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Updated Results of Ongoing Multicenter Phase I Study of bb2121 anti-BCMA CAR T Cell Therapy Continue to Demonstrate Deep and Durable Responses in Patients with Late-Stage Relapsed/Refractory Multiple Myeloma at ASCO Annual Meeting

High rates of response that were both deep and durable were seen at the highest dose levels.

Median PFS of approximately one year achieved in heavily pre-treated patients in the active doses of the dose escalation cohort

Consistent response observed for both low and high BCMA expression levels

Adverse events have been manageable across doses

SUMMIT, N.J. & CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ:CELG) and bluebird bio, Inc. (NASDAQ:BLUE) today announced updated results from the ongoing CRB-401 phase I clinical study of bb2121, an investigational anti-B-cell maturation antigen (BCMA) CAR T cell therapy, in 43 patients with late-stage relapsed/refractory multiple myeloma. These data were the subject of an oral presentation by Noopur Raje, M.D. at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL.

"We are encouraged by the continuing deep and durable responses seen in this study and look forward to the results of our pivotal study, KarMMa, which is currently enrolling," said Jay Backstrom, Chief Medical Officer for Celgene. "We continue to see BCMA as an excellent target in multiple myeloma and we believe bb2121 has the potential to have a significant impact on the treatment approach and outcomes for these patients. We and our partners at bluebird bio are fully committed to the continued rapid clinical development of bb2121 and the evaluation of its potential in the treatment of patients with relapsed and refractory multiple myeloma."

"To see a median PFS of 11.8 months in this heavily pretreated patient population is very encouraging," said David Davidson, M.D., Chief Medical Officer, bluebird bio. "As the data from this program continue to mature, bb2121 has set a high bar as the leading investigational anti-BCMA CAR T cell candidate for relapsed and refractory multiple myeloma. In addition, the deep MRD-negative responses, the activity seen across myeloma with high and low levels of BCMA expression, as well as adverse events observed support the evaluation of bb2121 in earlier lines of multiple myeloma, where patients may experience more durable outcomes."

The open-label phase I CRB-401 study (NCT02658929) is evaluating the preliminary safety and efficacy of bb2121 anti-BCMA CAR T cell therapy in patients with relapsed/refractory multiple myeloma.

Patients in the study were heavily pre-treated, with a median of seven prior myeloma treatment regimens (min, max: 3,14) in the dose escalation cohort (n=21) and eight prior regimens (min, max: 3, 23) in the dose expansion cohort (n=22). More than 90% of patients had received prior treatment with two IMiD® therapies, two proteasome inhibitors, daratumumab and an autologous stem cell transplant.

As of the March 29, 2018 data cut-off, 43 patients had been enrolled and dosed in either the dose-escalation cohort of the study, at four dose levels (50×10^6, 150×10^6, 450×10^6 and 800×10^6 CAR+ T cells), or in the dose expansion cohort in a dose range between $150\text{-}450 \times 10^6$ CAR+ T cells.

Patients received a lymphodepleting conditioning regimen of fludarabine and cyclophosphamide, followed by an infusion of bb2121 anti-BCMA CAR T cells. The CAR T cells were produced from each patient's own blood cells, which were modified using a proprietary lentiviral vector encoding the anti-BCMA CAR.

Response outcomes in efficacy evaluable patients* in the study were as follows:

Measure	50 x 10^6 (n=3), median follow-up 84 days (59,94)	150 x 10^6 (n=14), median follow-up 87 days (36,638)	> 150 x 10^6 (n=22), median follow-up 194 days (46, 556)
Overall response (ORR)	33.3%	57.1%	95.5%
Complete response (CR)	0%	42.9%	50%
Very good partial response (VGPR)	0%	7.1%	36.4%
Median duration of response mDOR	1.9 months	Not estimable	10.8 months

*Patients with ≥2 months of response data or PD/death within < 2 months

Responses were dose-related and observed for both low and high BCMA expression levels. In patients treated with 450 x 10^6 CAR+ T cells whose myeloma cells expressed low levels of BCMA (0 to 50% of cells BCMA positive), 8 of 8 had a response. In those expressing high BCMA (≥50% BCMA positive), 10 of 11 had a response.

The median progression-free survival (PFS) estimate for patients in the dose-escalation phase treated at active doses (≥150 x 10^6 CAR+ T cells) was 11.8 months (95% CI 8.8, NE), while patients receiving 50 x 10^6 CAR+ T cells had a median PFS of 2.7 months (95% CI 1.0, 2.9).

