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): November 9, 2020

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 2.02 Results of Operation and Financial Condition.

On November 9, 2020, Krystal Biotech, Inc., a Delaware corporation (the "Company"), announced its financial results for the quarter ending September 30, 2020. A copy of the Company's press release is attached as Exhibit 99.1 hereto and incorporated by reference herein.

The information concerning financial results in this Form 8-K and in Exhibit 99.1 shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section. The information concerning financial results in this Form 8-K and in Exhibit 99.1 shall not be incorporated into any registration statement or other document filed with the Securities and Exchange Commission by the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific reference in such filing.

Item 7.01 Other Events.

In its press release, the Company also disclosed that new *in vivo* data from the ongoing preclinical development of KB407 for cystic fibrosis shows successful nebulization, distribution of vector and functional protein expression throughout the lung in mice and a nonhuman primate. A copy of the Company's presentation on the KB407 data and a copy of the Company's corporate presentation reflecting such updates regarding KB407 are attached hereto as Exhibit 99.2 and Exhibit 99.3, respectively, and are incorporated by reference herein. Each presentation is also available at the Company's website located at www.krystalbio.com.

The information concerning financial results in this Form 8-K and in Exhibits 99.2 and 99.3 shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section. The information concerning financial results in this Form 8-K and in Exhibits 99.2 and 99.3 shall not be incorporated into any registration statement or other document filed with the Securities and Exchange Commission by the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release, dated November 9, 2020.
99.2	Presentation on KB407 for the treatment of cystic fibrosis.
99.3	Corporate Presentation for November 2020.
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: November 9, 2020

KRYSTAL BIOTECH, INC.

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

Krystal Biotech Reports Third Quarter 2020 Financial Results and Provides Update on Operational Progress

- *Pivotal GEM-3 study of B-VEC in DEB expected to complete enrollment in early 2021*
- *Initiated the Phase 1 Study of KB301 in Facial Wrinkles and Acne Scars*
- *Today announced additional in vivo preclinical data supporting the development of KB407 in cystic fibrosis*
- *Strong balance sheet with cash, cash equivalents and short-term investments of $286.4 million as of September 30, 2020*
-

PITTSBURGH, November 9, 2020 – Krystal Biotech, Inc. (Nasdaq:KRYS), a fully integrated gene therapy company driven by its proprietary, engineered herpes simplex virus type 1 vector (HSV-1) platform, today reported financial results and key operational progress updates for the third quarter ended September 30, 2020.

“Despite the challenges presented by COVID in this quarter, we initiated a pivotal trial for DEB, a phase 2 trial in ARCI and a phase 1 trial in aesthetic skin conditions, and I thank my entire team for their efforts in these difficult times,” said Krish Krishnan, Chairman and CEO of Krystal Biotech, Inc. “I am particularly encouraged by progress with KB407 for the treatment of cystic fibrosis. The *in vivo* animal data reported today demonstrates our ability to deliver functional CFTR throughout the lung, which is encouraging in this indication and gives us confidence to explore additional diseases of the lung where delivery of a therapeutic transgene may be beneficial.” he added.

He further noted “With the granting of Rare Pediatric Designation for this program by the FDA this quarter, we are now eligible to receive a Priority Review Voucher for KB407 as well as for B-VEC, KB105, KB104.”

Program Highlights & Upcoming Events

Beremagene Geperpavec (B-VEC) for DEB

- Enrollment in the ongoing pivotal GEM-3 study is proceeding well and enrollment completion is anticipated in early 2021. The trial is a randomized, double-blind, intra patient placebo-controlled multicenter trial designed to evaluate the efficacy and safety of B-VEC for patients suffering from both recessive and dominant dystrophic forms of Epidermolysis Bullosa.

- Details of the pivotal study can be found at www.clinicaltrials.gov under NCT identifier NCT04491604.
- Top line data and BLA filing are anticipated in 2021, in line with prior guidance. Data from this trial will also form the basis of an MAA filing in the EU which is anticipated to occur shortly after the BLA filing.

KB105 for TGM1-ARCI

- In September 2020, preclinical data supporting the development of KB105 in TGM1-related Autosomal Recessive Congenital Ichthyosis (ARCI) were published online ahead of print in the peer-reviewed *Journal of Investigative Dermatology*.
- Dosing of the 4th patient in the Phase 1/2 study of KB105 in patients with TGM1 deficient autosomal recessive congenital ichthyosis (ARCI) has completed. Treatment of a larger area and therefore higher dose is being evaluated. Data from this patient together with the data from the 3 initial patients, will help determine next steps.
- Details of the Phase 2 study can be found at www.clinicaltrials.gov under NCT identifier NCT04047732.
- The Company plans to present an update on this program in the first half of 2021.

KB407 for Cystic Fibrosis

- New *in vivo* data from the ongoing preclinical development of KB407 shows successful nebulization, distribution of vector and functional protein expression throughout the lung in mice and a nonhuman primate. More detailed results are available in a corporate presentation available under the Investors section of our website, here.
- In September 2020, KB407 was granted Rare Pediatric Designation by the FDA.
- During the third quarter of 2020, we received a Notice of Allowance for our patent application covering methods of using KB407 for the treatment of Cystic fibrosis and other diseases causing progressive lung destruction, which is expected to issue as US Pat. No. 10,829,529 on November 10th, 2020. As previously announced, in August 2020, the FDA granted Orphan Drug Designation for KB407.
- Pre-clinical validation work is ongoing, and the Company is on track to initiate a clinical study in the first half of 2021.

KB301 for Aesthetic Indications

- In October 2020, positive preclinical data supporting the ongoing development of KB301 in aesthetic indications was presented at the American Society for Dermatologic Surgery (ASDS) 2020 Virtual Meeting.
- During the third quarter of 2020, the United States Patent Office (USPTO) granted U.S. Patent No. 10,786,438 which covers pharmaceutical compositions comprising HSV vectors encoding one or more cosmetic proteins, as well as methods of their use for improving skin condition, quality, and/or appearance.
- The Phase 1 study of KB301 for the treatment of shallow to moderately deep facial wrinkles and severe atrophic acne scars initiated in August 2020.
- Initial safety data from this study is anticipated in early 2021, followed by initial efficacy data in 2H21.

KB104 for Netherton Syndrome

- The Company continues to work towards an IND filing, which is anticipated in 2021.

Financial results for the quarter ended September 30, 2020

- Cash, cash equivalents and short-term investments totaled $286.4 million on September 30, 2020.
- Research and development expenses for the third quarter ended September 30, 2020 were $5.1 million, compared to $3.9 million for third quarter 2019.
- General and administrative expenses for the third quarter ended September 30, 2020 were $4.6 million, compared to $1.5 million for third quarter 2019.
- Net losses for the quarters ended September 30, 2020 and 2019 were $9.6 million and $4.3 million, or ($0.49) and ($0.25) respectively, per common share (basic and diluted).
- For additional information on the Company's financial results for the third quarter ended September 30, 2020, refer to form 10-Q filed with the SEC.

About Krystal Biotech

Krystal Biotech, Inc. (NASDAQ:KRYS) is a gene therapy company dedicated to developing and commercializing novel treatments for patients suffering from dermatological diseases. For more information, please visit http://www.krystalbio.com.

Forward-Looking Statements

Any statements in this press release about future expectations, plans and prospects for Krystal Biotech, Inc., including but not limited to statements about the development of Krystal's product candidates, such as plans for the design, conduct and timelines of ongoing clinical trials of beremagene geperpavec ("B-VEC"), KB105, KB104, KB301 and KB407; the clinical utility of B-VEC, KB105, KB104, KB301 and KB407, and Krystal's plans for filing of regulatory approvals and efforts to bring B-VEC, KB105, KB104, KB301 and KB407 to market; the market opportunity for and the potential market acceptance of B-VEC, KB105, KB104, KB301 and KB407; plans to pursue research and development of other product candidates; the sufficiency of Krystal's existing cash resources; the unanticipated impact of COVID-19 on Krystal's business operations, pre-clinical activities and clinical trials; 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 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 trials 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 including B-VEC, KB105, KB104, KB301 and KB407, the sufficiency of cash resources and need for additional financing and such other important factors as are set forth under the caption “Risk Factors” in Krystal’s annual and quarterly reports on file with the U.S. Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent Krystal’s views as of the date of this release. Krystal anticipates that subsequent events and developments will cause its views to change. However, while Krystal 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 Krystal’s views as of any date subsequent to the date of this release.

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TellMed Strategies
mary.coyle@tmstrat.com

Source: Krystal Biotech, Inc.

Exhibit 99.2

Krystal

Medicines for Rare Diseases –
An HSV-1-based Gene Therapy Company

KB407 for the treatment of cystic fibrosis

November 2020

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 B-VEC, KB105, KB301, KB407 and the Company's other product candidates; conduct and timelines of clinical trials, the clinical utility of B-VEC, KB105, KB301, KB407 and the Company's other product candidates; plans for and timing of the review of regulatory filings, efforts to bring B-VEC, KB105, KB301, KB407 and the Company's other product candidates to market; the market opportunity for and the potential market acceptance of B-VEC, KB105, KB301, KB407 and the Company's other product candidates, the development of B-VEC, KB105, KB301, KB407 and the Company's other product candidates for additional indications; the development of additional formulations of B-VEC, KB105, KB301, 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; the unanticipated impact of COVID-19 on the Company's business operations, preclinical activities and clinical trials; 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.

Despite recent approvals, there remains significant unmet need in CF

Approximately 10% of CF patients have mutations that are not amenable to current small molecule approaches

Cystic fibrosis (CF) is the most common fatal inherited disease in the United States

- It is autosomal recessive, caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR), a transmembrane anion channel expressed on the surface of epithelial cell responsible for maintaining proper fluid transport
- Loss of CFTR function causes acidification and mucus accumulation in the lungs, provoking recurrent lung infections, uncontrolled inflammation, and bronchiectasis

Currently therapies are not completely corrective, and 10% of patients are ineligible for any therapy at all

- Small molecule correctors work by improving trafficking and processing of the mutated CFTR, though only restore ~50% of protein function in patients with certain amenable mutations
- In the ~10% patients with mutations that do not produce any CFTR protein (null mutations) current therapies are ineffective
- Even in patients who are amenable to therapy, suboptimal efficacy or tolerability issues can limit benefit derived from treatment

Epidemiology of cystic fibrosis[1]

CF Prevalence & Incidence[2]

>70,000 patients with CF worldwide

>30,000 patients in US CF registry[2]

~1,000 new cases of CF diagnosed each year in the US

Krystal

1: World Health Organization (2004). "The molecular genetic epidemiology of cystic fibrosis".
2: US Cystic Fibrosis Foundation.

