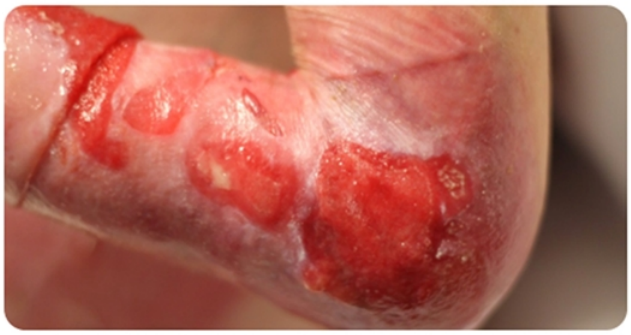
© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Dystrophic epidermolysis bullosa (DEB)

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

Dystrophic Epidermolysis Bullosa

- A rare, genetic skin disease that causes skin to tear or blister from minor contact
- Mutations in the *COL7A1* gene lead to absent or dysfunctional COL7 protein, without which the epidermis does not anchor to the dermis
- The recessive form (RDEB) is the classic, most severe form of the condition. Dominant DEB (DDEB) has a broader range in severity and is often characterized by blistering on the hands, feet, knees, and elbows



Epidemiology

- **Prevalence**: Up to 125,000 people are affected by DEB worldwide[1]
- We believe that there are, at present, approximately 3,000 DEB patients in the US
- **Incidence**: The incidence of DEB is 6.5 per million births in the US[2]

Current Standard of Care

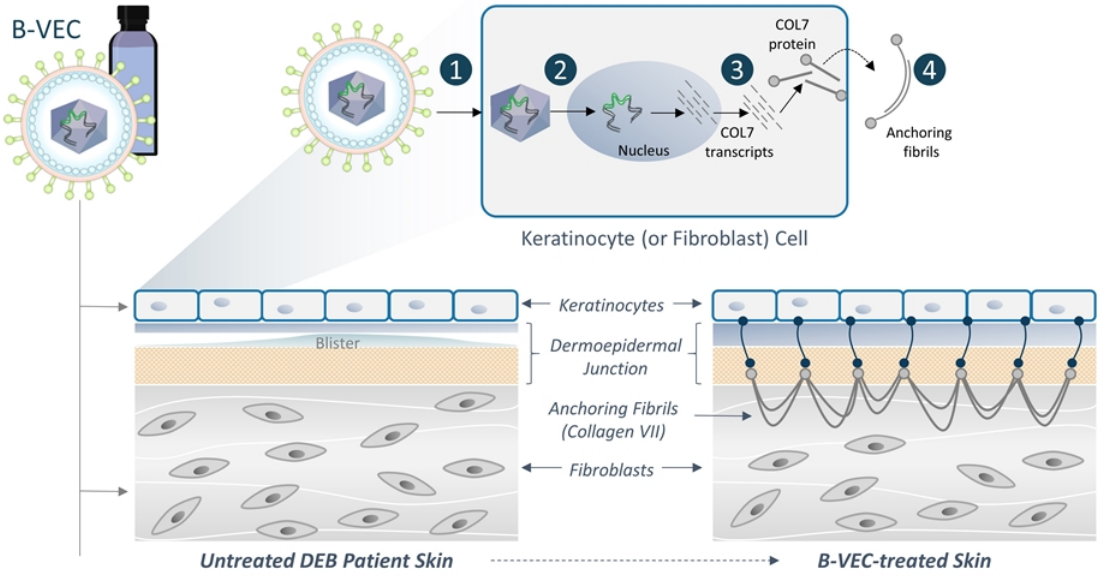
- There are no approved treatments for DEB
- Existing therapies limited to expensive and time-consuming palliative treatments
- Palliative treatments cost $200k – $400k annually[3,4]

1. DEBRA International, http://www.debra-international.org/epidermolysis-bullosa/causes-and-subtypes.html; http://www.debra-international.org/what-is-eb/causes-and-subtypes/deb.html
2. Pfendner EG, Lucky AW. Dystrophic Epidermolysis Bullosa. 2006 Aug 21 [Updated 2015 Feb 26]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet].
3. Rashidghamat E., Mellerio J.E., Management of chronic wounds in patients with dystrophic epidermolysis bullosa: challenges and solutions, Chronic Wound Care Management and Research Volume 2017:4, 45-54
4. GENEGRAFT Report Summary. (2015, February 16). Retrieved December 13, 2016, from http://cordis.europa.eu/result/rcn/156078_en.html

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Beremagene geperpavec (B-VEC) for DEB

Topically applied B-VEC gel is designed to deliver local COL7 expression and molecular correction



1. B-VEC enters the compromised skin of DEB patients and transduces both keratinocytes and fibroblasts
2. Once in the nucleus of transduced cells the vector genome is deposited (episomally)
3. As a result, *COL7A1* transcripts are generated, allowing the cell to produce and secrete functional COL7 protein
4. The secreted COL7 protein assembles into anchoring fibrils which hold the epidermis and dermis together

