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 5, 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 5, 2020, bluebird bio, Inc. (“bluebird”) and Bristol Myers Squibb Company issued a press release announcing updated data evaluating the companies’ investigational B-cell maturation antigen (BCMA) directed chimeric antigen receptor (CAR) T cell therapy, idecabtagene vicliueucel (ide-cel), in patients with relapsed and refractory multiple myeloma, were presented at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition.

Also on December 5, 2020, bluebird issued a press release announcing data presented at ASH of updated long-term efficacy and safety results reflecting up to six years of data for betibeglogene autotemcel gene therapy (beti-cel; formerly LentiGlobin™ for β-thalassemia) in patients with transfusion-dependent β-thalassemia (TDT).

The full text of bluebird’s press releases regarding these announcements are filed as Exhibit 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 5, 2020 (regarding data from ide-cel).
99.2	Press release issued by bluebird bio, Inc. on December 5, 2020 (regarding data from beti-cel).
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

Bristol Myers Squibb and bluebird bio Present Data Highlighting Anti-BCMA CAR T Cell Therapy, Ide-cel, in Relapsed and Refractory Multiple Myeloma at ASH 2020

Longer-term data from Phase 1 CRB-401 study evaluating ide-cel in relapsed and refractory multiple myeloma show ongoing deep and durable responses and median overall survival of 34.2 months[1]

Analyses from pivotal KarMMa study show clinically meaningful health-related quality of life benefits with ide-cel and underscore the potential value of ide-cel in elderly patients and in patients with high-risk multiple myeloma[2,3]

PRINCETON, NJ. and CAMBRIDGE, Mass. (BUSINESS WIRE) – December 5, 2020 - Bristol Myers Squibb (NYSE: BMY) and bluebird bio (BLUE) today announced updated data evaluating the companies' investigational B-cell maturation antigen (BCMA) directed chimeric antigen receptor (CAR) T cell therapy, idecabtagene vicluecel (ide-cel), were presented at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition. The data include longer-term updated results from the original Phase 1 CRB-401 study of ide-cel in relapsed and refractory multiple myeloma (RRMM), including the primary endpoint of safety and exploratory endpoints of progression-free survival (PFS) and overall survival (OS). Analyses of the pivotal registrational KarMMa trial will also be presented at the ASH meeting, including an analysis of health-related quality of life in patients with RRMM treated with ide-cel, and a subgroup analysis of outcomes for patients with high-risk RRMM. A subgroup analysis of elderly patients with RRMM treated with ide-cel in the KarMMa study were presented today. In addition, data from the ongoing Phase 1 CRB-402 study of bb21217, an investigational BCMA-directed CAR T cell therapy, were presented today at the meeting.

"Building on our experience in multiple myeloma, Bristol Myers Squibb is dedicated to delivering the promise of CAR T cell therapy to patients with relapsed and refractory multiple myeloma," said Kristen Hege, senior vice president, Early Clinical Development, Hematology/Oncology and Cell Therapy, Bristol Myers Squibb. "Ide-cel and bb21217 are part of our broad cell therapy development program intended to bring transformative therapies to patients in need, and these data from different studies, including the longest follow-up for any anti-BCMA CAR T cell therapy from the original CRB-401 study and important analyses from our pivotal KarMMa trial, further underscore the potential of ide-cel to improve patient outcomes with durable responses and clinical benefits for patients with triple-class exposed multiple myeloma."

"The breadth of data presented at ASH from across our studies underscores our commitment to the continued innovation of cell therapies for patients with multiple myeloma," said David Davidson, M.D., chief medical officer, bluebird bio. "We are encouraged by the longer-term results from the Phase 1 CRB-401 study, showing consistency with the depth and durability of responses observed in the Phase 2 KarMMa study, and reinforcing the role of ide-cel as an important potential therapeutic option for patients with triple-class exposed multiple myeloma. Additionally, we are pleased to see the updated results from the Phase 1 CRB-402 study, which continue to suggest promising response rates and durability. As had been hoped, early data also suggest that enrichment of bb21217 for memory-like T cells may be associated with sustained

response. We look forward to presenting additional data from across our ide-cel and bb21217 development programs in the future as we work to transform the treatment landscape for patients living with this devastating disease."

