# 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): December 17, 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 December 17, 2021, bluebird bio, Inc. (“bluebird” or the "Company") issued a press release announcing that the U.S. Food and Drug Administration (FDA) has accepted for priority review the Biologics License Application (BLA) for elivaldogene autotemcel (eli-cel,Lenti-D®), bluebird's gene therapy for cerebral adrenoleukodystrophy (CALD) in patients less than 18 years of age. Eli-cel is an investigational one-time gene therapy, custom-designed to treat the underlying cause of this irreversible neurodegenerative disease and to stabilize neurologic function. The agency set a Prescription Drug User Fee Act goal date of June 17, 2022.

On December 20, 2021, the Company announced that the FDA has placed its clinical program for lovotibeglogene autotemcel (lovo-cel) gene therapy for sickle cell disease (SCD) on partial clinical hold for patients under the age of 18. The partial, temporary suspension relates to an ongoing investigation by the Company into an adolescent patient with persistent, non-transfusion-dependent anemia following treatment with lovo-cel, now 18 months post-treatment. This patient is clinically well and there is no evidence of malignancy or clonal predominance. Enrollment and dosing for patients 18 and older living with SCD in the HGB-206, HGB-210 and LTF-307 clinical studies, as well as follow up for treated patients of all ages in all studies are continuing as planned.

Consistent with the FDA’s clinical hold procedures, the Company anticipates receiving written questions from the agency in early 2022 and will work quickly to respond in order to resolve the partial hold. The Company is evaluating what impact, if any, the partial clinical hold may have on first quarter 2023 projected timing for the lovo-cel biologics license application (BLA) submission. As previously communicated, the Company has treated all patients in HGB-206 Group C who will form the primary basis of efficacy for approval, with the demonstration of analytical comparability and validation of our commercial manufacturing process as the key remaining actions prior to submission of the planned BLA.

The full text of bluebird’s press releases regarding these announcements are filed as Exhibits 99.1 and 99.2 to this Current Report on Form 8-K and are 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 December 17, 2021. |
| 99.2 | Press release issued by bluebird bio, Inc. on December 20, 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: December 20, 2021

**bluebird bio, Inc.**

By: /s/ Helen C. Fu

Helen C. Fu

*Senior Vice President, General Counsel and Secretary*

**Exhibit 99.1**

# bluebird bio Announces FDA Priority Review of Biologics License Application for eli-cel Gene Therapy for Cerebral Adrenoleukodystrophy (CALD) in Patients Without a Matched Sibling Donor

*If approved, eli-cel will be the first and only gene therapy for the treatment of CALD, a rare neurodegenerative disease primarily affecting young children that can lead to progressive, irreversible loss of neurologic function and death*

*FDA set PDUFA date of June 17, 2022*

CAMBRIDGE, Mass. — (BUSINESS WIRE) — December 17, 2021— **bluebird bio, Inc**. (Nasdaq: BLUE) today announced that the U.S. Food and Drug Administration (FDA) has accepted for priority review the Biologics License Application (BLA) for elivaldogene autotemcel (eli-cel, Lenti-D®), the company's gene therapy for cerebral adrenoleukodystrophy (CALD) in patients less than 18 years of age. Eli-cel is an investigational one-time gene therapy, custom-designed to treat the underlying cause of this irreversible neurodegenerative disease and to stabilize neurologic function. The agency set a Prescription Drug User Fee Act (PDUFA) goal date of June 17, 2022.

"Eli-cel is an important potential therapeutic option for patients with CALD—a devastating neurodegenerative disease—and we are encouraged to be moving forward given the urgent unmet need for these children and their families," said Andrew Obenshain, chief executive officer, bluebird bio. "As the second BLA acceptance for bluebird bio this year, this is a meaningful milestone in our work to deliver one-time treatments for severe genetic diseases."

If approved, eli-cel will be the first approved treatment to address the underlying genetic cause of disease for patients living with CALD in the U.S. – offering appropriate patients an alternative to allogeneic hematopoietic stem cell transplant (allo-HSCT), which is associated with serious potential complications and mortality that increase in patients without a matched sibling donor. It is estimated that more than 70% of patients diagnosed with CALD do not have a matched sibling donor.