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

B-VEC is an investigational therapy being studied in clinical trials

Topical B-VEC was evaluated in a Phase1/2 study

Design

- GEM1/2 (NCT03536143) was an intra-patient comparison of wounds randomized to receive either topical B-VEC or placebo.
- Each patient on-study for ~6 months; 3 months of on-site visits followed by 3-month at-home imaging period
- *Study PI: Dr. Peter Marinkovich (Stanford University)*

Enrollment

- A total of 9 RDEB patients (adult and pediatric) were enrolled in the study; 3 subjects re-enrolled later in the study and were re-randomized for a total of 12 subjects

Dosing

- In the Ph1 portion (n=2) one wound was administered B-VEC and one wound was administered placebo at a dose of 1e8 PFU/wound with varying frequency throughout the study period
- In Phase 2 portion (n=10) 2 wounds were administered B-VEC and one wound was administered placebo (except 1 patient who was 1:1) at doses of either 2e8, 3e8, 6e8 or 8e8 PFU/wound with varying frequency throughout the study period

Key Endpoints

Safety measures

- AEs, including clinically significant changes in laboratory results, vitals, and physical exam findings
- Viral shedding was analyzed through the collection of blood, urine, and skin swabs, and antibodies to HSV and COL7 were analyzed through collection of serum

Efficacy measures

- Level of collagen VII (COL7) in B-VEC-administered skin as measured by immunofluorescence; presence of anchoring fibrils as measured by immunoelectron microscopy
- Wound closure (change in wound surface area relative to baseline), time to wound closure, and duration of wound closure, all relative to placebo

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Repeat doses of topical B-VEC were well tolerated; COL7 expression and molecular correction established

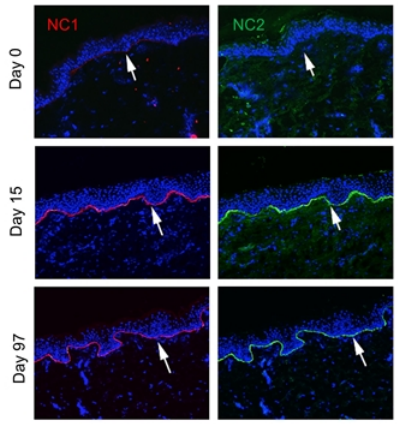
Increasing doses and dosing frequency were well tolerated

- In the Ph1/2 trial, the number of repeat doses per wound ranged from 4 to 41; the PFU per wound ranged from 1e8 to 8e8
- No treatment-related serious AEs were reported; AEs deemed possibly related were mild (n=7) or moderate (n=1) and self-limiting
- No immune response or blistering observed around the sites of administration following first and repeat doses
- Blood and urine samples collected throughout the study revealed:
  - No systemic viral shedding
  - No adverse events associated with routine labs (chemistry and hematology)
- Some patients had baseline COL7 and/or HSV-1 antibodies which did not impair efficacy or impact tolerance of therapy

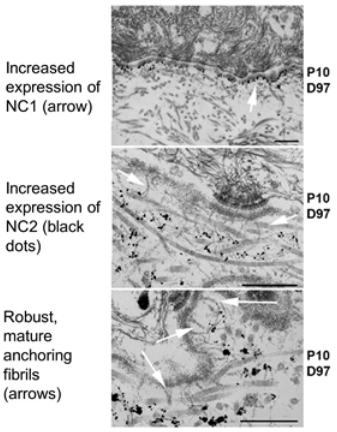
Molecular correction established and correlated with wound healing

- Expression and correct localization of full-length COL7 was observed following B-VEC therapy, evidenced by presence of *both* NC1 and NC2 domains and visible anchoring fibrils on IEM.

Baseline, Days 15 and 97 collagen VII expression using NC1 and NC2 specific antibodies (patient 10)



Immunoelectron microscopy shows mature anchoring fibrils at day 97 (patient 10)



