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

FORM 8-K

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

Date of Report (Date of earliest event reported): May 12, 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 8.01 Other Events.

On May 12, 2020, Krystal Biotech, Inc., a Delaware corporation (the "Company"), presented a poster on the *in vitro* pharmacology of KB407, an HSV-1-based gene therapy vector, for the treatment of cystic fibrosis at the American Society of Gene & Cell Therapy Annual Meeting. A copy of the Company's poster is attached as Exhibit 99.1 hereto and incorporated by reference herein and is also available at the Company's website located at www.krystalbio.com/select-scientific-publications.

Any statements in this Current Report on Form 8-K 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 and KB407; the clinical utility of B-VEC, KB105 and KB407, and Krystal's plans for filing of regulatory approvals and efforts to bring B-VEC, KB105 and KB407 to market; the market opportunity for and the potential market acceptance of B-VEC, KB105 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 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	In Vitro Pharmacology of KB407, An HSV-1-Based Gene Therapy Vector, for the Treatment of Cystic Fibrosis Poster, dated May 12, 2020

SIGNATURES

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

Date: May 13, 2020

KRYSTAL BIOTECH, INC.

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

In Vitro Pharmacology of KB407, an HSV-1-Based Gene Therapy Vector, for the Treatment of Cystic Fibrosis

ASGCT 2020
May 12, 2020

Court Freedman, Trevor Parry, Pooja Agarwal, Alexandra Collin de l'Hortet, and Suma Krishnan

Krystal Biotech, Inc. Pittsburgh, PA, 15203

INTRODUCTION

Cystic fibrosis (CF), the most common inherited genetic disorder in the United States, is caused by mutations in the gene encoding cystic fibrosis transmembrane conductance regulator (CFTR). Lack of functional CFTR in secretory airway epithelia results in defective Cl^-, bicarbonate, and thiocyanate secretion, coupled with enhanced Na^+ absorption and mucus production, leading to dehydration and acidification of the airway surface liquid[1-3]. CF is characterized by recurrent chest infections, increased airway secretions, and eventually, respiratory failure[4].

While FDA approval of four small molecule modulator therapies has been a boon to CF patients harboring the specific mutations responsive to these drugs, these modulators only treat a subset of the CF population. In particular need for effective drug intervention are the ~10% of CF patients harboring *CFTR* mutations that result in severely reduced or absent CFTR expression (class I mutations), as these patients suffer from the harshest and deadliest forms of CF[5]. Regrettably, no suitable therapies are approved for treating this most sensitive patient population. To this end, Krystal has developed KB407, a replication-defective herpes simplex virus type 1 (HSV-1) gene therapy vector encoding human CFTR, for molecular correction of CF.

MATERIALS & METHODS

Test Article
KB407: Krystal Biotech, Inc.'s propriety replication-incompetent, non-integrating HSV-1 vector expressing human CFTR.

Table 1. Critical Reagents

Reagent	Application	Source
Small airway epithelial cells	*In vitro* dose-ranging	Lonza (cat. no. CC-2933)
Organoid cultures	*Ex vivo* pharmacology[6]	Hubrecht Organoid Technology
Rhodamine 6G	R6G uptake assay[7]	Sigma (cat. no. 252433)
Anti-human CFTR	IF/western blot	R&D Systems (cat. no 25031)
Anti-human GAPDH	Western blot	Abcam (cat. no. ab9485)

RESULTS

In Vitro KB407 Dose-Ranging in CF Patient-Derived Small Airway Epithelial Cells (SAECs)

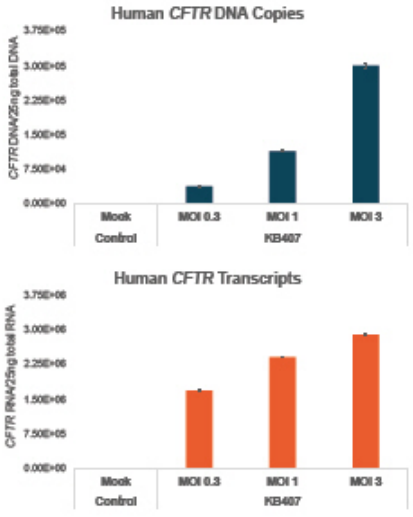

Figure 1. Dose-dependent increases in *CFTR* DNA and transcript levels upon KB407 infection of CF patient-derived SAECs. Data is presented as the average of three replicates ± standard error of the mean (SEM).