The BLA for eli-cel is supported by efficacy and safety data from the completed Phase 2/3 Starbeam study (ALD-102) (N=32). Additionally, the BLA contains data for 23 subjects dosed in the Phase 3 ALD-104 study. Study ALD-104 has subsequently completed enrollment and follow-up is ongoing. All patients who completed ALD-102, as well as those who will complete ALD-104, are invited to participate in a long-term follow-up study (LTF-304).

In ALD-102, 90.6% (29/32) of patients met the primary endpoint of Major Functional Disabilities (MFD)-free survival at 24 months. As previously reported, two patients withdrew from study ALD-102 at investigator discretion, and one additional subject experienced rapid disease progression early in the study, resulting in MFDs and subsequent death. All patients who completed ALD-102 enrolled in follow-up study LTF-304. The median duration of follow-up is 3.5 years (42.3 months; 13.4, 83.7).

Adverse reactions attributed to eli-cel observed in clinical trials include myelodysplastic syndrome, cystitis viral, pancytopenia, and vomiting. There have been no reports of graft-versus-host-disease, graft failure or rejection, transplant-related mortality, or replication competent lentivirus in the 55 patients who received eli-cel in clinical studies (ALD-102/LTF-304 and ALD-104).

On August 9, bluebird bio announced that the eli-cel clinical program was placed on a clinical hold, following a Suspected Unexpected Serious Adverse Reaction (SUSAR) of myelodysplastic syndrome

(MDS). Available evidence suggests that the event was likely mediated by Lenti-D lentiviral vector (LVV) insertion. Consistent with this known risk, two additional cases of MDS have subsequently been reported and details have been shared with the FDA and study investigators. The FDA clinical hold for eli-cel is ongoing and all patients who received eli-cel in the clinical program continue to be closely monitored, per study protocols. Given the devastating and fatal nature of CALD and lack of other treatment options for patients without a matched sibling donor, bluebird bio continues to assess the overall benefit/risk profile of the product as favorable for patients with CALD who do not have a matched sibling donor.

The FDA's Priority Review designation is granted to therapies that have the potential to provide significant improvements in the treatment, diagnosis or prevention of serious conditions, and targets a review timeline of six months after the 60-day FDA BLA filing decision, compared to a standard review timeline of 10 months after the 60-day FDA filing decision.

The FDA previously granted eli-cel Orphan Drug status, Rare Pediatric Disease designation, and Breakthrough Therapy designation.

**About CALD**

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 leads to 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 that nerve cells need to function effectively, especially for thinking and muscle control. The onset of symptoms of CALD typically occurs in childhood (median age 7). Early diagnosis and treatment of CALD is essential, as nearly half of patients who do not receive treatment die within five years of symptom onset.

**About elivaldogene autotemcel (eli-cel, Lenti-D®) gene therapy**

eli-cel 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 stem cells (HSCs). The addition of the functional *ABCD1* gene allows patients to produce the ALD protein (ALDP), which is thought to facilitate the breakdown of very long-chain fatty acids (VLCFAs). The expression of ALDP and effect of eli-cel is expected to be life-long. The goal of treatment with eli-cel is to stop the progression of CALD and, consequently, preserve as much neurological function as possible, including the preservation of motor function and communication ability. Importantly, with eli-cel, there is no need for donor HSCs from another person.

bluebird bio's clinical development program for eli-cel includes the completed pivotal Phase 2/3 Starbeam study (ALD-102) and the ongoing Phase 3 ALD-104 study, which has completed enrollment. Additionally, bluebird bio is conducting a long-term safety and efficacy follow-up study (LTF-304) for patients who have received eli-cel for CALD and completed two years of follow-up in ALD-102 or ALD-104. Clinical studies of eli-cel are currently on hold with the FDA.

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

**About bluebird bio, Inc.**

bluebird bio is pursuing curative gene therapies to give patients and their families more bluebird days.

