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 21, 2021

bluebird bio, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-35966**	**13-3680878**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

60 Binney Street, Cambridge, MA	**02142**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (339) 499-9300

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

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 (see General Instructions A.2. below):

☐ 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, $0.01 par value per share	BLUE	The NASDAQ Stock Market LLC

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 21, 2021, bluebird bio, Inc. ("bluebird") issued a press release to announce that it received a positive opinion recommending marketing authorization from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) for SKYSONA™ (elivaldogene autotemcel, Lenti-D™), a one-time gene therapy for the treatment of early cerebral adrenoleukodystrophy (CALD) in patients less than 18 years of age with an *ABCD1* genetic mutation, and for whom a human leukocyte antigen (HLA)-matched sibling hematopoietic stem cell (HSC) donor is not available.

The full text of bluebird's press release regarding the announcement is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release issued by bluebird bio, Inc. on May 21, 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, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: May 21, 2021

bluebird bio, Inc.

By: /s/ Jason F. Cole

Jason F. Cole

Chief Operating and Legal Officer

Exhibit 99.1

bluebird bio Receives Positive CHMP Opinion for SKYSONA™ (elivaldogene autotemcel, Lenti-D™) Gene Therapy for Patients Less Than 18 Years of Age with Early Cerebral Adrenoleukodystrophy (CALD)

SKYSONA is the first and only gene therapy recommended for approval for patients with CALD, a progressive, neurodegenerative disease

As of the data cutoff date, 90% of patients (27/30) treated with SKYSONA in the pivotal ALD-102 clinical study met the primary endpoint of major functional disability (MFD)-free survival at two years of follow-up

Data from the long-term follow-up study (LTF-304) suggest that SKYSONA continues to show a durable effect on MFD-free survival, with the longest follow-up of nearly seven years (82.7 months)

Among 51 patients treated with SKYSONA across clinical studies to date, there have been no reports of graft-versus-host disease (GVHD), graft failure or rejection, or transplant-related mortality (TRM)

CAMBRIDGE, Mass. – (BUSINESS WIRE) May 21, 2021 – bluebird bio, Inc. (Nasdaq: BLUE) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending marketing authorization for SKYSONA™ (elivaldogene autotemcel, Lenti-D™), a one-time gene therapy for the treatment of early cerebral adrenoleukodystrophy (CALD) in patients less than 18 years of age with an *ABCD1* genetic mutation, and for whom a human leukocyte antigen (HLA)-matched sibling hematopoietic stem cell (HSC) donor is not available. If approved by the European Commission (EC), SKYSONA will be the first one-time gene therapy approved to treat CALD, a rare neurodegenerative disease that occurs in childhood and can lead to progressive, irreversible loss of neurological function and death.

The CHMP's positive opinion will now be reviewed by the EC, which has the authority to grant marketing authorization for SKYSONA in the European Union (EU). A CHMP positive opinion is one of the final steps before the EC decides whether to authorize a new medicine. A final decision by the EC for SKYSONA is anticipated in mid-2021. SKYSONA is not approved for any indication in any geography.

"The goal of treatment with SKYSONA is to stabilize disease progression in children with CALD for whom a matched sibling donor is not available, in order to prevent further neurological decline and improve survival for these young patients," said Richard Colvin, M.D., Ph.D., interim chief medical officer, bluebird bio. "This positive opinion from the CHMP marks the first regulatory approval recommendation for any gene therapy for CALD, bringing us closer to a one-time, durable treatment option that stabilizes neurological disease while reducing the risk of the serious immune complications associated with allogeneic stem cell transplantation (allo-HSCT), which is the only therapeutic option for children with this devastating disease. Together with the ALD community and clinical investigators, we are all optimistic that new hope could soon be provided to patients suffering from this unbearable condition."

Adrenoleukodystrophy (ALD) is a rare, X-linked metabolic disorder that primarily affects males; worldwide, an estimated one in 21,000 male newborns are diagnosed with ALD. The disorder is caused by mutations in the *ABCD1* gene that affect the production of adrenoleukodystrophy protein (ALDP) and subsequently cause toxic accumulation of very long-chain fatty acids (VLCFAs), primarily in the adrenal gland and white matter of the brain and spinal cord. Approximately 40% of boys with ALD will develop CALD, the most severe form of ALD. CALD is a progressive and irreversible neurodegenerative disease that involves the breakdown of myelin, the protective sheath of the nerve cells in the brain responsible for thinking and muscle control. The onset of symptoms of CALD typically occurs in childhood (median age 7).