Updated Results from CRB-401 Study of Ide-cel

In the Phase 1 CRB-401 study, 62 patients with heavily pretreated relapsed or refractory multiple myeloma were treated with ide-cel across dose levels of 50, 150, 450, or 800 × 10^6 CAR positive T cells (Presentation #131). The primary endpoint was safety, and secondary and exploratory endpoints included response rates, PFS, OS, and minimal residual disease (MRD).

Safety remained consistent with previously reported results from CRB-401. The most frequent adverse events (AEs) were neutropenia (92%), cytokine release syndrome (CRS; 76%), anemia (76%), and thrombocytopenia (74%). The most frequent Grade 3/4 AEs were neutropenia (89%), leukopenia (61%), anemia (57%), and thrombocytopenia (57%). Most CRS events were Grade 1 or 2. Four patients (7%) had Grade 3 CRS; there were no Grade 4 or 5 CRS events reported.[1]

Among 62 patients treated with ide-cel in this study, the overall response rate (ORR) was 76%, including 24 patients (39%) who achieved a complete response (CR). The median duration of response (DoR) was 10.3 months. Median PFS was 8.8 months and median OS was 34.2 months, with a median follow-up of 14.7 months. Full results from the CRB-401 study will be presented today in an oral presentation (Presentation #131).[1]

"The CRB-401 study continues to demonstrate the potential of ide-cel to provide deep and durable responses for heavily pre-treated relapsed and refractory multiple myeloma patients," said Yin Lin, M.D., Ph.D., presenting author, associate professor of hematology at Mayo Clinic. "This longer-term data is also important as it reflects a meaningful median duration of response for hard-to-treat patients, further highlighting the importance of ide-cel as a potential innovative treatment for patients with significant unmet treatment needs."

Analyses of Pivotal KarMMa Study: Subgroup Analyses of Ide-cel Outcomes in High-Risk and Elderly Patients and Health-Related Quality of Life

Ide-cel demonstrated deep and durable responses in the pivotal phase 2 KarMMa study of patients with triple-class exposed relapsed and refractory multiple myeloma. A subgroup analysis was conducted to assess outcomes of treatment with ide-cel across target dose levels of 150 to 450 × 10^6 CAR positive T cells in patients with poor prognosis, including those with extramedullary disease, high-risk cytogenetics, and high tumor burden.

In the analysis of 128 patients, ide-cel demonstrated deep and durable responses across the majority of subgroups, including those with the highest risk. The ORR and CR rate were ≥65% and ≥20%, respectively for the majority of high-risk subgroups. Additionally, in the majority of the high-risk subgroups, the median DoR was ≥9.2 months and the median PFS was ≥7.5 months. Results will be presented in a poster presentation on Monday, December 7 (Presentation #3234).[2]

A separate subgroup analysis was conducted to evaluate the outcomes of treatment with ide-cel in elderly patients (Presentation #1367). Multiple myeloma occurs most commonly among the older population, with a median age of 69 at diagnosis. Advanced age has been shown to negatively affect prognosis and limit treatment options.[3]

Of the 128 patients treated with ide-cel in the KarMMa study, 45 patients (35%) were aged ≥65 years and 20 patients (16%) were aged ≥70 years. Response rates for both age groups were comparable and consistent with the overall ide-cel treated population, across all target dose levels, with ORRs of 84% to 90% and CR rates of 31% to 35%.[3]

Likewise, median DoR among responders in both age groups (10.7 months in patients aged ≥65 years and 11.0 months in patients aged ≥70 years) was similar to that of the overall ide-cel treated population. Median PFS was 8.6 months (95% CI, 4.9-12.2) in patients aged ≥65 years and 10.2 months (95% CI, 3.1-12.3) in patients aged ≥70 years. Additionally, no new safety signals were observed.[3]

In an analysis of the impact of ide-cel treatment on health-related quality of life (HRQoL) measures in patients with relapsed and refractory multiple myeloma from the KarMMa study, ide-cel was associated with clinically meaningful QoL benefits without compromising any HRQoL domains (Presentation #437). Patients demonstrated a clinically meaningful improvement in most functioning and symptom scores from baseline to Month 3 through 15, with statistical significance ($p<0.05$) reached at various time points for different subscales throughout the follow-up period. Full results from the HRQoL analysis will be presented tomorrow, Sunday, December 6, in an oral presentation (Presentation #437).[4]

Phase 1 CRB-402 Study of bb21217

Updated safety and efficacy results from the ongoing Phase 1 study (CRB-402) of bb21217, an investigational BCMA-directed CAR T cell therapy being studied in patients with relapsed and refractory multiple myeloma, were also presented today in an oral presentation (Presentation #130). bb21217 uses the ide-cel CAR molecule and is cultured with the PI3 kinase inhibitor (bb007) to enrich for T cells displaying a memory-like phenotype with the intention of increasing the *in vivo* persistence of CAR T cells.