Gene therapy is an attractive approach; our vector is uniquely positioned to overcome prior limitations

CF is a monogenic disease; replacing the missing or dysfunctional protein could fundamentally correct the defect

Various gene therapy approaches have been tried and ultimately 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

Our HSV-1 vector has potential to overcome prior limitations of CF gene therapy

- ✓ Accommodates large genes and necessary regulatory elements
- ✓ Is amenable to rapid, non-invasive inhaled administration
- ✓ Natural tropism to epithelial cells, e.g., those lining the airways
- ✓ Non-cytotoxic
- ✓ Non-immune stimulating
- ✓ Well suited for repeated administration in highly inflammatory environments

	LV	AAV	HSV-1	LNP
In Vivo Dosing?	No	Yes	**Yes**	Yes
Baseline antibody exclusion criteria?	No (ex-vivo)	Yes	**No**	No
Repeat-dose capabilities?	No	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

Krystal

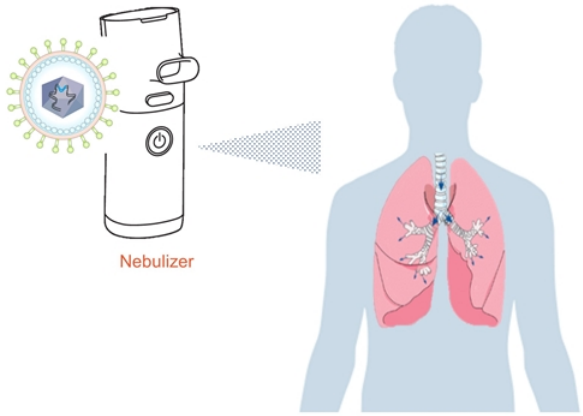
1. Lundstrom, K. Viral Vectors in Gene Therapy. *Diseases* 2018, 6, 42.
2. Generation Bio (GBIO) Prospectus. (2020, June 11). Retrieved September 4, 202020, https://www.sec.gov/Archives/edgar/data/1733294/000119312520167812/d924849d424b4.htm

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

KB407 is an inhaled gene therapy for the treatment of CF

KB407 product characteristics:

- 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

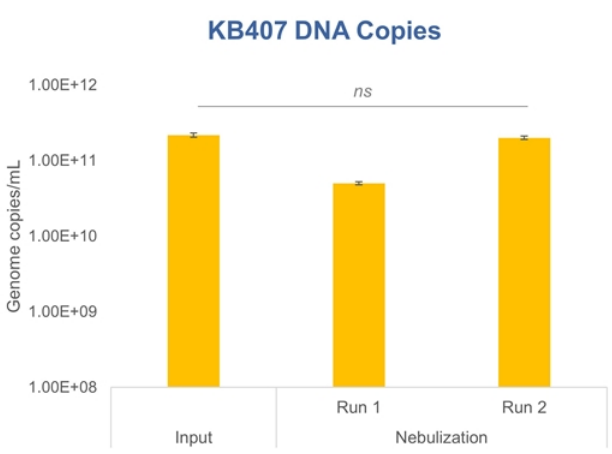


In vitro data shows KB407 can be nebulized, successfully transduce target lung cells and induce expression of fully functional and properly localized CFTR

Krystal

KB407 is amenable to aerosolization without loss of titer

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



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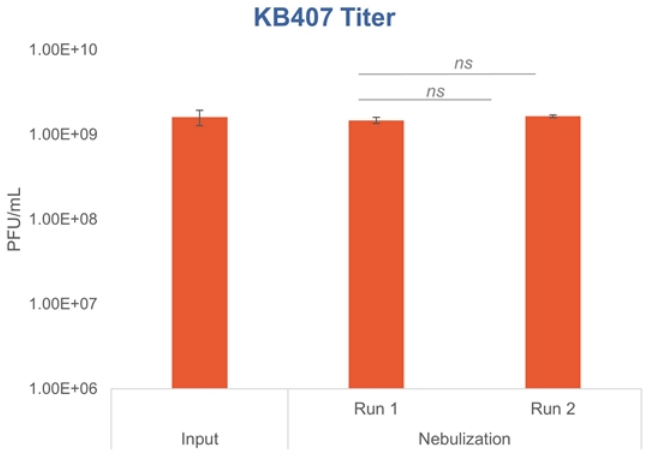
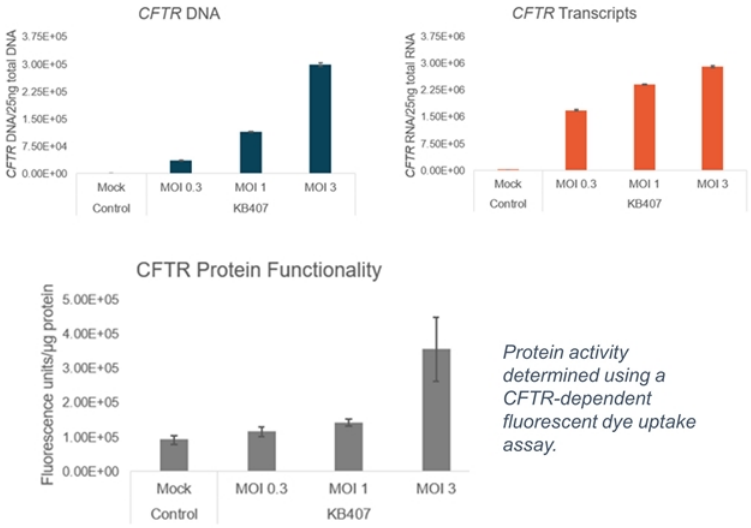


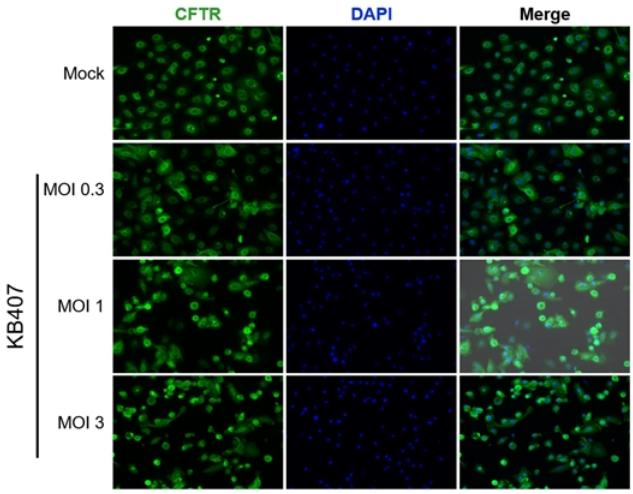
Dose dependent expression observed in CF patient derived airway epithelial cells

KB407 infects primary CF cells in a dose-dependent manner, resulting in robust expression of human CFTR at the transcript and protein levels



Protein activity determined using a CFTR-dependent fluorescent dye uptake assay.

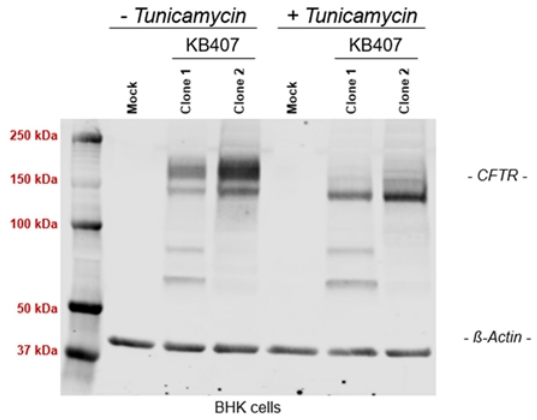
KB407-expressed human CFTR properly localized to the plasma membrane of transduced cells



KB407-Expressed CFTR is Properly Glycosylated in Mammalian Cells

Proper glycosylation indicates the protein has been produced and processed correctly into mature CFTR

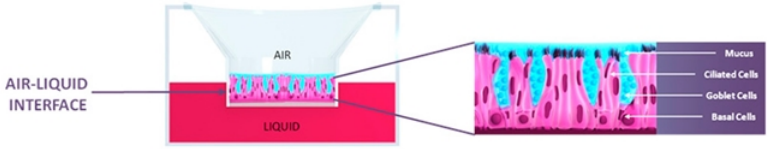
- CFTR protein is assembled on the endoplasmic reticulum-associated ribosome and is eventually trafficked to the cell membrane where it resides
- As the protein moves from one place to the other, various post-translational modifications are made which ultimately produce the complex glycosylated fully mature form of the protein
- Western blot analysis shows that CFTR produced from our backbone is fully glycosylated and would therefore be expected to be properly trafficked and fully functional



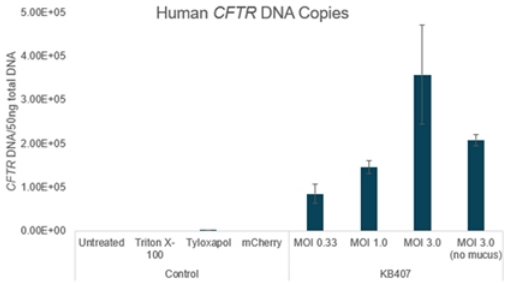
Preliminary *in vitro* data supports KB407 ability to penetrate CF mucus

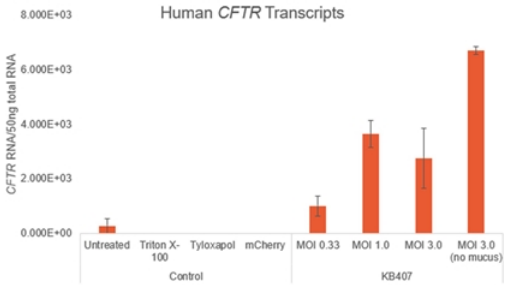
Collaboration with Epithelix using MucilAir™ system derived from F508del CF patient biopsy

