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): August 29, 2020

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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 August 29, 2020, bluebird bio, Inc. (“bluebird”) announced updated results from the clinical development program for its investigational elivaldogene autotemcel (eli-cel, Lenti-D) gene therapy in patients with cerebral adrenoleukodystrophy (CALD), including long-term results from Phase 2/3 Starbeam study (ALD-102) and first disclosure of data from Phase 3 study (ALD-104). These data were shared at the 46th Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT 2020), taking place virtually from August 29 – September 1, 2020.

The full text of bluebird’s press release regarding this 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 August 29, 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, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: August 31, 2020

bluebird bio, Inc.

By: /s/ Jason F. Cole

Jason F. Cole

Chief Operating and Legal Officer

Exhibit 99.1

bluebird bio Presents New Results from Clinical Development Program of elivaldogeneautotemcel (eli-cel, Lenti-D™) Gene Therapy for Cerebral Adrenoleukodystrophy (CALD),Including Updated Long-Term Data, at the 46th Annual Meeting of the EBMT

Long-term results from Phase 2/3 Starbeam study (ALD-102/LTF-304) suggest durability of response post eli-cel with all 20 patients who were free of major functional disabilities (MFDs) at two years (out of 23 evaluable patients) remaining MFD-free through last available follow-up, including all 10 patients who reached at least Year 5 follow-up visit

31 out of 32 patients in ALD-102 had stable Neurologic Function Scores following treatment with eli-cel, including 24 patients with a score of zero as of the last available visit

In clinical studies of eli-cel to date, there have been no reports of graft failure, graft rejection, graft-versus-host disease (GVHD), replication competent lentivirus, or insertional oncogenesis

Company on track to submit Marketing Authorization Application in EU by year-end 2020, and Biologics License Application in U.S. in mid-2021

CAMBRIDGE, Mass.--(BUSINESS WIRE)— August 29, 2020—bluebird bio, Inc. (Nasdaq: BLUE) announced updated results from the clinical development program for its investigational elivaldogene autotemcel (eli-cel, Lenti-D™) gene therapy in patients with cerebral adrenoleukodystrophy (CALD), including long-term results from the Phase 2/3 Starbeam study (ALD-102/LTF-304) and data from the Phase 3 ALD-104 study. These data were presented today at the 46th Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT 2020), taking place virtually from August 29 - September 1, 2020.

“CALD is a fatal neurodegenerative disease primarily affecting young boys. Currently, the only treatment available is allogeneic hematopoietic stem cell transplantation (allo-HSCT), which comes with associated, significant risks, including transplant-related mortality, graft failure or rejection, and graft-versus-host disease (GVHD),” said David Davidson, M.D., chief medical officer, bluebird bio. “Eighty-seven percent of patients in our Phase 2/3 Starbeam study of eli-cel are alive and free of major functional disabilities (MFDs) at 24 months or more of follow-up. Importantly, there were no reports of graft failure, graft rejection, or GVHD. It is gratifying to see the consistent outcomes with eli-cel and the durability of the treatment effect demonstrated in the children participating in our long-term follow-up study – including 10 boys who have now reached at least their Year 5 follow-up visit.”

Adrenoleukodystrophy (ALD) is a rare, X-linked metabolic disorder that is estimated to affect one in 21,000 male newborns worldwide. ALD 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 cortex and white matter of the brain and spinal cord.

Approximately 40% of boys with adrenoleukodystrophy will develop CALD, the most severe form of ALD. CALD is a progressive neurodegenerative disease that involves breakdown of myelin, the protective sheath of the nerve cells in the brain that are responsible for thinking and muscle control. Symptoms of CALD usually occur in early childhood and progress rapidly, if untreated, leading to severe loss of neurologic function, and eventual death, in most patients. CALD is associated with six MFDs, which severely compromise a patient’s ability to function independently: loss of communication, cortical blindness, need for tube feeding, total incontinence, wheelchair dependence, and complete loss of voluntary movement. Nearly half of boys with CALD who do not receive treatment will die within five years of symptom onset.

“Patients with CALD experience a rapid decrease in neurologic function after the initial onset of clinical symptoms, so early diagnosis and treatment is critical in order to stop the disease progression and preserve

their neurological function. In the Phase 2/3 Starbeam study, 31 of 32 patients had a stable neurologic function score, suggesting that disease progression had stabilized and minimal neurological function was lost, following eli-cel infusion," said Dr. Jörn-Sven Kühl, Department of Pediatric Oncology, Hematology and Hemostaseology, Center for Women's and Children's Medicine, University Hospital Leipzig. "These results presented at EBMT 2020 are very encouraging and suggest treatment with eli-cel may prevent neurological decline in boys with CALD."