"The rapid and progressive decline of cognitive and physical functions for a child living with CALD is agonizing for parents, families and healthcare providers to witness. With CALD, each day truly counts, as nearly half of

the patients who do not receive treatment will die within five years of symptom onset,"[1] said Jean-Hugues Dalle, M.D., Ph.D., HSCT and Gene Therapy program director, Robert Debré Hospital, GH Nord Université de Paris, France. "As a clinician, I stand with my fellow investigators in our continued dedication to improve outcomes for children diagnosed with CALD, including the advancement of an approved treatment option like SKYSONA."

"Families affected by CALD face a critical diagnosis, as symptoms that generally develop in childhood result in a progressive loss of autonomy and rapid neurological decline. There is an urgent need for treatment options," said Guy Alba, President of ELA International and founder of the ELA association. "The ELA association has shown the way by investing massively in CALD research since 1992. We support all initiatives that, like gene therapy, could change the lives of patients. This milestone is a very important step forward in options for the care of patients with CALD."

SKYSONA is a one-time investigational gene therapy that uses ex vivo transduction with the Lenti-D lentiviral vector (LVV) to add functional copies of the *ABCD1* gene into a patient's own hematopoietic (blood) stem cells (HSCs). The addition of the functional *ABCD1* gene allows patients to produce the ALD protein, which is thought to facilitate the breakdown of VLCFAs. The goal of treatment with SKYSONA is to stabilize the progression of CALD and, consequently, preserve as much neurological function as possible, including the preservation of motor function and communication ability. Importantly, with SKYSONA, there is no need for donor HSCs from another person.

In October 2020, the EMA accepted bluebird bio's Marketing Authorisation Application (MAA) for its investigational SKYSONA gene therapy for the treatment of patients with CALD. SKYSONA was accepted into the EMA's Priority Medicines scheme (PRIME) in July 2018 and was previously granted Orphan Medicinal Product status.

Data Supporting Clinical Profile of SKYSONA
The positive CHMP opinion is supported by efficacy and safety data from the Phase 2/3 Starbeam study (ALD-102). All patients who completed ALD-102, plus those who will complete a second Phase 3 study (ALD-104), will be asked to participate in a long-term follow-up study (LTF-304).

The primary efficacy endpoint of the pivotal ALD-102 study was the proportion of patients who did not have any of the six MFDs, were alive, did not receive a second allo-HSCT or rescue cell administration and had not withdrawn or been lost to follow-up at Month 24. To date, 32 patients have been treated with SKYSONA in ALD-102, and 30/32 patients were evaluable for follow-up at Month 24. As of the last data cutoff date, 90% (27/30) of the patients met the Month 24 MFD-free survival endpoint. In addition, as previously reported, two patients withdrew from the study at investigator discretion, and one experienced rapid disease progression early on in the study, resulting in MFDs and subsequent death.

In ALD-102, 26/28 evaluable patients maintained a neurologic function score (NFS) less than or equal to 1 through Month 24, and 24 of those patients had no change in their NFS, which showed maintenance of neurological function in the majority of patients. All patients who completed ALD-102 enrolled for long-term follow-up in the LTF-304 study. The median duration of follow-up was 38.59 months (min.: 13.4; max.: 82.7).

The treatment regimen, comprising mobilization/apheresis, conditioning and SKYSONA infusion, had a safety/tolerability profile primarily reflective of the known effects of mobilization/apheresis and conditioning.

Adverse reactions attributed to SKYSONA observed in clinical trials include cystitis viral, pancytopenia and vomiting.

There have been no reports of GVHD, graft failure or rejection, TRM or replication competent lentivirus in the 51 patients treated with SKYSONA in clinical studies (ALD-102/LTF-304 and ALD-104). Additionally, there have

[1] Reported Kaplan-Meier estimated five-year survival rates among untreated patients are 55% (from the time of CALD diagnosis) and 59% (from the time of onset of first clinical symptoms).

been no reports of lentiviral vector-mediated insertional mutagenesis resulting in oncogenesis, including myelodysplasia, leukemia or lymphoma, associated with SKYSONA. Nevertheless, there is a theoretical risk of malignancy after treatment with SKYSONA. Clonal expansion resulting in clonal predominance without clinical evidence of malignancy has been detected in some patients treated with SKYSONA.