The MucilAir™ system provides an *in vitro* replication of the CF airway, including active mucus production



- After 7 days of mucus production, KB407 (in solution) was applied to the apical surface at increasing MOI and compared to control viruses as well as a high MOI
- applied to washed cells (no mucus).
- KB407 transduction and subsequent CFTR increased in a dose dependent manner in the setting of CFTR mucus; CFTR expression no different in the absence of mucus suggesting KB407 penetrates CF mucus





KB407 corrects CF phenotype in clinically translatable organoid model

Krystal

Efficacy in patient derived organoids correlates with clinical efficacy

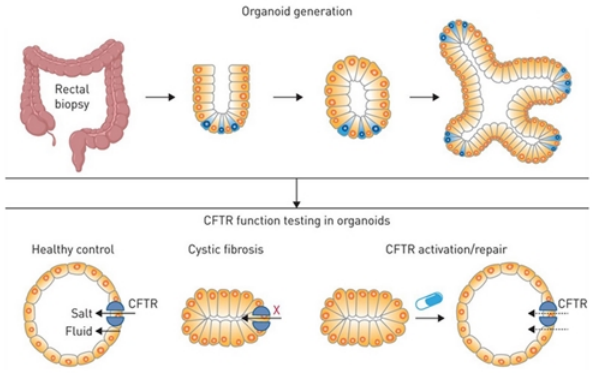
Organoids have proven to be valuable disease models in CF

- They enable high-throughput screening and validation of medicines preclinically
- Patient derived organoids (PDOs) are 3D models that retain the specific genetic and phenotypic characteristics of diseased tissue

KB407 was evaluated in organoids derived from CF patients with class I mutations

- PDOs sourced from Hubrecht Organoid Technology (HUB) provide mutation specific assays for preclinical efficacy assessment
- Cells derived from patients with class I mutations do not create any functional CFTR, thus currently approved CFTR correctors are ineffective

In vitro **drug responses in rectal organoids[1] have been shown to correlate with clinical changes in FEV1 and Sweat Chloride Concentration[2]**



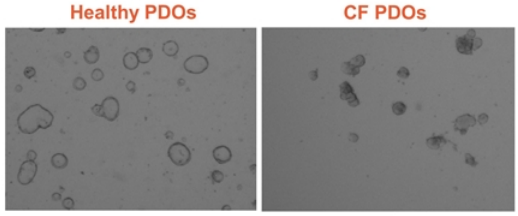
1. Van Mourik *et al.* (2019). "Intestinal organoids to model cystic fibrosis".
2. Berkers et al. (2019). "Rectal Organoids Enable Personalized Treatment of Cystic Fibrosis".

Treatment with KB407 corrected PDO morphology within 24 hours

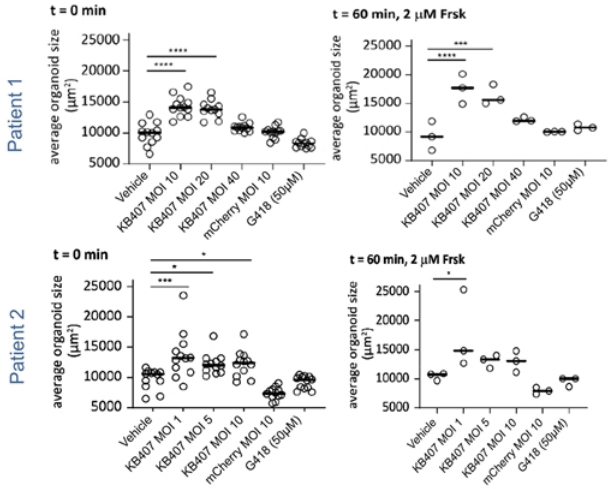
Reference Images

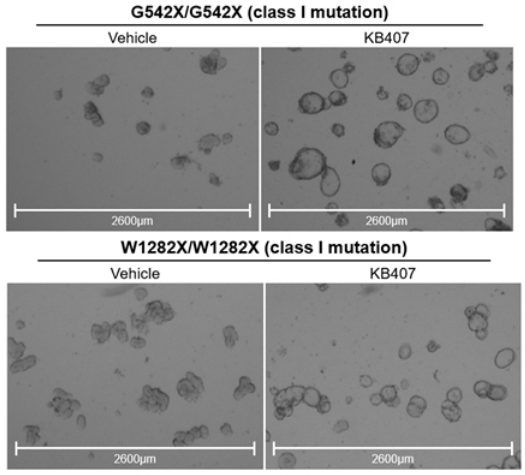
In **healthy patient derived organoids** (left), CFTR protein functions properly and enables water transport across the membrane leading to **plump, round appearing PDOs**

In **PDOs derived from CF patients** (right), CFTR does not work properly and water is not transported causing PDOs to **appear shrunken or shriveled**



Class I PDOs Before and After KB407 Treatment





KB407 is an investigational therapy being studied in preclinical trials

Krystal

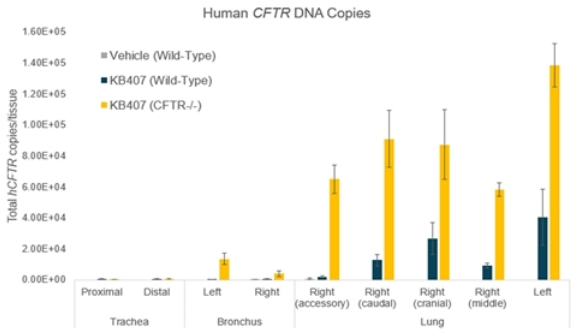
In vivo studies (mice and nonhuman primate) demonstrate successful nebulization of KB407 with broad distribution throughout the lung; no toxicity or significant safety findings were observed

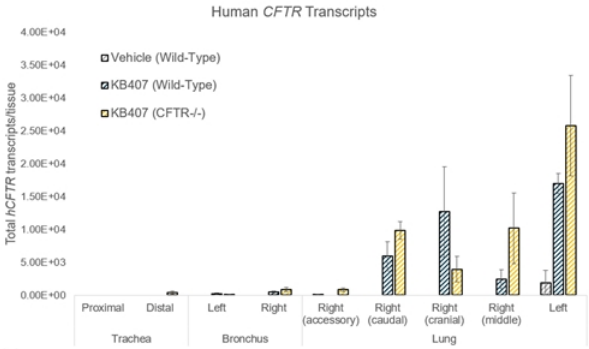
Krystal

KB407 is effectively delivered to the lungs of healthy and CFTR-/- mice

- 3 groups of 4 mice were simultaneously dosed with a single, low dose of KB407
- Mice were observed and vitals were monitored for 2 days with no adverse findings
- After 2 days, whole blood and lung tissue were analyzed for presence of KB407 vector.
- All blood samples below the limit of detection suggesting no systemic exposure
- qPCR analysis shows vector transduction and CFTR expression evenly throughout the lung

Group No.	Mouse Strain	Test Article	Route of Administration	Termination
1	C57BL/6J	Vehicle	Nebulization	48h
2	C57BL/6J	KB407	Nebulization	48h
3	Cftr^{tm1Unc}Tg(FABPCFTR)1 Jaw/J	KB407	Nebulization	48h

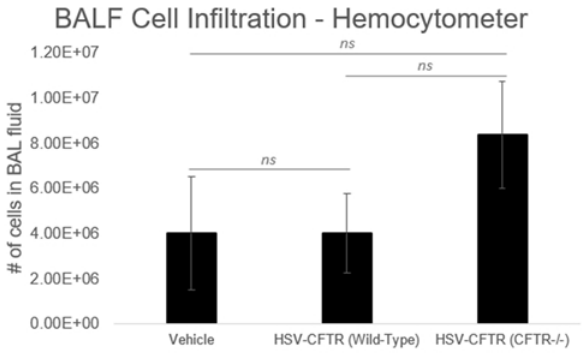


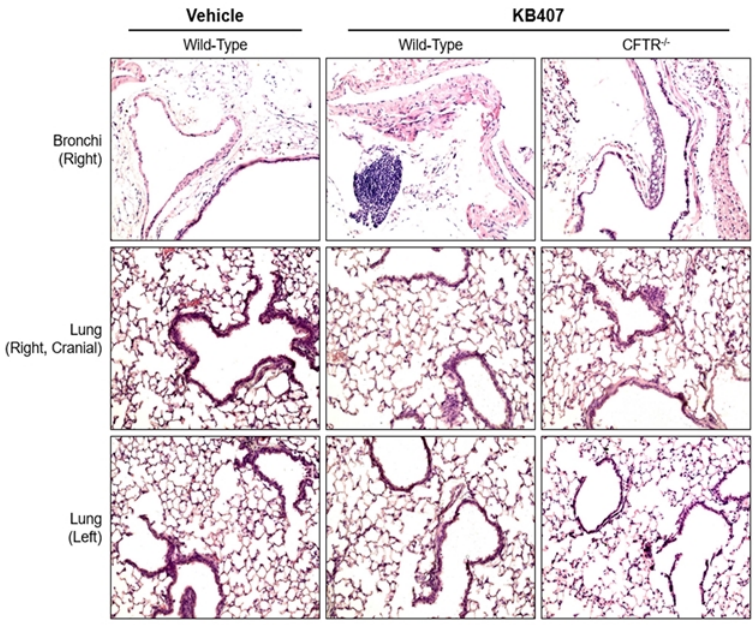


Nebulized KB407 does not induce inflammation or cell infiltration

Qualitative (right) and quantitative (below) analysis shows no evidence of local immune activation

- Certified pathologist found no adverse safety findings (fibrosis, necrosis, immune cell infiltration or immune activation) in any examined lung tissues
- There were no significant changes in cell infiltration between placebo or KB407 exposed animals