RESULTS (CONTINUED)

In Vitro CFTR Protein Analysis in KB407-Transduced CF Patient-Derived SAECs

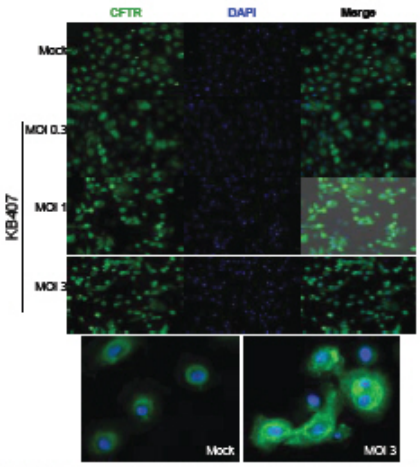

Figure 2. CFTR protein expression and relative cellular localization upon KB407 infection of CF patient-derived SAECs.

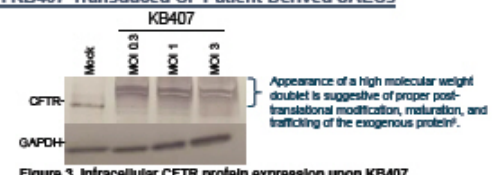

Figure 3. Intracellular CFTR protein expression upon KB407 infection of CF patient-derived SAECs.

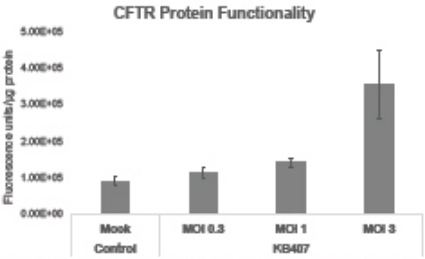

Figure 4. Dose-depend increase in CFTR-mediated R6G uptake upon KB407 infection in CF patient-derived SAECs. Data is presented as the average of three replicates ± SEM.

Ex Vivo KB407 Dose-Ranging and Pharmacodynamics in 3D Organotypic Cultures

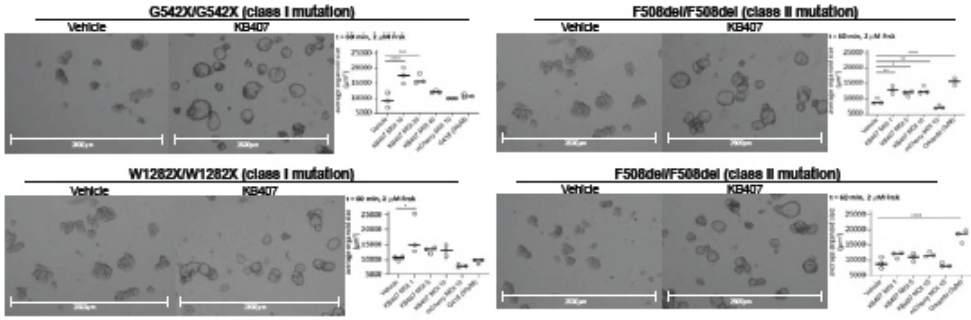

Figure 5. KB407-mediated functional correction to cystic phenotype of CF patient-derived intestinal organoids (PDOs) 48 hours post-infection, as assessed by a forskolin-induced swelling (FIS) assay. Organoids were stained with calcein green and imaged before and every 10 minutes after 2µM forskolin (Frsk) addition for 60 minutes. G418 or Orkambi were used as positive controls where appropriate; vehicle alone or HSV-mCherry were used as negative controls. Representative brightfield images show PDO morphology 24 hours after vehicle or KB407 treatment. *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001

CONCLUSIONS

- KB407 infects primary CF SAECs 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 cystic organoid phenotype exhibiting wild-type characteristics, 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.
- These data support KB407 as a novel gene therapy for the treatment of cystic fibrosis.

ACKNOWLEDGEMENTS

We kindly thank Hubrecht Organoid Technology (HUB) for all of their work on our collaboration utilizing KB407 in the CF patient–derived organoid model.

REFERENCES

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