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 7, 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 December 7, 2020, bluebird bio, Inc. ("bluebird") issued a press release announcing data presented at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition from its Phase 1/2 HGB-206 study of investigational LentiGlobin™ gene therapy (bb1111) for adult and adolescent patients with sickle cell disease.

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 December 7, 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: December 7, 2020

bluebird bio, Inc.

By: /s/ Jason F. Cole

Jason F. Cole

Chief Operating and Legal Officer

Exhibit 99.1

Treatment with Investigational LentiGlobin™ Gene Therapy for Sickle Cell Disease (bb1111) Results in Complete Elimination of SCD-Related Severe Vaso-Occlusive Events in Group C of Phase 1/2 HGB-206 Clinical Study Presented at 62nd Annual ASH Meeting

No severe vaso-occlusive events (VOEs) reported through 24 months of follow-up in Group C patients who had a history of at least four severe VOEs and at least six months of follow-up (n=19)

At up to 30 months follow-up and 32 patients treated, Group C patients continue to produce consistent levels of gene therapy-derived anti-sickling hemoglobin (HbA^{T87Q}), reducing levels of abnormal sickle hemoglobin (HbS) that cause symptoms of SCD

Positive patient-reported quality of life outcomes assessed with validated PROMIS-57 demonstrate clinically meaningful reductions in pain intensity at Month 12 post-LentiGlobin for SCD treatment

CAMBRIDGE, Mass.— (BUSINESS WIRE)— December 7, 2020 - **bluebird bio, Inc.** (Nasdaq: BLUE) announced that new data from Group C of its ongoing Phase 1/2 HGB-206 study of investigational LentiGlobin™ gene therapy (bb1111) for adult and adolescent patients with sickle cell disease (SCD) show a complete elimination of severe VOEs and VOEs between six and 24 months of follow-up. These data are being presented at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition, taking place virtually from December 5-8, 2020.

“Now with more than two years of data, we continue to observe promising results in our studies of LentiGlobin for SCD that further illustrate its potential to eliminate the symptoms and devastating complications of sickle cell disease. Consistently achieving the complete resolution of severe vaso-occlusive events (VOEs) and VOEs between Month 6 and Month 24 follow-up is unprecedented other than with allogeneic stem cell transplantation. Importantly, our data show the potential for LentiGlobin for SCD to produce fundamentally disease-modifying effects with sustained pancellular distribution of gene therapy-derived anti-sickling HbA^{T87Q} and improvement of key markers of hemolysis that approach normal levels,” said David Davidson, M.D., chief medical officer, bluebird bio. “In addition to these clinical outcomes, for the first time with a gene therapy we now have patient-reported outcomes through the validated PROMIS-57 tool, showing reduction in pain intensity at 12 months after treatment with LentiGlobin for SCD. These results provide insight into the potential real-life impact LentiGlobin for SCD may offer patients.”

SCD is a serious, progressive and debilitating genetic disease. In the U.S., the median age of death for someone with sickle cell disease is 43 – 46 years. SCD is caused by a mutation in the β-globin gene that leads to the production of abnormal sickle hemoglobin (HbS). HbS causes red blood cells to become sickled and fragile, resulting in chronic hemolytic anemia, vasculopathy and unpredictable, painful VOEs.

In the HGB-206 study of LentiGlobin for SCD, VOEs are defined as episodes of acute pain with no medically determined cause other than a vaso-occlusion, lasting more than two hours and severe enough to require care at a medical facility. This includes acute episodes of pain, acute chest syndrome (ACS), acute hepatic sequestration and acute splenic sequestration. A severe VOE requires a 24-hour hospital stay or emergency room visit or at least two visits to a hospital or emergency room over a 72-hour period, with both visits requiring intravenous treatment.

LentiGlobin for SCD was 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 can produce anti-sickling hemoglobin (HbA^{T87Q}) that decreases the proportion of HbS, with the goal of reducing sickled red blood cells, hemolysis and other complications.