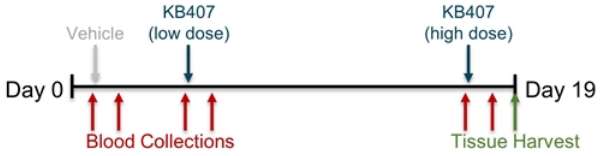




KB407 was safe and well tolerated a nonhuman primate

A single cynomolgus macaque received 2 doses of KB407 two weeks apart

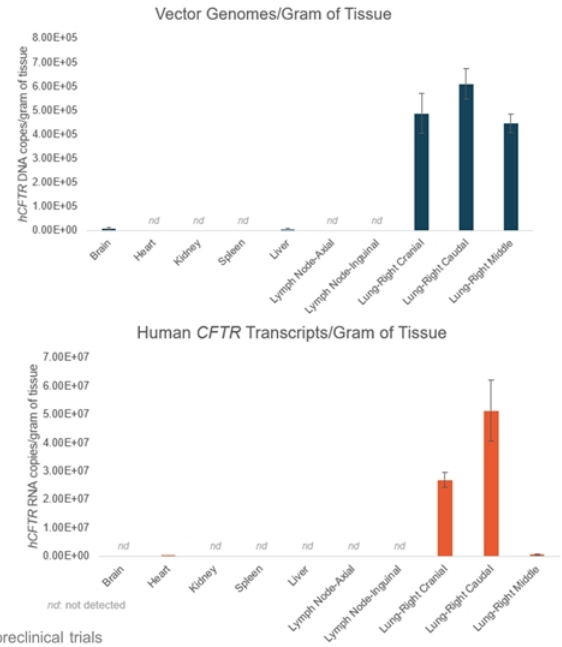
- A single monkey received 3 serial doses of vehicle alone, KB407 low dose and KB407 high dose over 19 days
- At day 19 (2 days following high dose KB407) animals were sacrificed and fill body bioanalysis was conducted
- The left lung was used for microscopic analysis, the right lung was evaluated via qPCR and qRT-PCR



KB407 was safe and well tolerated

- No abnormal cage-side/clinical observations throughout study
- All blood samples below the limit of detection for KB407
- No gross findings noted at time of necropsy
- Hematology and clinical chemistry testing showed no significant changes before vs after any dose administered

KB407 and CFTR was detected throughout lung tissue



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KB407 is an investigational therapy being studied in preclinical trials

KB407 Program Summary

- KB407 infects cells derived from CF patient airways in a dose-dependent manner, resulting in robust expression of human CFTR at the transcript and protein levels
- The vector efficiently produces functional, full-length CFTR protein that properly traffics to the cell membrane
- KB407 transduction leads to a striking alteration of organoid morphology, from a compact budding CF phenotype to a wild-type phenotype, irrespective of the underlying CFTR mutation, within 24 hours of infection at MOIs ranging from 1 to 40
- The corrected cystic morphology of multiple CF PDOs exposed to low doses of KB407 suggests that high levels of exogenous CFTR expressed in a minority of cells is sufficient to establish disease correction
- When delivered via nebulization, KB407 was distributed broadly throughout the lung of mice and a nonhuman primate, resulting in robust human CFTR expression
- Nebulized KB407 was safe and well tolerated, with no toxicity or significant adverse findings after the initial or repeat dose of vector

KB407 Next Steps

- GLP toxicity study in 40 nonhuman primates ongoing
- Clinical trial initiation anticipated in 2021

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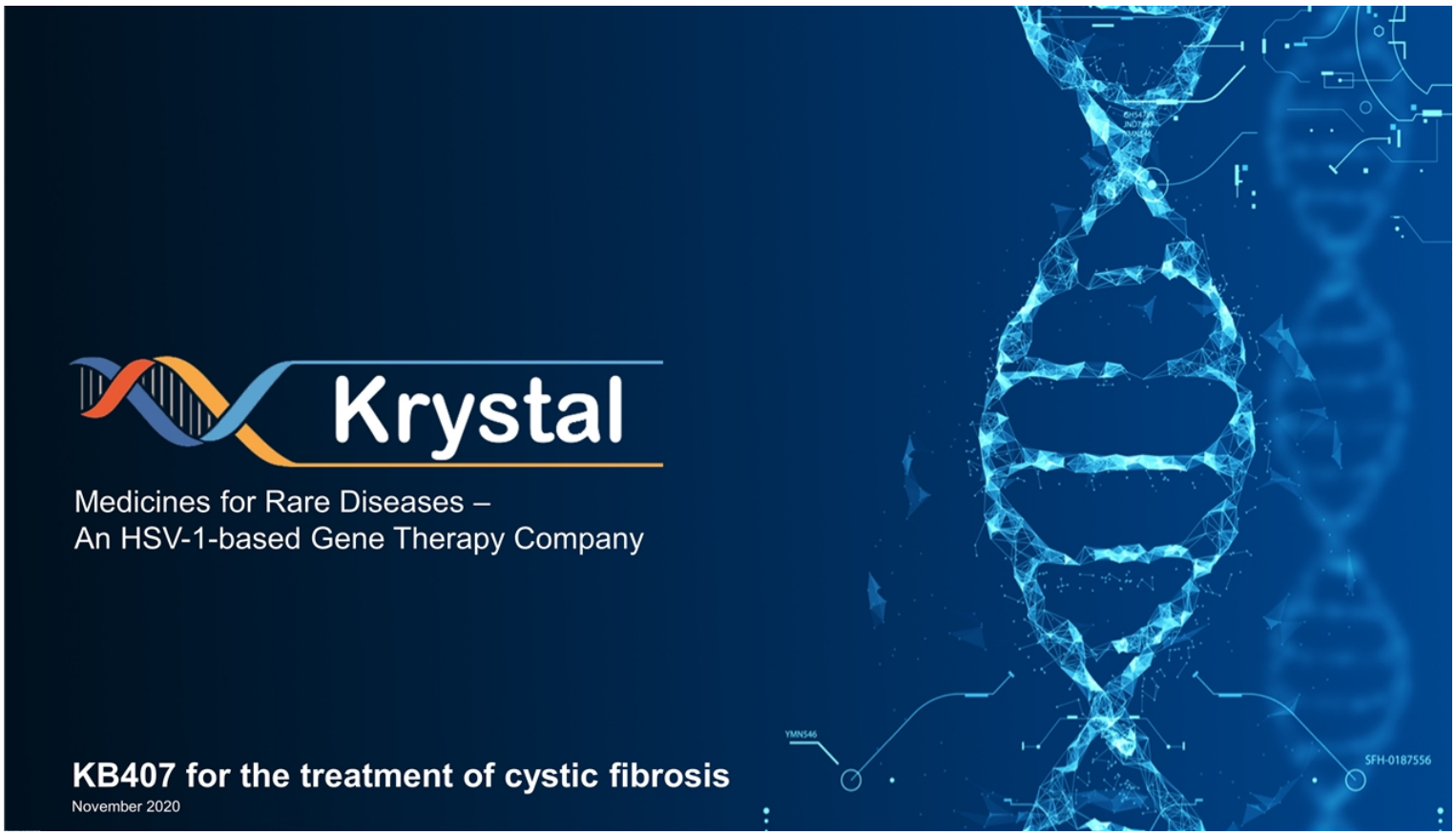
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Medicines for Rare Diseases –
An HSV-1-based Gene Therapy Company
KB407 for the treatment of cystic fibrosis
November 2020
YMN546
SFH-0187556

Exhibit 99.3

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Medicines for Rare Diseases –
An HSV-1 Based Gene Therapy Company

CORPORATE PRESENTATION
November 2020

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 B-VEC, KB105, KB301, KB407 and the Company's other product candidates; conduct and timelines of clinical trials, the clinical utility of B-VEC, KB105, KB301, KB407 and the Company's other product candidates; plans for and timing of the review of regulatory filings, efforts to bring B-VEC, KB105, KB301, KB407 and the Company's other product candidates to market; the market opportunity for and the potential market acceptance of B-VEC, KB105, KB301, KB407 and the Company's other product candidates, the development of B-VEC, KB105, KB301, KB407 and the Company's other product candidates for additional indications; the development of additional formulations of B-VEC, KB105, KB301, 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; the unanticipated impact of COVID-19 on the Company's business operations, preclinical activities and clinical trials; 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.

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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

- Platform powered by proprietary, engineered *replication incompetent* HSV-1 vector
- Pre-clinical and clinical data shows maintenance of safety and transgene expression with repeat dosing; additional 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

In house GMP manufacturing to support both clinical and commercial needs

- Current ~7,500 sqft GMP facility (ANCORIS) is producing pivotal material at commercial scale, and BLA readiness is underway
- Investing in additional capacity via construction of an ~150,000 sqft facility (ASTRA) which is expected to be operational in 2022

Leveraging platform to address larger indications, new tissues while investing in next gen tech

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

Differentiated HSV-1 Based Platform Enables *In Vivo*, Repeat Dose Gene Therapies

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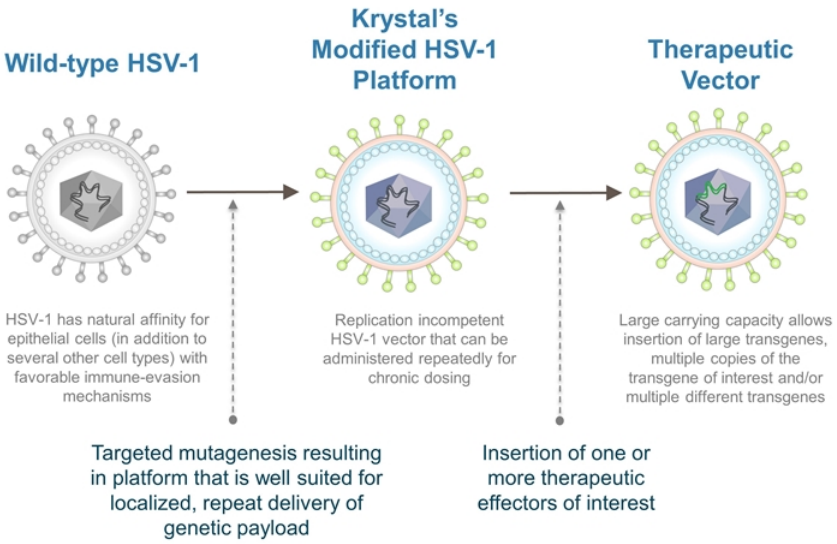
HSV-1 is Positively Differentiated vs. Other Gene Therapy Technologies