With a dedicated focus on severe genetic diseases, bluebird has industry-leading clinical and research programs for sickle cell disease, β-thalassemia and cerebral adrenoleukodystrophy and is advancing research to apply new technologies to these and other diseases. We custom design each of our therapies to address the underlying cause of disease and have developed in-depth and effective analytical methods to understand the safety of our lentiviral vector technologies and drive the field of gene therapy forward.

Founded in 2010, bluebird has the largest and deepest ex-vivo gene therapy data set in the world—setting the standard for industry. Today, bluebird continues to forge new paths, combining our real-world experience with a deep commitment to patient communities and a people-centric culture that attracts and grows a diverse flock of dedicated birds.

For more information, visit **bluebirdbio.com** or follow us on social media at **@bluebirdbio**, **LinkedIn**, **Instagram** and **YouTube**.

Lenti-D and bluebird bio are registered trademarks of bluebird bio, Inc.

**bluebird bio Cautionary Statement Regarding Forward-Looking Statements**
*This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. Such forward-looking statements are based on historical performance and current expectations and projections about our future financial results, goals, plans and objectives and involve inherent risks, assumptions and uncertainties, including internal or external factors that could delay, divert or change any of them in the next several years, that are difficult to predict, may be beyond our control and could cause our future financial results, goals, plans and objectives to differ materially from those expressed in, or implied by, the statements. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many risks and uncertainties that affect bluebird bio's business, particularly those identified in the risk factors discussion in bluebird bio's Annual Report on Form 10-K, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. These risks include, but are not limited to: the risk that the efficacy and safety results from our prior and ongoing clinical trials will not continue or be seen in additional patients treated with our product candidates; the risk that additional insertional oncogenic or other safety events associated with lentiviral vector, drug product, or myeloablation will be discovered or reported over time; and the risk that any one or more of our product candidates will not be successfully developed, approved or commercialized. The forward-looking statements included in this document are made only as of the date of this document and except as otherwise required by applicable law, bluebird bio undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.*

Investors:
Courtney O'Leary, 978-621-7347
**coleary@bluebirdbio.com**

or

Media:
Jess Rowlands, 857-299-6103
**jess.rowlands@bluebirdbio.com**

**Exhibit 99.2**

# bluebird bio Announces Partial Clinical Hold for Patients Under 18 in Sickle Cell Gene Therapy Clinical Program

CAMBRIDGE, Mass.— (BUSINESS WIRE) — December 20, 2021 — **bluebird bio, Inc.** (NASDAQ: BLUE) today announced that the FDA has placed its clinical program for lovotibeglogene autotemcel (lovo-cel) gene therapy for sickle cell disease (SCD) on partial clinical hold for patients under the age of 18. The partial, temporary suspension relates to an ongoing investigation by bluebird bio into an adolescent patient with persistent, non-transfusion-dependent anemia following treatment with lovo-cel, now 18 months post-treatment. This patient is clinically well and there is no evidence of malignancy or clonal predominance. Enrollment and dosing for patients 18 and older living with SCD in the HGB-206, HGB-210 and LTF-307 clinical studies, as well as follow up for treated patients of all ages in all studies are continuing as planned.

“The safety of patients treated with our gene therapies is always our top priority,” said Richard Colvin, MD, Chief Medical Officer, bluebird bio. “Consistent with the FDA’s direction, we have paused enrollment and treatment of patients younger than 18 in our SCD clinical program, and we will continue to work collaboratively with the FDA to understand and address their concerns. While the partial hold is in place, we intend to continue planned follow-up on previously treated patients from HGB-206 and HGB-210 and plan to enroll and treat new adult patients with lovo-cel through study HGB-210 to further characterize the efficacy and safety of lovo-cel for patients with SCD and to continue to advance the field of gene therapy.”

Consistent with the FDA’s clinical hold procedures, bluebird anticipates receiving written questions from the agency in early 2022 and will work quickly to respond in order to resolve the partial hold. The company is evaluating what impact, if any, the partial clinical hold may have on first quarter 2023 projected timing for the lovo-cel biologics license application (BLA) submission. As previously communicated, bluebird has treated all patients in HGB-206 Group C who will form the primary basis of efficacy for approval, with the demonstration of analytical comparability and validation of our commercial manufacturing process as the key remaining actions prior to submission of the planned BLA.