As of the September 1, 2020 cutoff date, 69 patients were treated with bb21217 and updated results include new data following the introduction of a manufacturing process change. The study has completed enrollment and follow-up is ongoing as data continue to mature and the durability of response at the RP2D is assessed.[5]

About ide-cel

Ide-cel is a B-cell maturation antigen (BCMA)-directed genetically modified autologous chimeric antigen receptor (CAR) T cell immunotherapy. The ide-cel CAR is comprised of a murine extracellular single-chain variable fragment (scFv) specific for recognizing BCMA, attached to a human CD8 α hinge and transmembrane domain fused to the T cell cytoplasmic signaling domains of CD137 (4-1BB) and CD3-ζ chain, in tandem. Ide-cel recognizes and binds to BCMA on the surface of multiple myeloma cells leading to CAR T cell proliferation, cytokine secretion, and subsequent cytolytic killing of BCMA-expressing cells.

Bristol Myers Squibb and bluebird bio's broad clinical development program for ide-cel includes clinical studies (KarMMa-2, KarMMa-3, KarMMa-4) in earlier lines of treatment for patients with multiple myeloma, including newly diagnosed multiple myeloma. For more information visit clinicaltrials.gov.

Ide-cel is being developed as part of a Co-Development, Co-Promotion and Profit Share Agreement between Bristol Myers Squibb and bluebird bio.

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

About bb21217

bb21217 is an investigational BCMA-targeted CAR T cell therapy that uses the ide-cel CAR molecule and is cultured with the PI3 kinase inhibitor (bb007) to enrich for T cells displaying a memory-like phenotype with the intention of increasing the *in vivo* persistence of CAR T cells. bb21217 is being studied for patients with multiple myeloma in partnership between bluebird bio and Bristol Myers Squibb.

The companies' clinical development program for bb21217 includes the ongoing Phase 1 CRB-402 study. CRB-402 is the first-in-human study of bb21217 in patients with relapsed and refractory multiple myeloma (RRMM), designed to assess safety, pharmacokinetics, efficacy and duration of effect. CRB-402 is a two-part (dose escalation and dose expansion), open-label, multi-site Phase 1 study of bb21217 in adults with RRMM. A total of 69 patients have been treated with bb21217 and the study has completed enrollment. For more information visit: clinicaltrials.gov using identifier NCT03274219.

bb21217 is not approved for any indication in any geography.

Bristol Myers Squibb: Creating a Better Future for People with Cancer

Bristol Myers Squibb is inspired by a single vision—transforming people's lives through science. The goal of the company's cancer research is to deliver medicines that offer each patient a better, healthier life and to make cure a possibility. Building on a legacy across a broad range of cancers that have changed survival expectations for many, Bristol Myers Squibb researchers are exploring new frontiers in personalized medicine, and through innovative digital platforms, are turning data into insights that sharpen their focus. Deep scientific expertise, cutting-edge capabilities and discovery platforms enable the company to look at cancer from every angle. Cancer can have a relentless grasp on many parts of a patient's life, and Bristol Myers Squibb is committed to taking actions to address all aspects of care, from diagnosis to survivorship. Because as a leader in cancer care, Bristol Myers Squibb is working to empower all people with cancer to have a better future.

About Bristol Myers Squibb

Bristol Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol Myers Squibb, visit us at BMS.com or follow us on LinkedIn, Twitter, YouTube, Facebook and Instagram.

Celgene and Juno Therapeutics are wholly owned subsidiaries of Bristol-Myers Squibb Company. In certain countries outside the U.S., due to local laws, Celgene and Juno Therapeutics are referred to as, Celgene, a Bristol Myers Squibb company and Juno Therapeutics, a Bristol Myers Squibb company.

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 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.

Bristol Myers Squibb 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 regarding, among other things, the research, development and commercialization of pharmaceutical products. 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. These risks, assumptions, uncertainties and other factors include, among others, that future study results will be consistent with the results to date, that idecabtagene vicluecel (ide-cel) may not receive regulatory approval for the indications described in this release in the currently anticipated timeline or at all and, if approved, whether such product candidate for such indications described in this release will be commercially successful. 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 Bristol Myers Squibb's business and market, particularly those identified in the cautionary statement and risk factors discussion in Bristol Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2019, 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. 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, Bristol Myers Squibb 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.