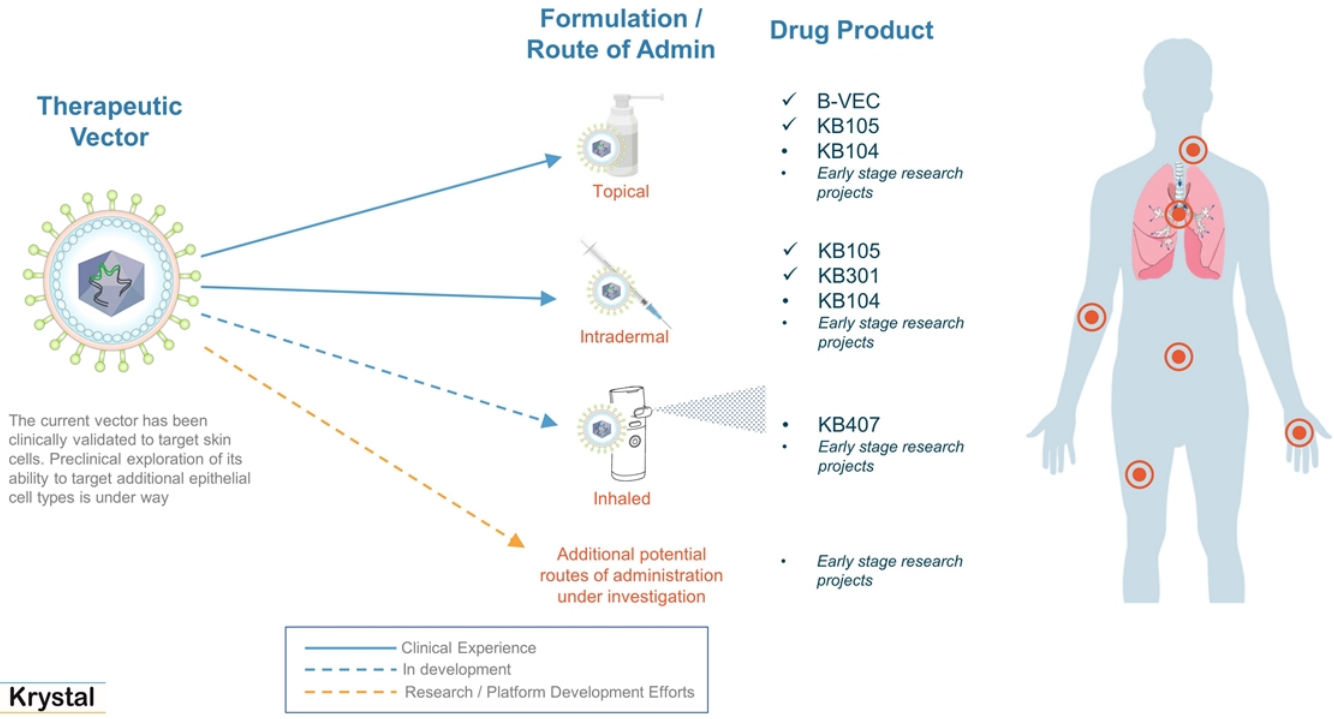
Current Status of Viral and Non-Viral Gene Therapy Vectors

	LV	AAV	HSV-1	LNP
In Vivo Dosing?	No	Yes	**Yes**	Yes
Baseline antibody exclusion criteria?	No *(ex-vivo)*	Yes	**No**	No
Repeat-dose capabilities?	No	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

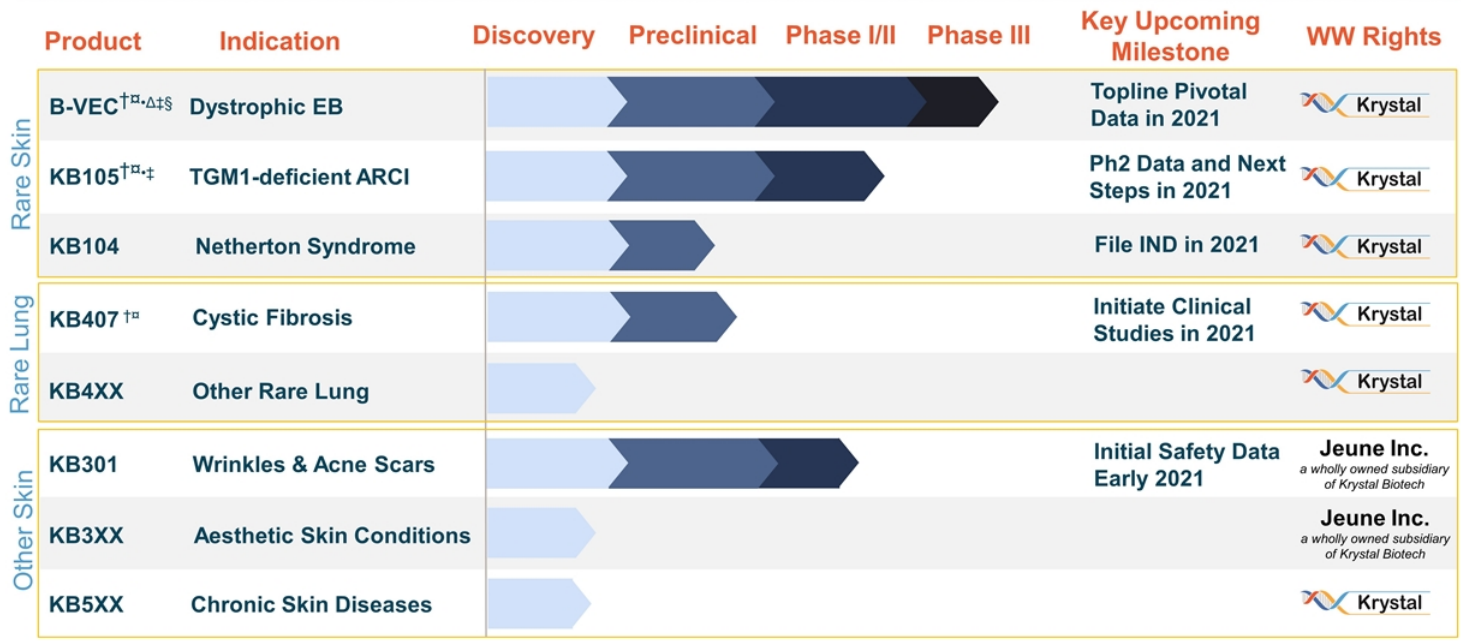
1. Lundstrom, K. Viral Vectors in Gene Therapy. *Diseases* 2018, 6, 42.
2. Generation Bio (GBIO) Prospectus. (2020, June 11). Retrieved September 4, 202020, https://www.sec.gov/Archives/edgar/data/1733294/000119312520167812/d924849d424b4.htm

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

Clinically Validated Platform Targeting Skin; Ongoing Investment in Next-Gen Technology to Broaden Platform Applicability



Pipeline



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

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

Initial Focus on Rare Skin Diseases Led to Rapid Clinical POC and Pipeline

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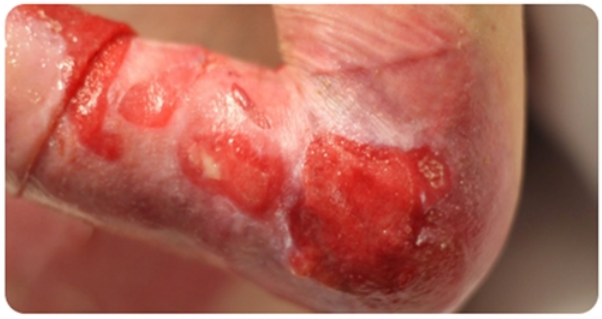
Dystrophic Epidermolysis Bullosa (DEB)

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

Dystrophic Epidermolysis Bullosa

- A rare, genetic connective tissue 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) can be milder with blistering often limited to 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 diagnosed DEB patients in the United States.

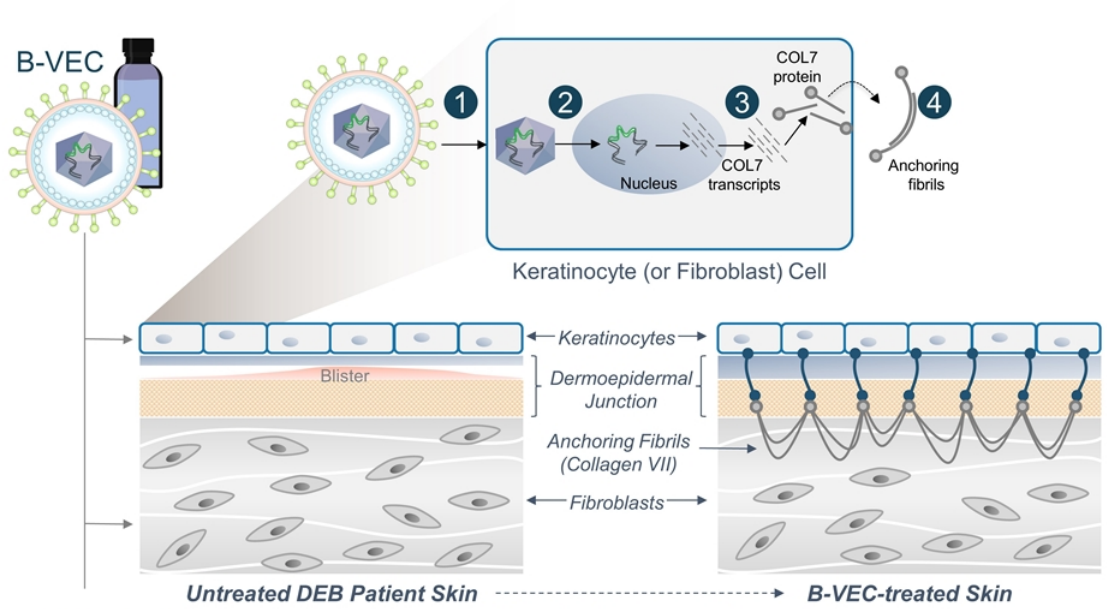
Current Standard of Care

- 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

Beremagene Geperpavec (B-VEC) for DEB

B-VEC is a topically administered, replication-deficient HSV-1 vector containing two functional COL7A1 genes applied directly to DEB patient wounds in an outpatient setting.