SKYSONA continues to be evaluated in the Phase 3 ALD-104 study and the long-term follow-up study LTF-304. If approved by the EC, patients treated with SKYSONA in Europe will be expected to enroll in the REG-502 Stargazer registry.

About SKYSONA (elivaldogene autotemcel, formerly Lenti-D™ gene therapy)
The U.S. Food and Drug Administration (FDA) granted SKYSONA Orphan Drug status, Rare Pediatric Disease designation and Breakthrough Therapy designation for the treatment of CALD. bluebird bio is currently on track to submit the Biologics License Application (BLA) in the U.S. by mid-2021.

SKYSONA is not approved for any indication in any geography.

The Phase 3 ALD-104 study, designed to assess the efficacy and safety of SKYSONA after myeloablative conditioning using busulfan and fludarabine in patients with CALD, is approaching enrollment completion; enrollment in Europe is expected to be closed at the end of May.

The Phase 2/3 Starbeam study (ALD-102) is complete. For more information about our studies, visit: **www.bluebirdbio.com/our-science/clinical-trials** or **clinicaltrials.gov**.

Additionally, bluebird bio is conducting a long-term safety and efficacy follow-up study (LTF-304) for patients who have been treated with SKYSONA for CALD and completed two years of follow-up in bluebird bio-sponsored studies. If approved by the EC, patients treated with SKYSONA in Europe will be expected to enroll in the REG-502 Stargazer registry.

About CALD Early Diagnosis
Early diagnosis of CALD is essential, as treatment must be administered before the disease progresses too far, as the outcome of treatment varies with the clinical stage of the disease. Newborn screening is a critical enabler of early diagnosis for ALD and provides access to a window of opportunity for the timely commencement of available therapies. Once a patient has been diagnosed with ALD, regular MRI scans are critical to detect white matter changes indicative of progression to CALD as currently, there is no way to predict who with ALD will develop CALD. In the absence of newborn screening for ALD, early detection of ALD symptoms is crucial to allow for timely treatment.

Unfortunately, in most EU countries, there is no newborn screening for ALD, and therefore it is difficult to detect patients at risk of developing CALD. To date, the Netherlands is the only country in Europe that has approved the addition of ALD to their newborn screening panel.

In the U.S., newborn screening for ALD was added to the Recommended Universal Screening Panel in February 2016 and is currently active in 19 states and the District of Columbia, accounting for ≥60% of U.S. newborns.

About bluebird bio, Inc.
bluebird bio is pioneering gene therapy with purpose. From our Cambridge, Mass., headquarters, we're developing gene and cell therapies for severe genetic diseases and cancer, with the goal that people facing potentially fatal conditions with limited treatment options can live their lives fully. Beyond our labs, we're working to positively disrupt the healthcare system to create access, transparency and education so that gene therapy can become available to all those who can benefit.

bluebird bio is a human company powered by human stories. We're putting our care and expertise to work across a spectrum of disorders: cerebral adrenoleukodystrophy, sickle cell disease, β-thalassemia and

multiple myeloma, using gene and cell therapy technologies including gene addition, and (megaTAL-enabled) gene editing.

bluebird bio has additional nests in Seattle, Wash.; Durham, N.C.; and Zug, Switzerland. For more information, visit bluebirdbio.com.

Follow bluebird bio on social media: @bluebirdbio, LinkedIn, Instagram and YouTube.

SKYSONA, eli-cel, Lenti-D and bluebird bio are trademarks of bluebird bio, Inc.

Forward-Looking Statements

This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the company's expectations and plans for regulatory submissions and approvals for eli-cel in the European Union and the United States. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: the risk that the EC does not grant marketing authorization to eli-cel on the timeline that we expect, or at all, the risks that the efficacy and safety results for eli-cel from the Starbeam Study and ALD-104 seen to date will not continue or persist; the risks regarding future potential regulatory approvals of eli-cel, including the risk that the Starbeam Study will be insufficient to support regulatory submissions or marketing approval in the U.S., or that the FDA may require additional data or information beyond our current expectations, the risk that our submissions for regulatory approval in the U.S. will not be submitted or accepted for filing by the FDA on the timeframe we expect or at all; and the risk that eli-cel is associated with insertional oncogenesis or other safety events that impact the risk-benefit profile of the therapy. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and bluebird bio undertakes no duty to update this information unless required by law.

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