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 regarding, among other things, the research, development and commercialization of ide-cel and bb21217. 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. These risks, assumptions, uncertainties and other factors include, among others, the possibility that the product candidates may not receive the FDA's approval for the indication described in this release, and, if approved, may not be commercially successful; that the results observed in ongoing clinical trials and described in this release may not continue in additional clinical trials, that the product candidates may not receive marketing approval in the EU or in any jurisdictions outside of

the US and the EU; and that the collaboration with Bristol Myers Squibb may not continue or be successful. 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 for the year ended December 31, 2019, 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. 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.

Hyperlinks are provided as a convenience and for informational purposes only. Neither Bristol Myers Squibb nor bluebird bio bears responsibility for the security or content of external websites or websites outside of their respective control.

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References

1. Lin, Y., et al., Idecabtagene Vicleucel (ide-cel, bb2121), a BCMA-Directed CAR T Cell Therapy, in Patients with Relapsed and Refractor Multiple Myeloma: Updated Results from Phase 1 CRB-401 Study. American Society of Hematology Annual Meeting. Presentation #131.
2. Raje, N., et al., Idecabtagene Vicleucel (ide-cel, bb2121) in Relapsed and Refractory Multiple Myeloma: Analyses of High-Risk Subgroups in the KarMMa Study. American Society of Hematology Annual Meeting. Presentation #3234.
3. Berdeja, J., et al., Efficacy and Safety of Idecabtagene Vicleucel (ide-cel, bb2121) in Elderly Patients with Relapsed and Refractory Multiple Myeloma: KarMMa Subgroup Analysis. American Society of Hematology Annual Meeting. Presentation #1367.

4. Shah, N., et al., Secondary Quality-of-Life Domains in Patients with Relapsed and Refractory Multiple Myeloma Treated with the BCMA-Directed CAR T Cell Therapy Idecabtagene Vicleucel (ide-cel, bb2121): Results from the KarMMa Clinical Trial. American Society of Hematology Annual Meeting. Presentation #437.
5. Alsina, M., et al., Updated Results from the Phase 1 CRB-402 Study of Anti-BCMA CAR T Cell Therapy bb21217 in Patients with Relapsed and Refractory Multiple Myeloma: Correlation of Expansion and Duration of Response with T Cell Phenotypes. American Society of Hematology Annual Meeting. Presentation #130.

Exhibit 99.2

Long-Term Data for bluebird bio's betibeglogene autotemcel (beti-cel) Gene Therapy Show Patients Across Ages and β-thalassemia Genotypes Achieve Transfusion Independence and Remain Free from Transfusions Up to Six Years Presented at 62nd ASH Meeting

All patients who achieved transfusion independence continue to remain transfusion free in ongoing long-term follow-up study

87% (13/15) of pediatric patients in Phase 3 studies achieved transfusion independence with median weighted average hemoglobin of 11.3 (9.4 – 12.8) g/dL and remain transfusion free

In long-term follow-up, 53% (9/17) of patients who achieved transfusion independence and restarted iron chelation have since stopped; 30% (7/23) who achieved transfusion independence now receive phlebotomy to reduce iron levels

CAMBRIDGE, Mass.— (BUSINESS WIRE)— December 5, 2020 - bluebird bio, Inc. (Nasdaq: BLUE) today presented updated long-term efficacy and safety results reflecting up to six years of data for betibeglogene autotemcel gene therapy (beti-cel; formerly LentiGlobin™ for β-thalassemia) in patients with transfusion-dependent β-thalassemia (TDT). The company also presented results for pediatric patients in the Phase 3 HGB-207 (Northstar-2) and HGB-212 (Northstar-3) studies. These data were presented at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition, taking place virtually from December 5-8, 2020.

"Our vision for beti-cel gene therapy is that a one-time treatment would enable lifelong, stable production of functional hemoglobin at sufficient levels to allow patients with β-thalassemia to stop and remain free from blood transfusions," said David Davidson, M.D., chief medical officer, bluebird bio. "All of the patients in our Phase 3 studies who achieved transfusion independence have maintained it, with the durability of the treatment effect underscored by patients from our earlier studies reaching their five-year anniversaries of freedom from transfusions. Moreover, transfusion independence has been observed in pediatric, adolescent and adult patients, and across genotypes – suggesting consistent outcomes with beti-cel regardless of age or genotype."