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

Topical B-VEC Was Evaluated in a Phase 1/2 Study at Stanford

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*

Enrollment

- A total of 9 RDEB subjects (adult and pediatric) were enrolled in the study; 3 subjects enrolled early and completed the study were subsequently re-enrolled and new wounds were randomized

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

In Ph1/2 Topical B-VEC was safe and well tolerated; COL7 expression and molecular correction observed

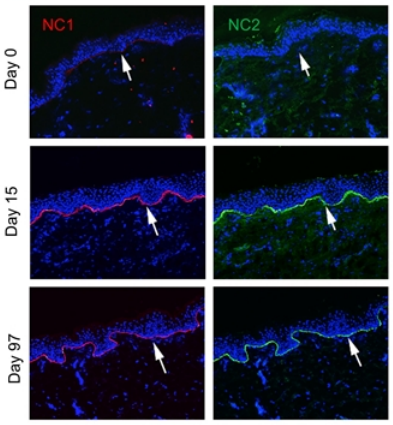
B-VEC was well tolerated following first and repeat dosing

- **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 HSV-1 antibodies which did not impair efficacy or impact tolerance of therapy**

Molecular correction established and correlated with wound healing

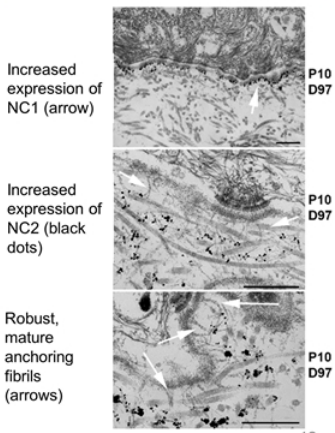
- Expression and correct localization of full-length COL7 following B-VEC therapy, which *promoted the formation of mature anchoring fibrils in all biopsy samples*

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



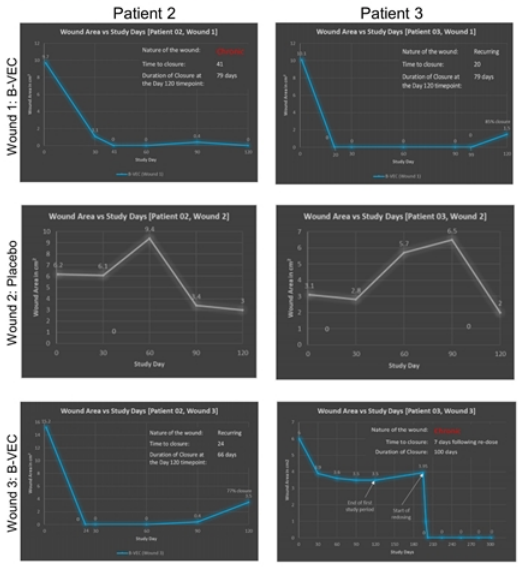
Arrows indicate basement membrane zone

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

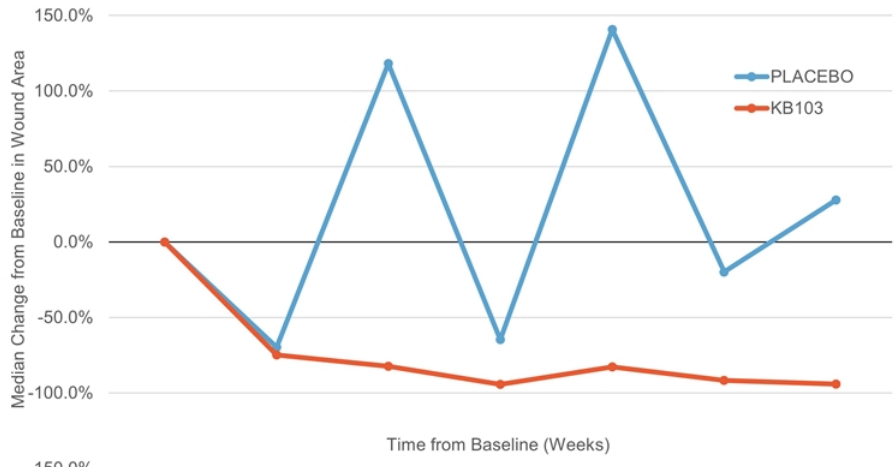


Statistically Significant Reduction in Wound Area achieved in Weeks 8,10 and 12

Efficacy was observed in both recurrent and chronic wounds



Median change in wound area across Phase 1/2 study

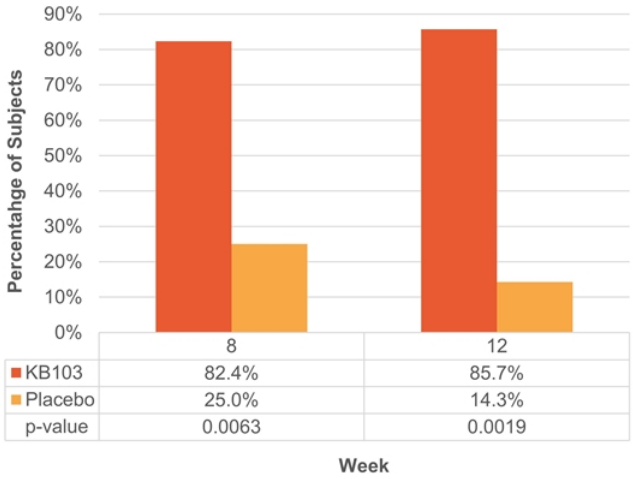


	0	2	4	6	8	10	12
PLACEBO	0.0%	-69.7%	118.3%	-64.7%	140.7%	-19.9%	27.8%
KB103	0.0%	-74.9%	-82.3%	-94.4%	-82.8%	-91.8%	-94.1%
p-value **		0.298	0.004	0.071	0.002	0.015	0.020

** Based on Wilcoxon Rank-Sum Test

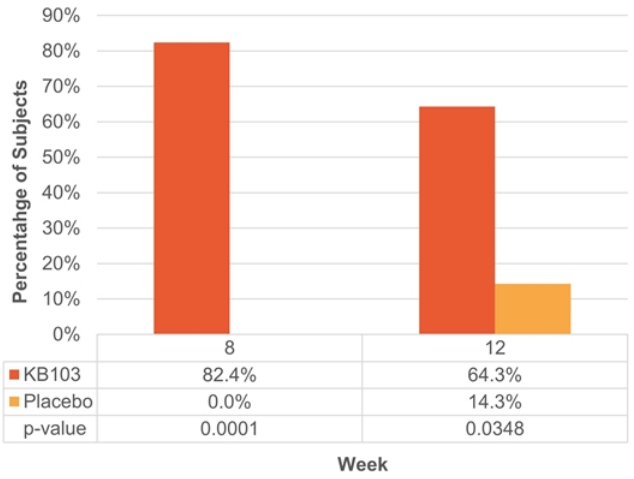
Wound Closure (>75% and 100%) for B-VEC vs. Placebo at Weeks 8 and 12

Change from baseline wound area ≥75%



	8	12
KB103	82.4%	85.7%
Placebo	25.0%	14.3%
p-value	0.0063	0.0019

Change from baseline wound area = 100%



	8	12
KB103	82.4%	64.3%
Placebo	0.0%	14.3%
p-value	0.0001	0.0348

**p-values are based on Cochran-Mantel Haenszel (CMH) Test Without Adjusting for Week-to-Week Placebo Variability*

The Pivotal GEM-3 Study is Currently Enrolling

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

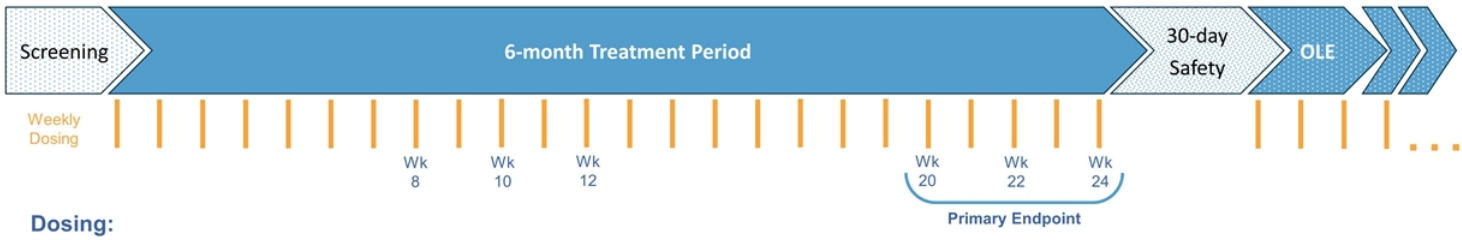
- Complete wound healing, determined by the Investigator, as compared to baseline in B-VEC treated wounds versus placebo treated at weeks 20, 22 and 24

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

Phase 3 Design Optimized for Clinical and Commercial Success

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

Autosomal Recessive Congenital Icthyosis Associated With TGM1 mutations

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).