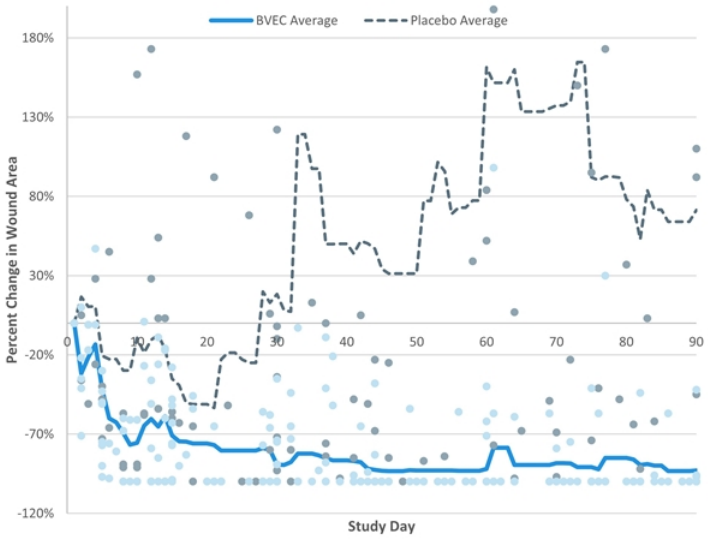
Arrows indicate basement membrane zone

B-VEC is an investigational therapy being studied in clinical trials

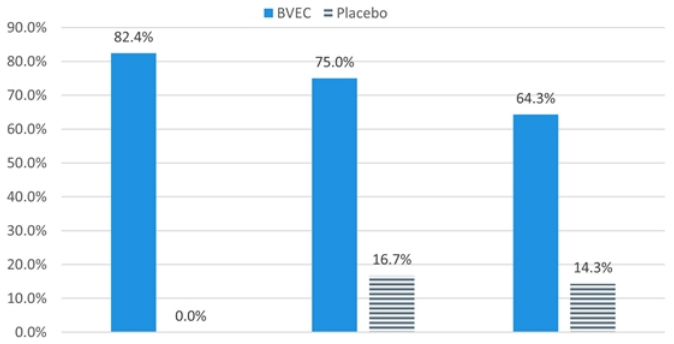
© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

B-VEC showed statistically significant benefit in wound healing relative to placebo

Percent change in wound area from (individual measurements and average) from Day 0 to 90



Percentage of wounds reaching 100% closure at weeks 8, 10 and 12



	Week 8	Week 10	Week 12
B-VEC	82.4% (14/17)	75.0% (12/16)	64.3% (9/14)
Placebo	0.0% (0/8)	16.7% (1/6)	14.3% (1/7)
p-value*	0.0001	0.0155	.0384
Combined p-value*	<0.0001		

*based on Cochran-Mantel Haenszel (CMH) Test Without Adjusting for Week-to-Week Placebo Variability
** based on the Breslow-Day for Homogeneity and Cochran-Mantel-Haenszel (CMH)Tests

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

B-VEC is an investigational therapy being studied in clinical trials

The pivotal GEM-3 study is enrolling; top line data expected in 2021

Design

- GEM-3 (NCT04491604) is a randomized, double-blind, intra-patient comparison of wounds randomized to receive either topical B-VEC or placebo.
- Each patient on-study for approximately 7 months: the 6-month dosing period followed by a 30-day safety follow up

Enrollment

- Approximately 30 DEB subjects (adult and pediatric) will be enrolled across 6 trial sites in the US
- Each subject provides at least 1 pair (up to 3) of primary target wounds, 1 randomized to B-VEC and the other to placebo
- In addition to the primary target wound pair(s), additional wounds (secondary wounds) may be selected to be treated with B-VEC in an open-label manner

Efficacy Endpoints

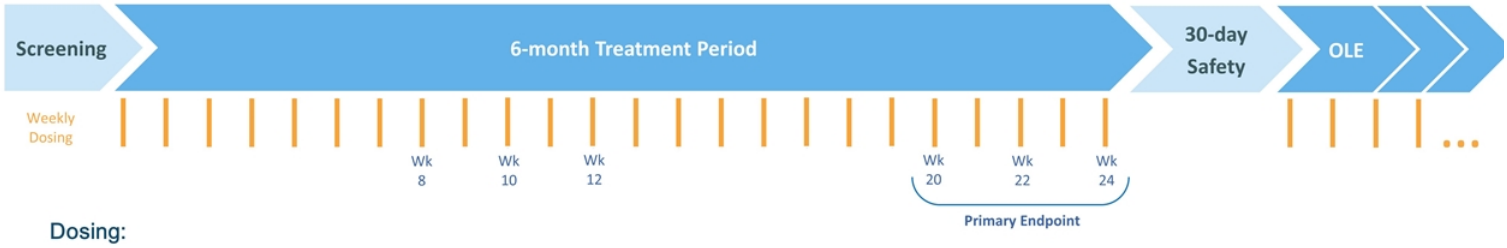
- Primary
- Complete wound healing, determined by the Investigator, as compared to baseline in B-VEC treated wounds versus placebo treated at weeks 20, 22 and 24
- Secondary
- Complete wound healing, determined by the Investigator, as compared to baseline in B-VEC treated wounds versus placebo at weeks 8, 10 and 12
- Mean change in pain severity (using either a VAS or FLACC-R Scale) per primary wound site associated with wound dressing changes
- The proportion of primary wound sites with ≥75% would healing as compared to baseline at Week 24 using Canfield photography quantitation