Eli-cel is a one-time investigational gene therapy designed to address the underlying genetic cause of CALD by adding functional copies of the *ABCD1* gene into a patient's own hematopoietic (blood) stem cells (HSCs) that have been transduced *ex vivo* with the Lenti-D lentiviral vector (LVV). The addition of a functional gene allows patients to produce the ALDP, which is thought to break down the toxic accumulation of VLCFAs in the brain. There is no need for donor HSCs from another person, as is required for allo-HSCT.

Starbeam Study (ALD-102)/Long-Term Follow-Up Study (LTF-304)
The ALD-102 study has completed enrollment. All reported data below are as of January 2020 and reflect a total population of 32 patients with a median follow-up time of 30.0 months (9.1 – 70.7 months).

Of the 32 patients who have received eli-cel as of January 2020, 20 have completed ALD-102 and enrolled in a long-term follow-up study (LTF-304). Nine additional patients continue to be followed in ALD-102 and have not reached 24 months post-treatment. As previously reported, two patients withdrew from the study at investigator discretion, and one experienced rapid disease progression early on-study resulting in MFDs and death. To date, 104.3 patient-years of follow-up have been reported for ALD-102 and LTF-304.

The primary efficacy endpoint in the study is the proportion of patients who are alive and free of MFDs at Month 24. Of those patients who have or would have reached Month 24, 87% have met the primary endpoint and continue to be alive and MFD-free at more than two years of follow-up (N=20/23). Fourteen patients have at least four years of follow-up, including 10 patients who have reached at least their Year 5 follow-up visit. The nine patients from ALD-102 that have not reached Month 24 have shown no evidence of MFDs.

Data on several secondary and exploratory efficacy outcomes are reported, including changes in neurologic function score (NFS), a 25-point score used to evaluate the severity of gross neurologic dysfunction across 15 symptoms in six categories; resolution of gadolinium enhancement (GdE), an indicator of active inflammation in the brain; and change in Loes score, an MRI measurement of white matter changes in CALD. Of the 32 patients treated, 31 had stable NFS following treatment with eli-cel, defined as NFS $\leq$4, without a change of >3 from baseline, and 24 patients maintained an NFS of 0. An NFS of 0 indicates that there are no concerns with the neurologic functions that are assessed on the 25-point scale. Loes scores generally stabilized within 12-24 months and GdE was no longer seen in most patients following eli-cel treatment.

The primary safety endpoint is the proportion of patients who experience acute (≥Grade 2) or chronic GvHD by Month 24. GvHD is a condition that may occur after an allo-HSCT, where the donated cells view the recipient's body as foreign and attack the body. No events of acute or chronic GvHD have been reported post-eli-cel treatment. There have been no reports of graft failure or graft rejection.

In addition, there have been no cases of replication competent lentivirus or insertional oncogenesis to date. Integration site analysis (ISA) was conducted to determine the pattern of integration post-eli-cel infusion and assess whether dominant or expanding clones were present. In one patient, now enrolled in LTF-304 for long-term follow up, a case of benign clonal expansion was observed with three separate integrations in the DNA of the cell at *ACER3*, *RFX3*, and *MECOM*. As of the patient's Month 62 visit in March 2020, the patient remained clinically stable. Bone marrow analyses showed no dysplasia (abnormal cell growth) or molecular abnormalities.

The treatment regimen, comprising mobilization/apheresis, conditioning, and eli-cel infusion, had a safety and tolerability profile primarily reflective of the known effects of mobilization/apheresis and conditioning. In ALD-102, as previously reported, three adverse events (AE) were considered possibly related to drug product

and include one serious AE (SAE), BK viral cystitis (N=1, SAE, Grade 3), and two non-serious AEs, vomiting (N=2, Grade 1). All three AEs resolved using standard measures.

ALD-104 Study

bluebird bio is currently enrolling patients for ALD-104, a Phase 3 study designed to assess the efficacy and safety of eli-cel in patients with CALD after myeloablative conditioning using busulfan and fludarabine, a different chemotherapy conditioning regimen than what is used in ALD-102 (busulfan and cyclophosphamide). The primary efficacy endpoint is the proportion of patients who are alive and free of MFDs at Month 24, and the primary safety endpoint is the proportion of patients with neutrophil engraftment after eli-cel infusion. All reported data below are as of February 2020.

In ALD-104, the 13 patients currently on study have a median of 6.1 months of follow-up to date (min-max: 2.2 – 10.3 months). All 13 patients achieved neutrophil engraftment and 12/13 evaluable patients had platelet engraftment (platelet engraftment pending in one patient as of data cut date). Due to the limited duration of follow-up, only safety data are being presented.