“As a hematologist, I regularly see the debilitating effects of pain events caused by sickle cell disease. Pain has an overwhelmingly negative impact on many facets of my patients’ lives and can lead to prolonged hospitalizations,” said presenting study author Alexis A. Thompson, M.D., professor of pediatrics at Northwestern University Feinberg School of Medicine and head of hematology at Ann and Robert H. Lurie Children’s Hospital of Chicago. “The results observed with LentiGlobin gene therapy for SCD include the complete elimination of severe vaso-occlusive pain episodes, which is certainly clinically meaningful, but also for the first time, we have documented patients reporting that they are experiencing improved quality of life. This degree of early clinical benefit is extraordinarily rewarding to observe as a provider."

As of the data cut-off date of August 20, 2020, a total of 44 patients have been treated with LentiGlobin for SCD in the HGB-205 (n=3) and HGB-206 (n=41) clinical studies. The HGB-206 total includes: Groups A (n=7), B (n=2) and C (n=32).

HGB-206: Group C Updated Efficacy Results
The 32 patients treated with LentiGlobin for SCD gene therapy in Group C of HGB-206 had up to 30.9 months of follow-up (median of 13.0; min-max: 1.1 – 30.9 months).

In patients with six or more months of follow-up whose hemoglobin fractions were available (n=22), median levels of gene therapy-derived anti-sickling hemoglobin, HbA^{T87Q}, were maintained with HbA^{T87Q} contributing at least 40% of total hemoglobin at Month 6. At last visit reported, total hemoglobin ranged from 9.6 – 15.1 g/dL and HbA^{T87Q} levels ranged from 2.7 – 8.9 g/dL. At Month 6, the production of HbA^{T87Q} was associated with a reduction in the proportion of HbS in total hemoglobin; median HbS was 50% and remained less than 60% at all follow-up timepoints. All patients in Group C were able to stop regular blood transfusions by three months post-treatment and remain off transfusions as of the data cut-off.

Nineteen patients treated in Group C had a history of severe VOEs, defined as at least four severe VOEs in the 24 months prior to informed consent (annualized rate of severe VOE min-max: 2.0 – 10.5 events) and at least six months follow-up after treatment with LentiGlobin for SCD. There have been no reports of severe VOEs in these Group C patients following treatment with LentiGlobin for SCD. In addition, all 19 patients had a complete resolution of VOEs after Month 6.

Hemolysis Markers
In SCD, red blood cells become sickled and fragile, rupturing more easily than healthy red blood cells. The breakdown of red blood cells, called hemolysis, occurs normally in the body. However, in sickle cell disease, hemolysis happens too quickly due to the fragility of the red blood cells, which results in hemolytic anemia.

Patients treated with LentiGlobin for SCD in Group C demonstrated near-normal levels in key markers of hemolysis, which are indicators of the health of red blood cells. Lab results assessing these indicators were available for the majority of the 25 patients with ≥ 6 months of follow-up.

The medians for reticulocyte counts (n=23), lactate dehydrogenase (LDH) levels (n=21) and total bilirubin (n=24) continued to improve compared to screening values and stabilized by Month 6. In patients with Month 24 data (n=7), these values approached the upper limit of normal by Month 24. These results continue to suggest that treatment with LentiGlobin for SCD may improve biological markers to near-normal levels for SCD.

Pancellularity
As previously reported, assays were developed by bluebird bio to enable the detection of HbA^{T87Q} and HbS protein in individual red blood cells, as well as to assess if HbA^{T87Q} was pancellular, or present throughout all of a patient’s red blood cells. In 25 patients with at least six months of follow-up, on average, more than 80% of red blood cells contained HbA^{T87Q}, suggesting near-complete pancellularity of HbA^{T87Q} distribution and with pancellularity further increasing over time.

HGB-206: Improvements in Health-Related Quality of Life
Health-related quality of life (HRQoL) findings in Group C patients treated with LentiGlobin for SCD in the HGB-206 study were generated using the Patient Reported Outcomes Measurement Information System 57 (PROMIS-57), a validated instrument in SCD.

Data assessing pain intensity experienced by nine Group C patients were analyzed according to baseline pain intensity scores relative to the general population normative value: 2.6 on a scale of 0-10, where 10 equals the most intense pain. Data were assessed at baseline, Month 6 and Month 12.