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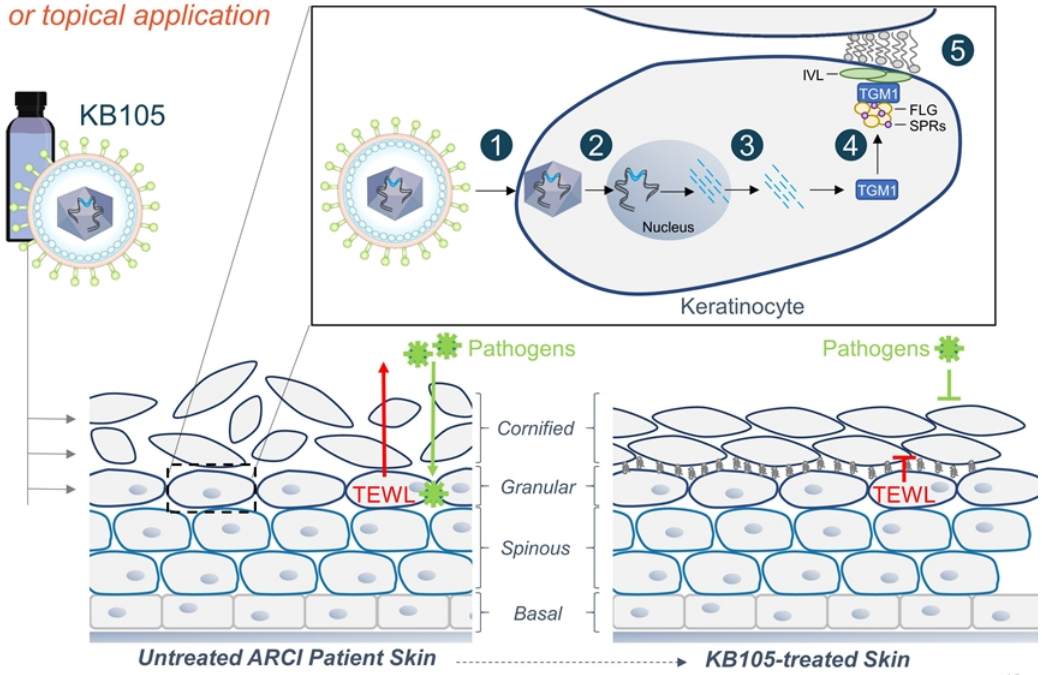
KB105 for TGM1 associated ARCI

KB105 is a replication-deficient HSV-1 vector that delivers multiple copies of human transglutaminase 1 ("TGM1") via intradermal injection or topical application

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 Being Evaluated in a Phase 1/2 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*

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 University (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

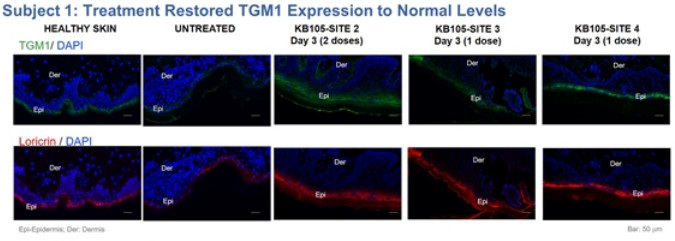
- Level of transglutaminase 1 in KB105-administered skin as measured by immunofluorescence microscopy
- Improvement of disease severity in the treatment area assessment through Investigator's Global Assessment (IGA)
- Improvement of disease severity in the treatment area through use of the Visual Index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

Ph1 Data Shows KB105 safe; Molecular and Phenotypic Improvement Evident

KB105 as 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 evaluated
- 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

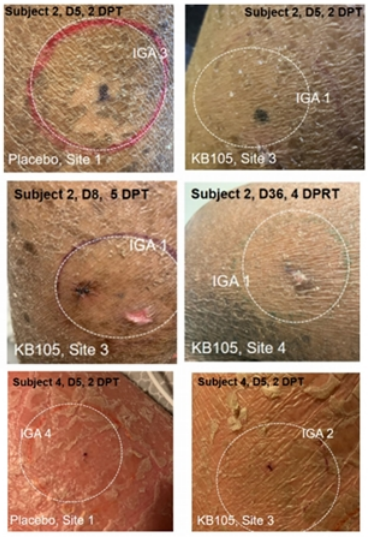


Phenotypic improvement evident after topical and microneedle application

- Similar delivery efficacy with and without microneedling; no microneedling required in future studies
- 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



In-House GMP Manufacturing to Support both Clinical and Commercial Needs

Krystal

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 Production Process

- Proprietary engineered vectors and complementary/supporting cell lines developed in-house are used in established methods for production of consistent batches
- Scalable from clinical phase to commercial

Downstream Purification Process

- Work conducted in an aseptic closed system process
- Process accommodates ever-expanding vector pipeline with minimal redevelopment effort between product candidates
- Compliant to global regulatory requirements

Facility operational;
Validated to produce pivotal and clinical materials
Size: 7500 sq. ft.


ASTRA (rendering)

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

Leveraging Platform to Target New Tissues and Larger Indications

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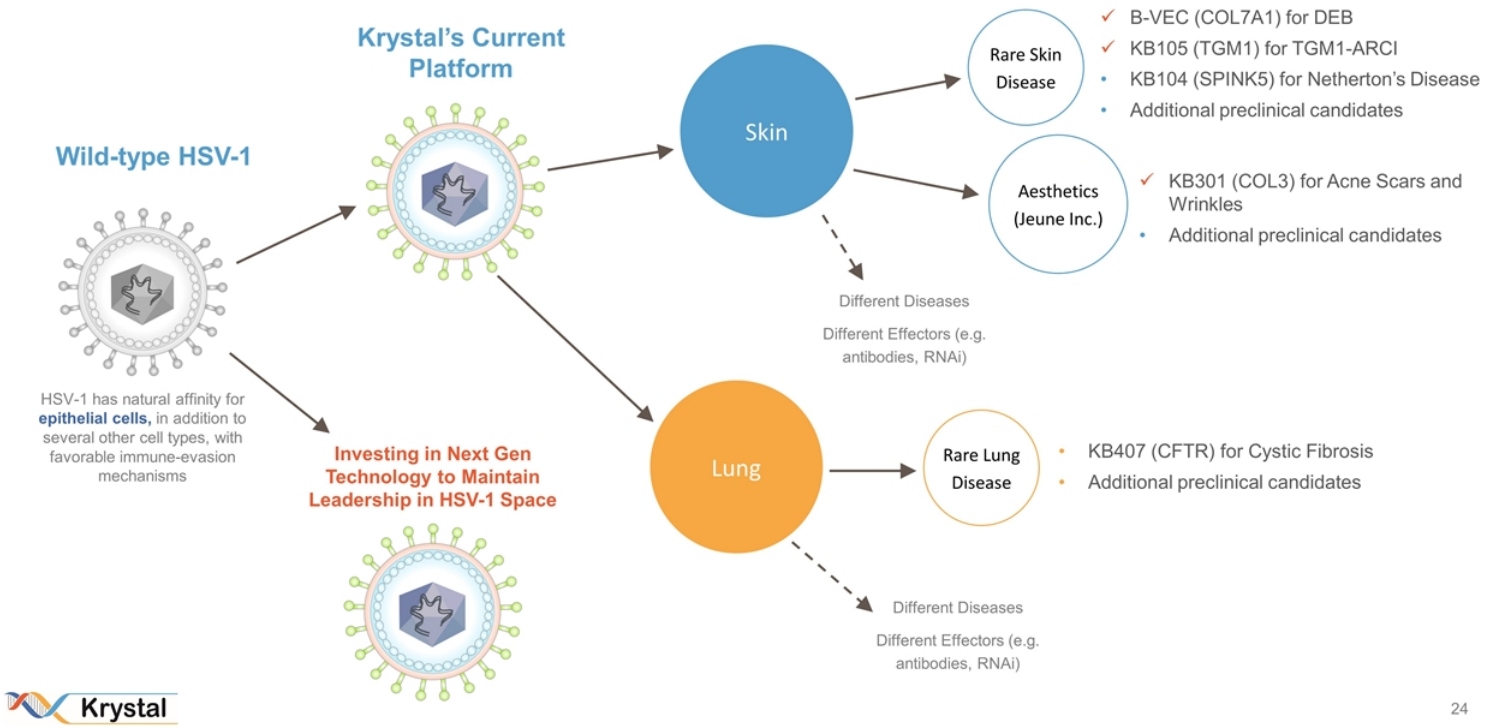
HSV-1 Has Potential Beyond Rare Skin



KB301 for Facial Wrinkles and Acne Scars

KB301 is designed to functional full-length human type III collagen (COL3) via injection

Many Characteristics of skin aging are due to aberrant collagen homeostasis

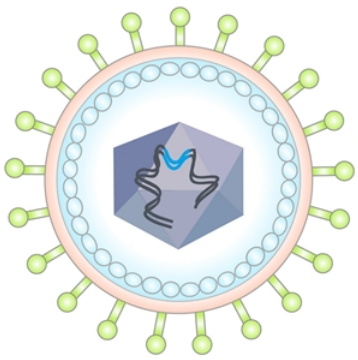
- The skin is largely composed of collagen-rich connective tissue, with dermal collagen, composed primarily of types 1 and 3 collagen fibrils, representing >90% (dry weight) of human skin
- Declining levels of collagen are caused by reduced collagen biosynthesis and increased collagen fibril fragmentation 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 the only off-the-shelf therapy designed to directly increase production of the body's own collagen

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

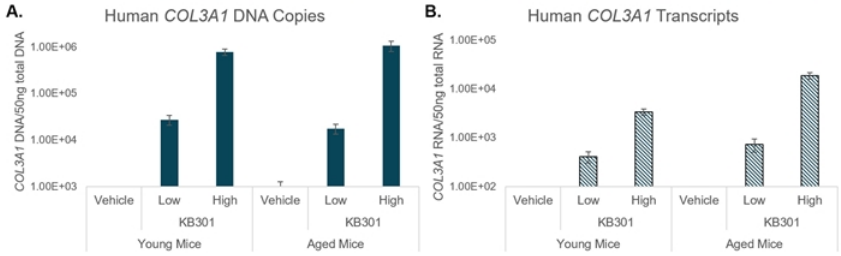
KB301



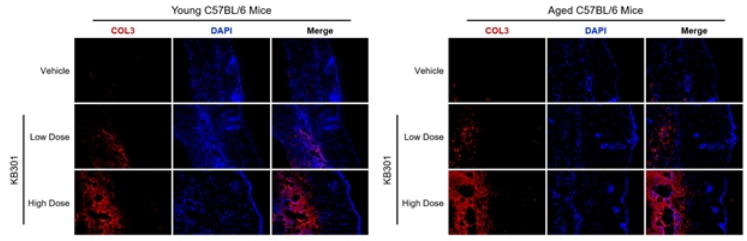
A replication-incompetent HSV-1 vector expressing full-length human COL3