**About lovotibeglogene autotemcel (lovo-cel; formerly LentiGlobin® for SCD, bb1111)**
lovotibeglogene autotemcel (lovo-cel) gene therapy is an investigational one-time treatment being studied for sickle cell disease (SCD), that is designed to add functional copies of a modified form of the β-globin gene ($\beta^{A\text{-}T87Q}$-globin gene) into a patient’s own hematopoietic (blood) stem cells (HSCs). Once patients have the $\beta^{A\text{-}T87Q}$-globin gene, their red blood cells (RBCs) can produce anti-sickling hemoglobin ($HbA^{T87Q}$) that decreases the proportion of HbS, with the goal of reducing sickled RBCs, hemolysis, and other complications. bluebird bio’s clinical development program for lovo-cel includes the completed Phase 1/2 HGB-205 and ongoing Phase 1/2 HGB-206 and Phase 3 HGB-210 studies. bluebird bio is also conducting a long-term safety and efficacy follow-up study (LTF-307) for people who have participated in bluebird bio sponsored clinical studies of lovo-cel.

The safety profile of the lovo-cel treatment regimen is predominately reflective of the known risks of autologous stem cell transplantation and myeloablative single-agent busulfan conditioning, as well as underlying SCD. Adverse drug reactions due to lovo-cel include hot flush, decreased blood pressure, acute myeloid leukemia (AML), and anemia.

As of February 17, 2021, a total of 49 patients have been treated with lovo-cel, with up to six years of patient follow-up, in the HGB-205 (n=3), HGB-206 (n=44), and HGB-210 (n=2) clinical studies. The HGB-206 total includes: Group A (n=7), B (n=2), and C (n=35), representing progressive adaptations to

the manufacturing and treatment processes. In the Group C cohort of the Phase 1/2 HGB-206 study, no severe vaso-occlusive events (VOEs) were reported with up to 24 months of follow-up in patients with a history of at least four severe VOEs and at least six months of follow-up.

In the initial cohort (Group A) of the HGB-206 study, two patients treated with lovo-cel developed AML. After thorough investigations into the cases, bluebird bio determined that these were unlikely related to the insertion of bluebird's lentiviral vector (LVV) gene therapy for SCD.

For more information on lovo-cel studies, visit: **https://www.bluebirdbio.com/our-science/clinical-trials** or **clinicaltrials.gov**.

The FDA has granted orphan drug designation, fast track designation, regenerative medicine advanced therapy (RMAT) designation, and rare pediatric disease designation for lovo-cel.

lovo-cel is investigational and has not been approved in any geography.

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Founded in 2010, bluebird has the longest and deepest ex-vivo gene therapy data set in the world—setting the standard for industry. Today, bluebird continues to forge new paths, combining our real-world experience with a deep commitment to patient communities and a people-centric culture that attracts and grows a diverse flock of dedicated birds.

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*on Form 10-K, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. These risks include, but are not limited to: the risk that the written questions that we receive from the FDA may require us to collect additional data or information beyond what we currently expect; the risk that we may not be able to address the FDA's concerns regarding lovo-cel in the treatment of patients with sickle cell under the age of 18 quickly or at all; the risk that we may not be able to collect the manufacturing comparability data needed to support a BLA submission for lovo-cel on our projected timelines; the risk that our planned BLA submission for lovo-cel may be delayed or may be for a narrower indication or patient population than we expected; the risk that the efficacy and safety results from our prior and ongoing clinical trials will not continue or be seen in additional patients treated with our product candidates; the risk that additional insertional oncogenic or other safety events associated with lentiviral vector, drug product, or myeloablation will be discovered or reported over time; the risk that any one or more of our product candidates will not be successfully developed, approved or commercialized; and the risks related to the ongoing COVID-19 pandemic. The forward-looking statements included in this document are made only as of the date of this document and except as otherwise required by applicable law, bluebird bio undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.*

**Investors**:
Courtney O'Leary, 978-621-7347
**coleary@bluebirdbio.com**

or

**Media**:
Sarah Alspach, 215-287-6354
**sarah.alspach@bluebirdbio.com**

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