In the dose-escalation and expansion phase of the study, all patients who responded and were evaluable for minimal residual disease (MRD as measured by adaptive next-generation sequencing assay) (n=16) were MRD negative at one or more time points. Additionally, two patients who did not have a response and were evaluated for MRD were MRD positive at month one. The median PFS estimate in MRD negative responders was 17.7 months (95% CI: 5.8, NE).

Among all infused patients (n=43), 63% had cytokine release syndrome (CRS), mostly Grade 1 & 2, with 2 patients experiencing Grade 3 CRS (5%). Nine patients (21%) received tocilizumab, including 4 patients (9%) who also received steroids and the median duration of CRS was 6 days (1,32). For patients receiving 150 x 10^6 CAR+ T cells (n=18), the rate of CRS was 39% with no grade 3 cases. For patients receiving ≥150 x 10^6 CAR+ T cells (n=22), the rate of CRS was 82% with 9.1% of patients experiencing grade 3 events. Also among all infused patients, there were 14 patients (33%) who experienced neurotoxicity, with one patient experiencing a grade 3 or higher event. Other frequent Grade 3/4 AEs included cytopenias commonly associated with lymphodepleting chemotherapy such as neutropenia (79%), thrombocytopenia (51%) and anemia (44%), as well as infection (any grade) with a frequency of 61% overall and 23% in the first month. Grade 3 or higher infection occurred with a frequency of 21% overall and 5% in the first month.

"The continuing high, durable response rates and MRD-negative results in this heavily pre-treated population of multiple myeloma patients further illustrates BCMA as a promising target in this incurable disease and bb2121 as an investigational therapy of great potential in patients with relapsed and refractory multiple myeloma with both high and low BCMA expression," said Dr. Raje., Professor of Medicine at Harvard Medical School and Director of the Multiple Myeloma Center at Massachusetts General Hospital. "We will continue to evaluate the long-term effect of bb2121 as we learn more about the potential for this investigational therapy."

bb2121 is an investigational compound that is not approved for any use in any country. bb2121 received Breakthrough Therapy Designation from the U.S. FDA and PRIME eligibility from the EMA. Celgene has also sponsored an open-label, single-arm, pivotal, phase 2 study (KarMMa), which is recruiting in North America and Europe, to evaluate bb2121 further in patients with relapsed and refractory multiple myeloma (NCT03361748).

About Celgene

Celgene Corporation, headquartered in Summit, New Jersey, is an integrated global biopharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases through next-generation solutions in protein homeostasis, immuno-oncology, epigenetics, immunology and neuro-inflammation. For more information, please visit www.celgene.com. Follow Celgene on Social Media: @Celgene, Pinterest, LinkedIn, Facebook and YouTube.

About bluebird bio, Inc.

With its lentiviral-based gene therapies, T cell immunotherapy expertise and gene editing capabilities, bluebird bio has built an integrated product platform with broad potential application to severe genetic diseases and cancer. bluebird bio's gene therapy clinical programs include Lenti-D™ for the treatment of cerebral adrenoleukodystrophy, and LentiGlobin™ for the treatment of transfusion-dependent β-thalassemia, also known as β-thalassemia major, and severe sickle cell disease. bluebird bio's oncology pipeline is built upon the company's leadership in lentiviral gene delivery and T cell engineering, with a focus on developing novel T cell-based immunotherapies, including chimeric antigen receptor (CAR T) and T cell receptor (TCR) therapies. bluebird bio's lead oncology programs, bb2121 and bb21217, are anti-BCMA CAR T programs partnered with Celgene. bluebird bio also has discovery research programs utilizing megaTAL/homing endonuclease gene editing technologies with the potential for use across the company's pipeline.

bluebird bio has operations in Cambridge, Massachusetts, Seattle, Washington, Durham, North Carolina and Zug, Switzerland.

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Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding the potential benefits of, and plans relating to the collaboration between bluebird bio and Celgene; the potential of bb2121 as a therapeutic drug; and the benefit of each company's strategic plans and focus. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "would," "could," "potential," "possible," "hope" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from current expectations and beliefs. For example, there can be no guarantee that any product candidate will be successfully developed or complete necessary preclinical and clinical phases, or that development of any of product candidates will successfully continue. There can be no guarantee that any positive developments will result in stock price appreciation. Management's expectations and, therefore, any forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other important factors, including: results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. FDA and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; the ability to obtain and maintain requisite regulatory approvals and to enroll patients in planned clinical trials; unplanned cash requirements and expenditures; competitive factors; the ability to obtain, maintain and enforce patent and other intellectual property protection for any product candidates; the ability to maintain key collaborations; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in each company's public filings with the Securities and Exchange Commission. Any forward-looking statements contained in this press release speak only as of the date hereof, and neither company has any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required by law.

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