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

B-VEC is an investigational therapy being studied in clinical trials

Phase 3 trial is well powered and inclusive of a broad patient population

*The trial is designed to maximize chances of success while maintaining potential for a broad label, inclusive of **chronic and recurring wounds of any size** in RDEB or DDEB patients*



Dosing:

- Primary wounds will be treated once weekly with a fixed dose until wound closure; should a wound re-open, weekly dosing will resume at the assigned dose until wound closure
- The fixed dose per wound is dependent on the size of the wound at baseline and ranges from $4x10^8$ to $1.2x10^9$ PFU per wound
- Each patient is allowed a maximum weekly dose of B-VEC; if that maximum is not reached in dosing primary wounds, additional secondary wounds may be chosen and treated with B-VEC in an open label manner
- The maximum weekly dose, administered once weekly per patient, is defined by patient age (right)

Maximum Weekly Dose Per Subject:	
Age	**Max Weekly Dose**
≥ 6 months to < 3 years	1.6x10^9 PFU/week
≥ 3 years to < 6 years	2.4x10^9 PFU/week
≥ 6 years	3.2x10^9 PFU/week

Key Design Elements:

- No restriction on chronic or recurring wounds
- Maximum weekly dose allows for flexibility to treat multiple and / or larger wounds
- Inclusive of RDEB *and* DDEB patients

B-VEC is an investigational therapy being studied in clinical trials

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Autosomal Recessive Congenital Icthyosis associated with TGM1 mutations

Transglutaminase-1 deficiency is associated with increased mortality in the neonatal period and has a dramatic impact on quality of life

Autosomal Recessive Congenital Ichthyosis (ARCI) Associated with TGM1

- The most common form of ARCI is caused by an inactivating mutation in the TGM1 gene encoding the enzyme transglutaminase-1, a protein that is essential for the proper formation of the skin barrier
- The condition is characterized by thick, dry, scaly skin, increased trans-epidermal water loss (TEWL), risk for dehydration, sepsis, skin malignancies, etc

Epidemiology[1-8]

- **Prevalence:** There are approximately 20,000 people affected by TGMI related icthyosis worldwide (~1,800 US; 3,000 EU; 18,000 ROW)
- **Incidence:** It is estimated that around 350-400 babies are born with the condition each year, worldwide

Current Standard of Care

- There are no approved treatments for ARCI associated with TGM1
- Topical and systemic retinoids and time-consuming supportive treatments (up to 4 hours a day of skin care) are most often used

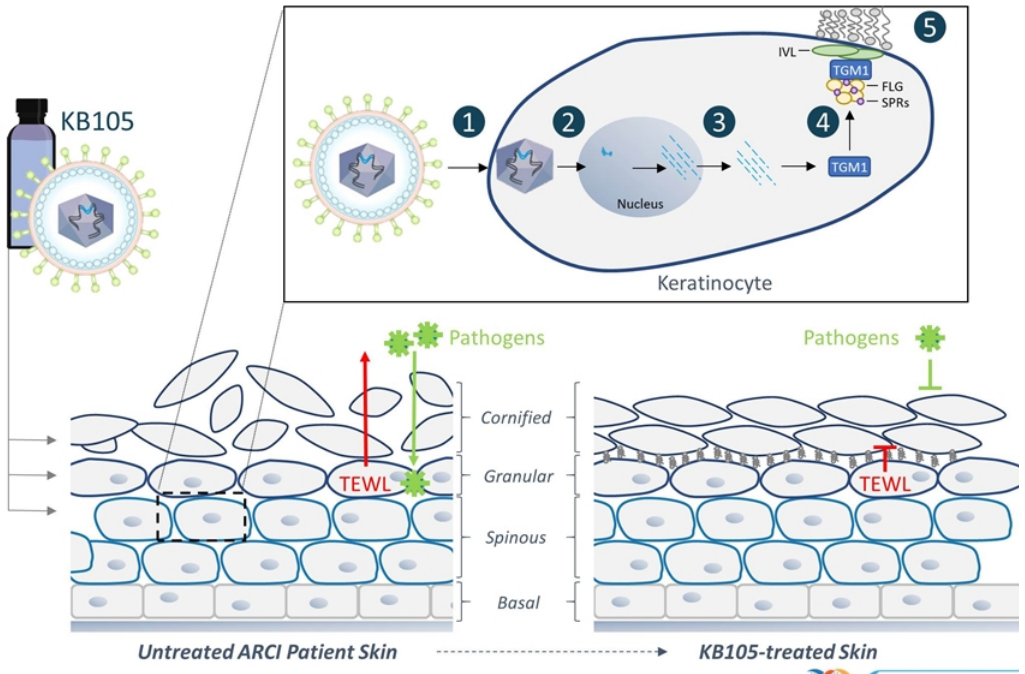
1. Rodriguez-Pazos et al. *Actas Dermosifiliogr.* 2013 May;104(4):270–284;
2. Dreyfus et al. *Orphanet J Rare Dis.* 2014 Jan 6;9:1;
3. Hernandez-Martin et al. *J Am Acad Dermatol.* 2012 Aug;67(2):240–244;
4. Pigg et al. *Eur J Hum Genet.* 1998 Nov-Dec;6(6):589–596.
5. Pigg et al. *Acta Derm Venereol.*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