TDT is a severe genetic disease caused by mutations in the β-globin gene that result in reduced or significantly reduced hemoglobin (Hb). In order to survive, people with TDT require chronic blood transfusions to maintain adequate Hb levels. These transfusions carry the risk of progressive multi-organ damage due to unavoidable iron overload.

Beti-cel is a one-time gene therapy that adds 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 a patient has the $\beta^{A\text{-}T87Q}$-globin gene, they have the potential to produce HbA^{T87Q}, which is gene therapy-derived adult Hb, at levels that may eliminate or significantly reduce the need for transfusions. In studies of beti-cel, transfusion independence (TI) is defined as no longer needing red blood cell transfusions for at least 12 months while maintaining a weighted average Hb of at least 9 g/dL.

As of the data cut-off of March 3, 2020, a total of 60 pediatric, adolescent and adult patients, including 10 patients with at least five years of follow-up and one with at least six years, across genotypes of TDT have been treated with beti-cel in the Phase 1/2 HGB-204 (Northstar) and HGB-205 studies, and the Phase 3 HGB-207 (Northstar-2) and HGB-212 (Northstar-3) studies. Data from bluebird bio's Phase 1/2 and Phase 3 clinical studies represent more than 160 years of patient experience with beti-cel.

Long-term follow-up study LTF-303: Efficacy
After participating in and completing the two years of follow-up in either Phase 1/2 studies (HGB-204, HGB-205), or in one of the Phase 3 studies (HGB-207, HGB-212), patients treated with beti-cel were invited to

enroll in the 13-year long-term follow-up study, LTF-303. As of March 3, 2020, 32 patients were enrolled in LTF-303 (22 treated in Phase 1/2 studies, 10 treated in Phase 3 studies) with a median post-infusion follow-up of 49.1 months (min-max: 23.3 – 71.8 months).

Of the 32 patients enrolled in LTF-303, TI was achieved in 14/22 (64%) patients treated in Phase 1/2 and in 9/10 (90%) patients treated in Phase 3. All patients who achieved TI remained free from transfusions [median duration of ongoing TI is 39.4 months (min-max: 19.4 – 69.4 months)].

Weighted average Hb in patients who achieved TI in the Phase 1/2 was 10.4 (min-max: 9.4 – 13.3) g/dL and 12.5 (min-max: 11.9 – 13.5) g/dL in patients who achieved TI in the Phase 3 studies.

Median gene therapy-derived hemoglobin (HbA^{T87Q}) in all patients treated in the Phase 1/2 studies was stable over time: 6.4 (min-max: 0.5 – 10.1) g/dL at Month 24 (n=22), 6.7 (min-max: 0.4 – 10.1) g/dL at Month 36 (n=22), 6.6 (min-max: 0.5 – 10.7) g/dL at Month 48 (n=22), and 7.1 (min-max: 2.8 – 11.2) g/dL at Month 60 (n=10). Median HbA^{T87Q} at Month 24 in all patients treated in the Phase 3 studies was 9.5 (min-max: 0.9 – 12.4) g/dL (n=10).

Following an initial increase in liver iron concentration (LIC) after infusion, LIC in patients who achieved TI decreased, particularly in patients with a high iron burden at baseline. Patients with severe (LIC >15 mg/g, n=2) and significant (LIC ≥7 – 15 mg/g, n=5) iron burden at baseline had a median reduction of 59% and 38%, respectively, from baseline to Month 48.

Prior to beti-cel infusion, all patients were on iron chelation, which is needed to reduce excess iron caused by chronic blood transfusions. Of the 23 patients who achieved TI following treatment with beti-cel, the majority (65%, n=15) discontinued iron chelation and 30% (7/23) were able to receive phlebotomy (blood removal), which is a preferred method for iron reduction.

Long-term follow-up study LTF-303: Safety
In LTF-303, there were no deaths, no graft-versus-host disease (GVHD), and no cases of replication-competent lentivirus, insertional oncogenesis or clonal dominance were observed. No drug-related adverse events (AEs) were reported >2 years post-infusion. Serious AEs during LTF-303 unrelated to beti-cel included gonadotropic insufficiency, ectopic pregnancy, gall bladder wall thickening/polyp, bacteremia, neutropenia and major depression (n=1 for each).