Of the five patients with baseline scores worse than the population normative value average, four demonstrated clinically meaningful reductions in pain intensity at Month 12; the group had a mean score of 6.0 at baseline and a mean score of 2.4 at Month 12. Of the four patients with better than or near population normative values at baseline, two reported improvement and two remained stable with a mean score of 2.3 at baseline and 0.8 at Month 12.

HGB-206: Group C Safety Results
As of August 20, 2020, the safety data from Group C patients in HGB-206 remain generally consistent with the known side effects of hematopoietic stem cell collection and myeloablative single-agent busulfan conditioning, as well as underlying SCD. One non-serious, Grade 2 adverse event (AE) of febrile neutropenia was considered related to LentiGlobin for SCD. There were no serious AEs related to LentiGlobin for SCD.

One patient with significant baseline SCD-related and cardiopulmonary disease died 20 months post-treatment; the treating physician and an independent monitoring committee agreed his death was unlikely related to LentiGlobin for SCD and that SCD-related cardiac and pulmonary disease contributed.

LentiGlobin for SCD Data at ASH
The presentation of HGB-206 Group C results and patient reported outcomes research are now available on demand on the ASH conference website:

- **Oral #677:** Resolution of Serious Vaso-occlusive Pain Crises and Reduction in Patient-Reported Pain Intensity: Results from the Ongoing Phase 1/2 HGB-206 Group C Study of LentiGlobin for Sickle Cell Disease (bb1111) Gene Therapy
- **Oral #365:** Improvements in Health-Related Quality of Life for Patients Treated with LentiGlobin for Sickle Cell Disease (bb1111) Gene Therapy

About HGB-206
HGB-206 is an ongoing, Phase 1/2 open-label study designed to evaluate the efficacy and safety of LentiGlobin gene therapy for sickle cell disease (SCD) that includes three treatment cohorts: Groups A (n=7), B (n=2) and C (n=32). A refined manufacturing process designed to increase vector copy number (VCN) and further protocol refinements made to improve engraftment potential of gene-modified stem cells were used for Group C. Group C patients also received LentiGlobin for SCD made from HSCs collected from peripheral blood after mobilization with plerixafor, rather than via bone marrow harvest, which was used in Groups A and B of HGB-206.

About LentiGlobin for SCD (bb1111)
LentiGlobin gene therapy for sickle cell disease (bb1111) is an investigational treatment being studied as a potential treatment for SCD. bluebird bio's clinical development program for LentiGlobin for SCD includes the completed Phase 1/2 HGB-205 study, the ongoing Phase 1/2 HGB-206 study, and the ongoing Phase 3 HGB-210 study.

The U.S. Food and Drug Administration granted orphan drug designation, fast track designation, regenerative medicine advanced therapy (RMAT) designation and rare pediatric disease designation for LentiGlobin for SCD.

LentiGlobin for SCD received orphan medicinal product designation from the European Commission for the treatment of SCD, and Priority Medicines (PRIME) eligibility by the European Medicines Agency (EMA) in September 2020.

bluebird bio is conducting a long-term safety and efficacy follow-up study (LTF-307) for people who have participated in bluebird bio-sponsored clinical studies of LentiGlobin for SCD. For more information visit: **https://www.bluebirdbio.com/our-science/clinical-trials** or **clinicaltrials.gov** and use identifier NCT04628585 for LTF-307.

LentiGlobin for SCD is investigational and has not been approved in any geography.

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**.

Forward-Looking Statements
This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. 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: regarding the potential for LentiGlobin for Sickle Cell Disease to treat SCD; the risk that the efficacy and safety results from our prior and ongoing clinical trials will not continue or be repeated in our ongoing or planned clinical trials; the risk that the current or planned clinical trials of our product candidates will be insufficient to support regulatory submissions or marketing approval in the United States and European Union; the risk that regulatory authorities will require additional information regarding our product candidates, resulting in delay to our anticipated timelines for regulatory submissions, including our applications for marketing approval; 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-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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