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

KB105 for TGM1 associated ARCI

Topically applied KB105 delivers multiple copies of the human transglutaminase 1 ("TGM1") gene

1. KB105 enters permeabilized skin and transduces keratinocytes (native TGM1-producing cells)
2. KB105 is transported into the nucleus of transduced cells and the vector genome is deposited (episomally)
3. *TGM1* transcripts are generated, which allows the cell to produce functional TGM1 protein that localizes to the cell membrane
4. TGM1 crosslinks target proteins (*e.g.*, filaggrin (FLG), involucrin (IVL), small proline-rich proteins (SPRs)) to aid in the formation of the cornified cell envelope
5. This layer, known as the stratum corneum, acts as a mechanical barrier to protect against transepidermal water loss (TEWL) and entry of infectious agents



KB105 is an investigational therapy being studied in clinical trials

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

KB105 is being evaluated in a Phase1/2 study

Design

- The Ph1/2 trial (NCT04047732) is an open label, intra-patient comparison of KB105 and placebo
- Each patient on-study for approximately six months; 3 months of on-site visits followed by 3-month at-home imaging period
- *Study PI: Dr. Amy Paller (Northwestern University)*

Enrollment

- ~6 TGM1-ARCI subjects will be enrolled across 2 sites; three Ph1 patients were enrolled at Paddington Testing Company (Philadelphia); Ph2 subjects will be enrolled at Northwestern (Chicago)

Dosing

- In the Ph1 portion (n=3) one or two ~20cm^2 target areas were administered placebo, and 3 target areas were administered 2x10^9 PFU with varying frequency over ~60-90 days
- In Ph1, topical and microneedle administration was evaluated; in Ph2 topical administration will be utilized

Key Endpoints

Safety measures

- AEs, including clinically significant changes in laboratory results, vitals, and physical exam findings
- Viral shedding analyzed through the collection of blood, urine, and skin swabs; antibodies to HSV and TGM1 analyzed through collection of serum

Efficacy measures

- Level of transglutaminase 1 in KB105-administered skin as measured by immunofluorescence microscopy
- Improvement of disease severity in the treatment area assessment through Investigator's Global Assessment (IGA)
- Improvement of disease severity in the treatment area through use of the Visual Index for Ichthyosis Severity scale, lamellar (VIIS-L) standard assessment

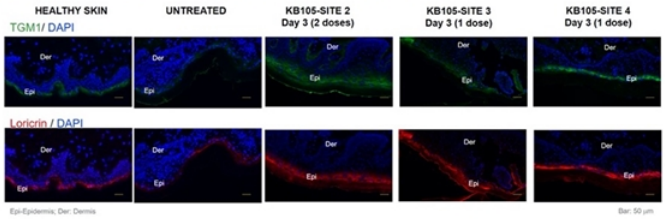
© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Initial data shows repeat dosing of KB105 to be well tolerated; molecular and phenotypic improvement evident

KB105 Was Well Tolerated and Generated Functional TGM1 protein

- Repeat dosing with KB105 was well tolerated with no drug related AEs and no immune response to HSV or TGM1
- No vector shedding detected in swabs, blood or urine in all three patients
- KB105 treatment restored functional TGM1 protein expression and activity in all treated sites
- KB105-expressed TGM1 was correctly localized in the epidermis, colocalizing with Loricrin, and was functionally active
- qPCR, IF, and in situ analyses demonstrated similar delivery efficacy of TGM1 DNA from single and repeat administration

Subject 1: Treatment Restored TGM1 Expression to Normal Levels

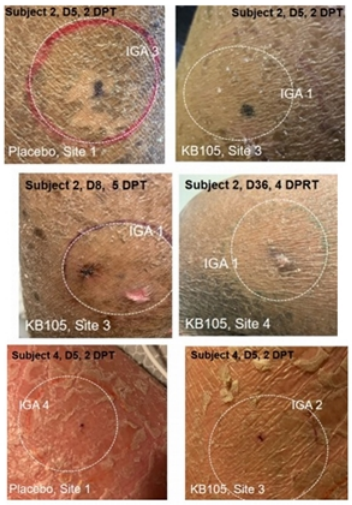


Phenotypic Improvement Evident After Topical and Microneedle Application

- Phenotypic evaluation limited by small treatment areas, but KB105 treated areas showed reduced reversion to ichthyotic scaling phenotype