Phase 3 Pediatric Patients: Efficacy
As of March 3, 2020; 24 pediatric patients (<12 years: n=13; ≥12 to <18 years: n=11) were treated and had a median follow-up of 15.5 months (min-max: 1.1 – 29.5 months) in Phase 3 HGB-207 (Northstar-2) and HGB-212 (Northstar-3) studies.

In these Phase 3 studies, the median age at which the children under 12 received their first transfusion was 11 months of age; for the adolescents between the ages of 12 and 18, the median was eight months of age.

Following treatment with beti-cel, 87% (13/15) of evaluable patients under the age of 18 years, including four patients under age 12, achieved TI. As of March 3, 2020, these patients continue to be free of transfusions for a median duration of 14.9 months (min-max: 12.2 – 21.6 months), with median weighted average total Hb levels of 11.3 g/dL (min-max: 9.4 – 12.8 g/dL).

Phase 3 Pediatric Patients: Safety
Drug-related AEs in pediatric patients during the HGB-207 and HGB-212 trials were non-serious and included tachycardia (Grade 1, n=1) and abdominal pain (Grade 1, n=2) on the day of infusion, and Grade 3 thrombocytopenia in one patient post-infusion. There were no deaths, no GVHD, no graft failures, and no cases of replication-competent lentivirus, insertional oncogenesis or clonal dominance were observed.

Post-infusion non-hematologic Grade ≥3 AEs in ≥3 patients < 18 years of age (N=24) included stomatitis (n=14), febrile neutropenia (n=12), decreased appetite (n=5), epistaxis (n=4), alanine aminotransferase increase (n=3), hypoxia (n=3) and pyrexia (n=3).

The presentations are now available on demand on the ASH conference website:

- **Oral #153:** Long-Term Efficacy and Safety of Betibeglogene Autotemcel Gene Therapy for the Treatment of Transfusion-Dependent β-Thalassemia: Results in Patients with up to 6 Years of Follow-up
- **Oral #154:** Favorable Outcomes in Pediatric Patients in the Phase 3 HGB-207 (Northstar-2) and HGB-212 (Northstar-3) Studies of betibeglogene autotemcel Gene Therapy for the Treatment of Transfusion-dependent β-thalassemia
- **Poster #776:** Improvement in Erythropoiesis Following Treatment with Betibeglogene Autotemcel Gene Therapy in Patients with Transfusion-Dependent β-Thalassemia in the Phase 3 HGB-207 Study
- **Poster #1699:** Response of Patients with Transfusion-dependent β-thalassemia (TDT) to betibeglogene autotemcel (beti-cel; LentiGlobin for β-thalassemia) Gene Therapy Based on HBB Genotype and Disease Genetic Modifiers

About betibeglogene autotemcel

The European Commission granted conditional marketing authorization (CMA) for beti-cel, marketed as ZYNTEGLO™ gene therapy, for patients 12 years and older with transfusion-dependent β-thalassemia (TDT) who do not have a β^0/β^0 genotype, for whom hematopoietic stem cell (HSC) transplantation is appropriate, but a human leukocyte antigen (HLA)-matched related HSC donor is not available.

Non-serious adverse events (AEs) observed during clinical studies that were attributed to beti-cel included abdominal pain, thrombocytopenia, leukopenia, neutropenia, hot flush, dyspnea, pain in extremity, tachycardia and non-cardiac chest pain. One serious adverse event (SAE) of thrombocytopenia was considered possibly related to beti-cel.

Additional AEs observed in clinical studies were consistent with the known side effects of HSC collection and bone marrow ablation with busulfan, including SAEs of veno-occlusive disease.

For details, **please see the Summary of Product Characteristics (SmPC).**

On April 28, 2020, the European Medicines Agency (EMA) renewed the CMA for beti-cel. The CMA for beti-cel is valid in the 27 member states of the EU as well as the UK, Iceland, Liechtenstein and Norway.

The U.S. Food and Drug Administration granted beti-cel Orphan Drug status and Breakthrough Therapy designation for the treatment of TDT. Beti-cel is not approved in the U.S. Beti-cel continues to be evaluated in the ongoing Phase 3 Northstar-2 (HGB-207) and Northstar-3 (HGB-212) studies.

bluebird bio is conducting a long-term safety and efficacy follow-up study (LTF-303) for people who have participated in bluebird bio-sponsored clinical studies of beti-cel.

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.**

ZYNTEGLO, LentiGlobin 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. 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 betibeglogene autotemcel to treat transfusion-dependent β-thalassemia and 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, or for a broader indication in the 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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