No events of acute or chronic GvHD have been reported and there have been no reports of graft failure, graft rejection, cases of insertional oncogenesis, or replication competent lentivirus.

The treatment regimen, comprising mobilization/apheresis, conditioning, and eli-cel infusion had a safety and tolerability profile primarily reflective of the known effects of mobilization/apheresis and conditioning. In ALD-104, two AEs of pancytopenia were considered possibly related to eli-cel. These two ongoing AEs were deemed as suspected unexpected serious adverse reactions (SUSARs) by the principal investigator and were diagnosed approximately two months post-eli-cel infusion in two patients (one Grade 2 and one Grade 3). An additional AE was ongoing as of February 2020, a Grade 3 SAE of transverse myelitis that was diagnosed in the presence of viral infection (adenovirus and rhinovirus/enterovirus positivity) approximately six months after eli-cel infusion and deemed unrelated to eli-cel.

eli-cel Presentation at EBMT

Lenti-D hematopoietic stem cell gene therapy stabilizes neurologic function in boys with cerebral adrenoleukodystrophy

Presenting Author: Dr. Jörn-Sven Kühl, Department of Pediatric Oncology, Hematology and Hemostaseology, Center for Women's and Children's Medicine, University Hospital Leipzig
Poster Session & Number: Gene Therapy; ePoster O077

Presentations will be available for virtual viewing throughout the duration of the live meeting on the EBMT 2020 website and content will be accessible online following the close of the meeting until November 1, 2020.

About elivaldogene autotemcel (eli-cel, formerly Lenti-D™)

In July 2020, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) granted an accelerated assessment to eli-cel gene therapy for cerebral adrenoleukodystrophy (CALD). bluebird bio is currently on track to submit the Marketing Authorization Application (MAA) in the EU for eli-cel for CALD by year-end 2020, and the Biologics License Application (BLA) in the U.S. in mid-2021.

bluebird bio is currently enrolling patients for a Phase 3 study (ALD-104) designed to assess the efficacy and safety of eli-cel after myeloablative conditioning using busulfan and fludarabine in patients with CALD. Contact **clinicaltrials@bluebirdbio.com** for more information and a list of study sites.

Additionally, bluebird bio is conducting a long-term safety and efficacy follow-up study (LTF-304) for patients who have been treated with eli-cel for CALD and completed two years of follow-up in bluebird bio-sponsored studies.

The Phase 2/3 Starbeam study (ALD-102) has completed enrollment.

For more information about bluebird bio-sponsored studies visit: **www.bluebirdbio.com/our-science/clinical-trials** or **clinicaltrials.gov**.

The European Medicines Agency (EMA) accepted eli-cel gene therapy for the treatment of CALD into its Priorities Medicines scheme (PRIME) in July 2018, and previously granted Orphan Medicinal Product designation to eli-cel.

The U.S. Food and Drug Administration (FDA) granted eli-cel Orphan Drug status, Rare Pediatric Disease designation, and Breakthrough Therapy designation for the treatment of CALD.

Eli-cel is not approved for any indication in any geography.

About CALD Early Diagnosis

Early diagnosis of CALD is important, as the outcome of available treatment varies with the clinical stage of the disease. Newborn screening for ALD is a critical enabler of early diagnosis and thus of successful treatment of ALD. Once a patient has been diagnosed with ALD, regular MRI scans are critical to detect white matter changes indicative of progression to CALD.

In the U.S., newborn screening for ALD was added to the Recommended Universal Screening Panel in February 2016 and is currently active in 17 states, accounting for ≥ 58 percent of U.S. newborns. Outside the U.S., the Minister of Health in the Netherlands has approved the addition of ALD to their newborn screening program. Even though ALD newborn screening has not been implemented in most EU countries, efforts to begin pilot programs are slowly progressing.

About bluebird bio, Inc.
bluebird bio is pioneering gene therapy with purpose. From our Cambridge, Mass., headquarters, we're developing gene 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 including cerebral adrenoleukodystrophy, sickle cell disease, β-thalassemia and multiple myeloma, using three gene therapy technologies: gene addition, cell therapy 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**.
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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 for eli-cel in the U.S. and E.U. 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: risks that the efficacy and safety results for eli-cel from the Starbeam Study seen to date will not continue or persist, the risk of cessation or delay of any of the ongoing clinical studies and/or our development of eli-cel, 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. and EU, the risk that our submissions for regulatory approvals will not be submitted or accepted for filing by the regulatory authorities on the timeframe we expect or at all, and the risk that any one or more of our product candidates will not be successfully developed, approved or commercialized. 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-K, 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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