DPT: Days Post Treatment

DPRT: Days Post Re-Treatment



KB105 is an investigational therapy being studied in clinical trials

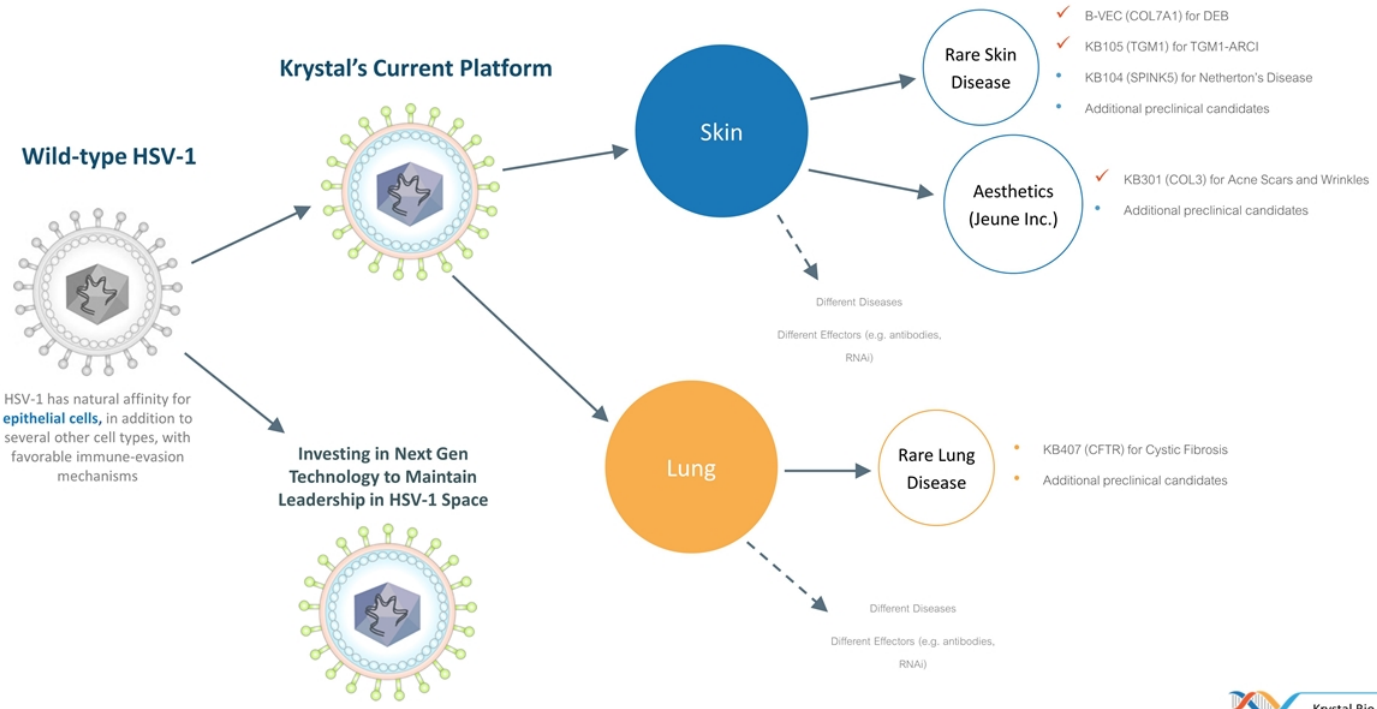
© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Krystal

Leveraging platform to target new tissues and larger indications

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

HSV-1 has potential beyond rare skin diseases



© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

KB407 for cystic fibrosis

Gene therapy approaches have been tried and failed in their attempts to replace CFTR protein

- Viral (adenovirus and AAV) and non-viral (DNA plasmids and stabilized mRNA) approaches have been tested in more than 25 clinical trials enrolling >470 patients
- Past approaches suffer from some combination of physical limitations for large cargo, low efficiency of gene transfer, toxicity, immune intolerance, product instability, and burdensome delivery

We are developing KB407 as an inhalable, repeat dose gene therapy that delivers the full human CFTR gene

- ✓ Replication incompetent HSV-1
- ✓ Delivers two copies of full length, human CFTR protein (mutation agnostic approach)
- ✓ Duration of nebulization expected to be under 30 minutes, using a commercially available nebulizer
- ✓ Episomal delivery of CFTR gene does not disrupt cell DNA
- ✓ Ability to re-dose and/or adjust dose over time as lung cells turnover

Our vector can be formulated and delivered via nebulizer with no significant change in activity

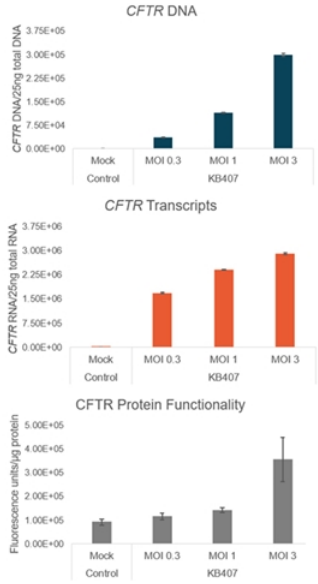
- In vitro data shows KB407 can be nebulized, successfully transduce target lung cells and induce expression of fully functional and properly localized CFTR