Preclinical Data Supports KB301 Development Aesthetic Indications

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

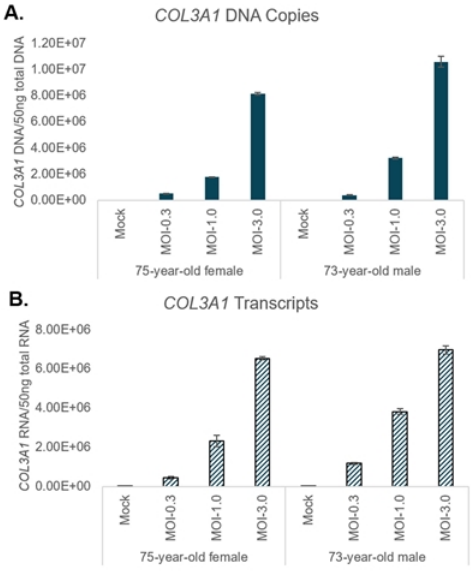


- Human COL3A1 DNA (A) and transcript (B) levels in treated skin 48-hours after intradermal administration of KB301 to young (6-8 weeks) and aged (13 mo) mice (above)
- COL3 protein localization 48-hours after intradermal administration of KB301 to young (6-8 weeks) and aged (13 mo) mice (below)



A 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



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KB301 is an investigational therapy being studied in preclinical trials

KB301 in Phase 1/2 with Initial Safety Data Expected Early 2021

Design

- PEARL-1 (NCT04540900) is an intra-patient comparison of KB301 or placebo
- 22 patients will be enrolled cross 3 cohorts:
  - Cohort 1 (n=6): Open label, dose ranging cohort will evaluate the safety and tolerability of two different dose levels (low and high) of KB301 in healthy buttock skin. Patients will be dosed on days 0 and 30 and followed for 12 months.
  - Cohorts 2 & 3 (n=8 each): Double-blind, placebo-controlled, intra-subject evaluations of the safety and efficacy of KB301 in either shallow-to-moderately deep facial wrinkles (Cohort 2) or moderate-to-severe atrophic acne scars (Cohort 3). Two patients in each cohort will be dosed on day 0 alone; 6 patients in each cohort will receive a 2nd dose at day 30. All patients will be followed for 12 months.

Endpoints

Safety Measures

- Safety and tolerability of KB301 based on the assessment of adverse events, physical examinations, vital signs, and clinical laboratory test results

Efficacy measures

- 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)

KB407 for Cystic Fibrosis

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

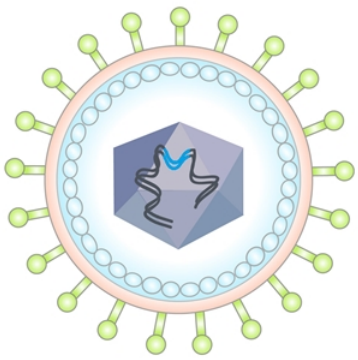
Gene therapy is an attractive modality for cystic fibrosis, though prior attempts have been unsuccessful

- 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

Our HSV-1 vector has potential to overcome prior limitations

- Accommodates large genes and necessary regulatory elements
- Is amenable to rapid, non-invasive inhaled administration
- Natural tropism to epithelial cells, e.g., those lining the airways
- Non-cytotoxic
- Non-immune stimulating
- Well suited for repeated administration in highly inflammatory environments

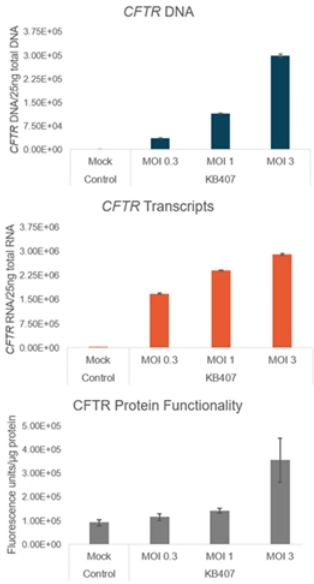
KB407



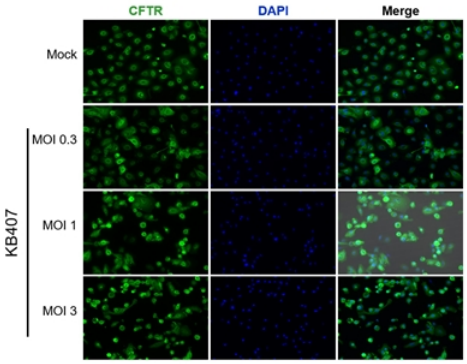
A replication-incompetent HSV-1 vector expressing full-length human CFTR

Efficient Cell Targeting, CFTR Expression and Function *In Vitro*

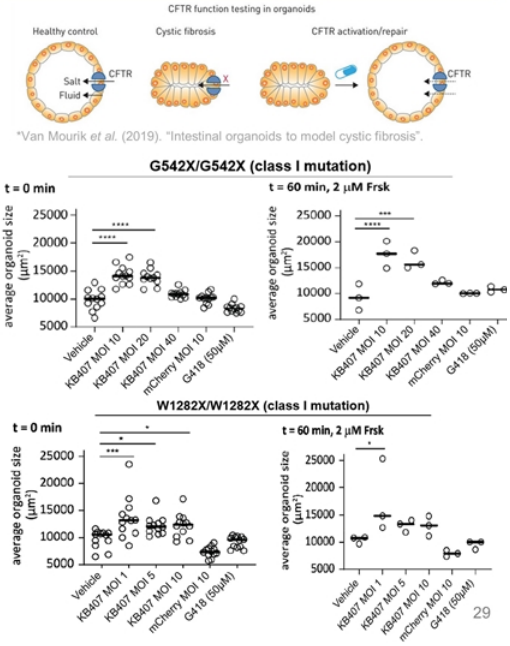
Robust, dose-dependent CFTR expression and functional correction in 2D Airway Epithelial Cell Culture



KB407-expressed human CFTR properly localizes to the plasma membrane of transduced cells



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



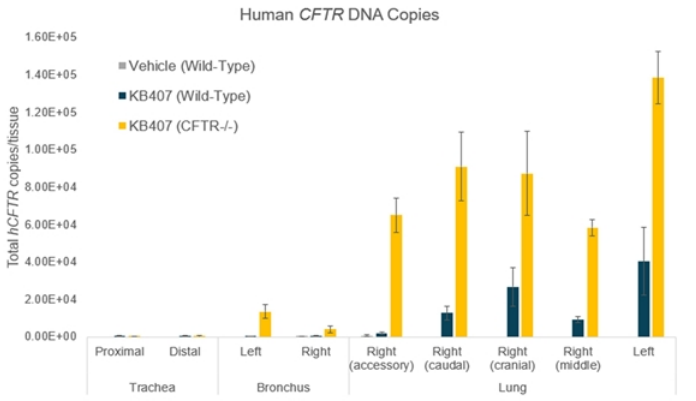
Krystal

KB407 is an investigational therapy being studied in preclinical trials

CFTR Protein Expression Distributed Throughout the Lung *In Vivo*

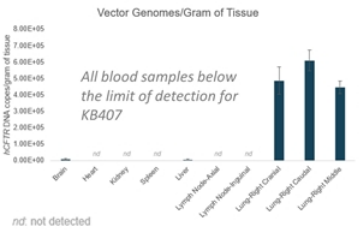
KB407 was effectively delivered to the lungs of **mice** using a clinically approved nebulizer

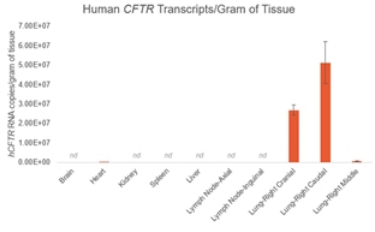
Group No.	Mouse Strain	Test Article	Route of Administration
1	C57BL/6J	Vehicle	Nebulization
2	C57BL/6J	KB407	Nebulization
3	Cftr^{tm1Unc}Tg(FABPCFTR)1 Jaw/J	KB407	Nebulization



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





Krystal

KB407 is an investigational therapy being studied in preclinical trials

Financials and Milestones

Krystal

Krystal Summary

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; topline data expected 2021. Commercial planning in US and EU underway
- **KB105:** 4th patient (first Ph2 patient) enrolled to evaluate higher dose and larger treatment area. Data from this patient will guide next steps in 2021
- **KB104:** preclinical work ongoing; IND anticipated in 2021

Aesthetics (Jeune Inc.)

- **KB301:** Phase 1 trial in acne scars and wrinkles ongoing; Initial Ph1 safety data anticipated in early 2021
- Update on Jeune Inc. / aesthetics strategy in 2021

Lung

- **KB407:** pre-IND work ongoing; clinical trial initiation anticipated in the first half of 2021

Platform

- **Manufacturing:** Astra facility 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


Krystal
Medicines for Rare Diseases –
An HSV-1 Based Gene Therapy Company
CORPORATE PRESENTATION
November 2020
YMN546
SFH-0187556

Appendix

Links to Scientific Presentations

B-VEC

- May 2020: Complete Phase 1/2 at SID 2020 – Link
- October 2019: Phase 1/2 Data Update – Link
- June 2019: Phase 1/2 Data Update – Link
- May 2018: Preclinical Poster at IID 2018 – Link
- September 2017: *In vitro* preclinical data at EB2017 - Link

KB105

- May 2020: Initial Phase 1/2 at SID 2020 - Link
- May 2019: *In vivo* preclinical data at SID 2019 – Link
- May 2019: *In vitro* preclinical data at SID 2019 – Link

KB104

- May 2019: *In vitro* preclinical data at SID 2019 - Link

KB301

- October 2020: *In vitro* and *in vivo* preclinical data at ASDS 2020 - Link

KB407

- May 2020: *In vitro* preclinical data at ASGCT 2020 – Link
- November 2020: Preclinical data overview including *in vivo* data - Link