



**bluebird bio and Celgene Corporation Present Initial Data from Ongoing Phase 1 Clinical Study of Next-Generation Anti-BCMA CAR T Cell Therapy bb21217 in Patients with Relapsed/Refractory Multiple Myeloma at ASH Annual Meeting**

*bb21217 early safety profile consistent with CAR T platform therapies*

*83 percent objective response rate in 12 heavily pretreated multiple myeloma patients at first dose level studied*

*Higher dose of bb21217 being assessed in the ongoing Phase 1 study*

**CAMBRIDGE, Mass. and SUMMIT, N.J. – December 2, 2018** – [bluebird bio, Inc.](#) (Nasdaq: BLUE) and Celgene Corporation (NASDAQ: CELG) announced initial data from the ongoing Phase 1 clinical study of bb21217 (CRB-402), an investigational next-generation anti-BCMA CAR T cell therapy being studied in patients with relapsed/refractory multiple myeloma. The data were presented by Nina Shah, M.D., University of California, San Francisco, as an oral presentation at the 60<sup>th</sup> Annual Meeting of the American Society of Hematology (ASH).

bb21217 is an investigational anti-BCMA CAR T cell therapy that uses the bb2121 chimeric antigen receptor (CAR) molecule with a manufacturing process designed to improve CAR T cell functional persistence. bb21217 has exhibited improved functional persistence and increased anti-tumor activity in preclinical animal studies.

“Anti-BCMA CAR T therapy with bb2121 has shown clinical responses in a substantial proportion of patients with relapsed/refractory multiple myeloma. With the bb21217 program we are pursuing an approach intended to improve the *in vivo* persistence of functional CAR T cells with the hope that this provides a more durable benefit for patients,” said David Davidson, M.D., chief medical officer, bluebird bio. “The safety results and promising response rate in the initial dose cohort, as well as the observation of detectable CAR T cells in the first three patients with follow up to the month 6 study visit and beyond, support advancing to a higher dose to further characterize the potential of bb21217 as a treatment option for patients with relapsed/refractory multiple myeloma.”

“The initial results of bb21217 are encouraging in terms of the adverse event profile, as well as the instances of ongoing, deep responses shown in these heavily pre-treated patients,” said Alise Reicin, M.D., President, Global Clinical Development for Celgene. “We look forward to further results from this next-generation agent in this area of continued medical need.”

bb21217 is being evaluated in the ongoing dose escalation part of the Phase 1 CRB-402 study in adults with relapsed/refractory multiple myeloma who have received at least three prior treatments, including a proteasome inhibitor and immunomodulatory agent (or are double refractory).



“Patients with multiple myeloma often undergo multiple cycles of treatment because there is currently no known cure for this aggressive cancer,” said Nina Shah, M.D., University of California, San Francisco, San Francisco, Calif. “The early clinical data from this Phase 1 study show manageable safety findings, and most patients in this initial group achieved an objective response. Future study is needed to assess durability of response at the current dose, as well as safety and activity at higher doses of bb21217.”

Patients included in these preliminary Phase 1 results (n=12) had a median age of 63 years (min; max: 44 – 69 years). They had received a median of seven prior lines of therapy (min; max: 4 – 17 lines) and 83 percent of patients received a prior autologous stem cell transplant. Fifty-eight percent (n=7) of patients had high-risk cytogenetics.

All treated patients received a dose of  $150 \times 10^6$  CAR+ T cells. The median follow-up after bb21217 infusion was 26 weeks (min; max: 4 – 51 weeks). The primary endpoint is safety measured by frequency of adverse events (AEs), dose limiting toxicity (DLT) and changes in laboratory results. Secondary endpoints include disease specific response criteria based on the International Myeloma Working Group (IMWG) Uniform Response Criteria for Multiple Myeloma.

### **Safety Results**

The safety results, reported as of the data extract of October 18, 2018, were manageable and consistent with known toxicities of CAR T therapies.

Eight of the 12 patients (67 percent) treated with bb21217 developed cytokine release syndrome (CRS); four Grade 1, three Grade 2, one Grade 3 case and no Grade 4 cases. Additionally, three of the 12 patients (25 percent) experienced neurotoxicity, including one Grade 1, one Grade 2 and one Grade 4 case. All CRS and neurotoxicity events resolved and no deaths occurred on study. Following the Grade 4 neurotoxicity event, patients were divided into two groups based on tumor burden and dosing continued at  $150 \times 10^6$  CAR+ T cells for a total of 12 subjects treated at this dose level.

### **Efficacy Results**

Of the 12 patients who received treatment with bb21217, 83 percent (n=10) achieved an objective clinical response by IMWG criteria. As of the data extract, responses are ongoing in nine of 10 patients, including three with a complete response (CR) or stringent complete response (sCR), two with a very good partial response (VGPR) and four with a partial response (PR).

Evidence of myeloma in the bone marrow, known as minimal residual disease (MRD), was undetectable at a minimum of two time points, by next-generation sequencing at a sensitivity level of  $10^{-5}$  or better in all responders who had evaluable bone marrow samples (n=4) with some as early as day 15.



CAR+ T cell expansion was observed during the first 30 days following treatment in all evaluable patients (n=11) with anti-BCMA CAR+T cells showing sustained persistence in all patients (3/3) with six or more months of follow-up.

The ongoing Phase 1 CRB-402 study is assessing a higher dose of  $300 \times 10^6$  CAR+ T cells in both high and low tumor burden cohorts.

### **About bb21217**

bb2121 and bb21217 are bluebird bio's lead investigational anti-BCMA CAR T therapies being developed in collaboration with Celgene.

Chimeric antigen receptors (CAR) are receptor proteins that have been engineered to give T cells the ability to target a specific protein. bb2121 and bb21217 are designed to recognize and kill plasma cells, notably malignant myeloma cells, that express the B cell maturation antigen (BCMA).

bluebird bio's clinical development program for bb21217 includes the ongoing Phase 1 CRB-402 two-part (dose escalation and dose expansion), non-randomized, open label study with sites in the United States. For more information visit: [clinicaltrials.gov](https://clinicaltrials.gov) using identifier NCT03274219.

bb21217 is not approved for any indication in any geography.

### **About Multiple Myeloma**

Multiple myeloma is a cancer of certain cells in the blood, called plasma cells. The cause of multiple myeloma is not known, and currently there is no cure. However, there are a number of treatment options available that can lead to remission. For some people with multiple myeloma, remission can last many years. Patients who have already been treated with some available therapies but continue to have progression of their disease have "relapsed" or "refractory" multiple myeloma, meaning their cancer has reoccurred after they have received initial treatments. Patients with relapsed/refractory multiple myeloma have fewer treatment options.

### **About bluebird bio, Inc.**

With its lentiviral-based gene therapies, T cell immunotherapy expertise and gene editing capabilities, bluebird bio has built a pipeline with broad potential application in severe genetic diseases and cancer.

bluebird bio's gene therapy clinical programs include investigational treatments for cerebral adrenoleukodystrophy, transfusion-dependent  $\beta$ -thalassemia and sickle cell disease.

bluebird bio's oncology pipeline is built upon the company's 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. The company's lead oncology programs are anti-BCMA CAR T programs partnered with Celgene.



bluebird bio's discovery research programs include 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. For more information, visit [www.bluebirdbio.com](http://www.bluebirdbio.com).

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### **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](http://www.celgene.com).

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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 in the development of bb2121 and bb21217; the potential of bb2121 and bb21217 as therapeutic drugs; 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, or that marketing approval will be granted. 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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