KB407 is an investigational therapy being studied in preclinical trials

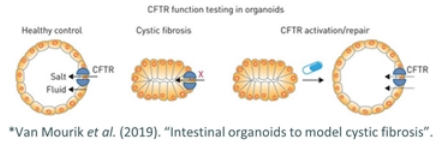
© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Preclinical data supports KB407 in CF and broader development in lung disease

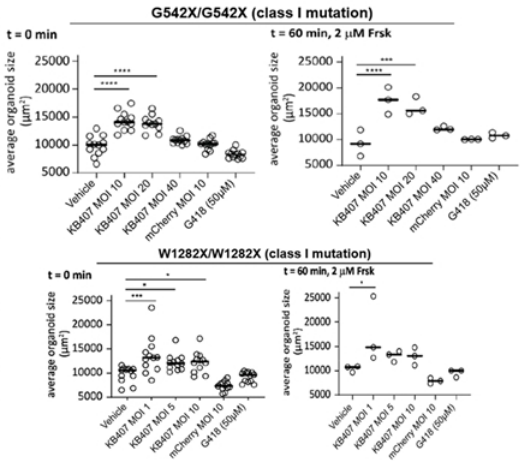
Robust, dose-dependent CFTR expression and functional correction in 2D airway epithelial cell culture



KB407-mediated functional correction of CF phenotype in clinically relevant 3D organotypic system (HUB)



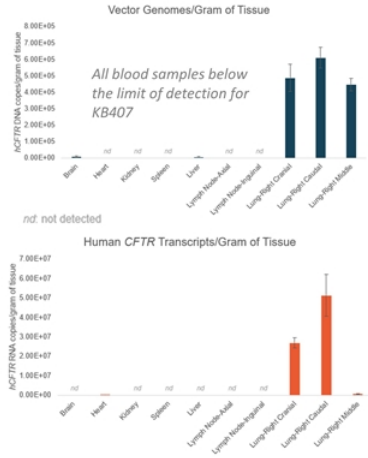
*Van Mourik *et al.* (2019). "Intestinal organoids to model cystic fibrosis".



KB407 is an investigational therapy being studied in preclinical trials

Two repeat doses of KB407 in a nonhuman primate were well tolerated and distributed broadly throughout the lung

- No abnormal cage-side/clinical observations throughout study
- No gross findings noted at time of necropsy



© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

KB301 for aesthetic indications

KB301 and other discovery programs in Aesthetics, are housed in our wholly owned subsidiary, Jeune Inc.

Many Characteristics of Skin Aging are Due to Aberrant Collagen Homeostasis

- Dermal collagen, composed primarily of types 1 and 3 collagen fibrils, representing >90% (dry weight) of human skin
- Declining levels of collagen are caused by reduced collagen biosynthesis and increased collagen fibril fragmentation resulting from both intrinsic (e.g., passage of time, genetics) and extrinsic (e.g., chronic light exposure, pollution) pressures

KB301 aims increase neocollagenesis, thereby correcting the molecular defect underlying the aged phenotype

- KB301 is designed to deliver the gene for full-length type III collagen (COL3)
- It is injected directly into the area of interest, with the goal of targeted collagen production by the body's own cells

KB301 is currently being evaluated in a Phase 1 trial (NCT04540900)

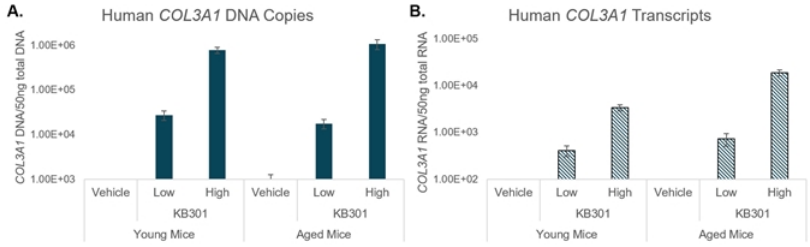
- The open label, dose ranging study will evaluate repeat dosing of KB301 injections
- Safety Endpoints
  - Safety and tolerability of KB301 based on the assessment of adverse events, physical examinations, vital signs, and clinical laboratory test results
- Efficacy Endpoints
  - Cohort 1 - COL3A1 transgene expression 2-days post-dose, as measured by qRT-PCR of skin biopsies.
  - Cohort 2 - Investigator assessment of wrinkle improvement over baseline through the use of a 5-point Lemperle Scale; subject assessment of aesthetic improvement over baseline based on a 5-point Subject Satisfaction Score (SSS).
  - Cohort 3 - Investigator assessment of acne scar improvement over baseline through the use of a 6-point Global Scale for Acne Scar Severity (SCAR-S); subject assessment of aesthetic improvement over baseline based on a 5-point Subject Satisfaction Score (SSS)

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

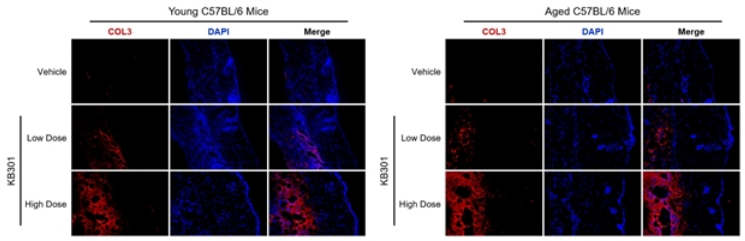
KB301 is an investigational therapy being studied in preclinical trials

Preclinical data supports KB301 development aesthetic indications

A dose dependent increase in COL3A1 observed in young and aged mice



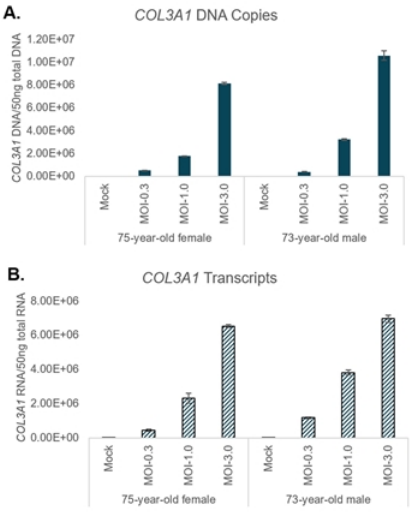
- Human COL3A1 DNA (A) and transcript (B) levels in treated skin 48-hours after intradermal administration of KB301 to young (6-8 weeks) and aged (13 mo) mice (above)
- COL3 protein localization 48-hours after intradermal administration of KB301 to young (6-8 weeks) and aged (13 mo) mice (below)



KB301 is an investigational therapy being studied in preclinical trials

Similar dose dependent effect was observed in primary human dermal fibroblasts

- COL3A1 DNA (A) and transcript levels (B) upon KB301 transduction of primary aged HDFs



© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Krystal

In-house GMP manufacturing to support clinical and commercial needs

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Platform supported by in-house manufacturing capacity and expertise

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

- Maintains control of IP/trade secrets relating to manufacturing process
- Adheres to internal process and production schedules, avoiding use of high demand gene therapy CMOs

Upstream process using stable producer cell lines has cost and regulatory benefits

- Stable complementary cell lines are developed in-house are used in established methods for production of consistent batches
- Eliminates the need for multiple cGMP qualifications of plasmids and variability in transfection efficiency from batch to batch
- Scalable from clinical phase to commercial

We have successfully developed a robust and reproducible downstream process

- Work conducted in an aseptic closed system process
- The same process is leveraged across pipeline with minimal redevelopment effort between product candidates
- Compliant with global regulatory requirements

Facility operational;
Validated to produce pivotal and clinical materials
Size: 7,500 sq. ft.


ASTRA (rendering)

Operational in 2022
Size: 150,000 sq. ft.

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Financials and Milestones

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Krystal summary (updated)

A fully integrated, clinical stage gene therapy company powered by proprietary HSV-1 vector technology

Current Status and Milestones

Rare Skin

- **B-VEC:** Pivotal GEM-3 trial currently enrolling with enrollment completion anticipated in 1Q21; topline data expected 2H21. Commercial planning in US and EU underway
- **KB105:** Phase 2 study ongoing; initial data from the first Phase 2 patient and an update on the next Phase 2 cohorts expected in 1H21
- **KB104:** Preclinical work ongoing; IND anticipated in 2H21

Aesthetics (Jeune Inc.)

- **KB301:** Phase 1 trial in acne scars and wrinkles ongoing; Initial cohort 1 safety data expected in 1Q21
- Update on Jeune Inc. / aesthetics strategy in 1Q21

Rare Lung

- **KB407:** pre-IND work ongoing; clinical trial initiation anticipated in 1H21
- Announcement of development candidate in a 2nd genetic lung disease anticipated in 1H21

Platform

- **Manufacturing:** Ancoris facility (7,500 sqft) currently supplying all clinical material and will supply initial phase of B-VEC launch; Astra facility (150,000 sqft) construction underway, completion anticipated in 2022
- **Next Gen Tech:** Evaluation of novel effectors, routes of administration, and tissue tropism underway

Cash balance as of September 30, 2020: $286.4M

- All four lead programs are PRV eligible

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.

Krystal

The Leader in Redosable Gene Therapy for Rare Disease

JANUARY 2021

© Copyright 2021 Krystal Biotech, Inc. All rights reserved.