



December 10, 2017

## **Celgene Corporation and bluebird bio Announce Updated Results from Ongoing Multicenter Phase 1 Study of bb2121 Anti-BCMA CAR T Cell Therapy in Patients with Late Stage Relapsed/Refractory Multiple Myeloma at ASH Annual Meeting**

*Overall response rate (ORR) of 94% in patients in active dose cohorts (doses above  $50 \times 10^6$  CAR + T-cells)*

*Complete Response (CR) rate of 56% observed in patients in active dose cohorts*

*Median progression free survival (PFS) not reached with median follow up of 40 weeks in active dose cohorts*

*Nine of 10 (90%) of patients evaluable for minimal residual disease (MRD) status were found to be MRD-negative*

SUMMIT, N.J. & CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ: CELG) and [bluebird bio, Inc.](http://bluebird.bio) (Nasdaq: BLUE) today announced that updated results from the ongoing CRB-401 Phase 1 clinical study of bb2121, an investigational anti-B-cell maturation antigen (BCMA) CAR T cell therapy, in 21 patients with late-stage relapsed/refractory multiple myeloma will be presented in an oral presentation at the American Society of Hematology (ASH) Annual Meeting in Atlanta, Georgia.

The objective of this Phase 1 dose-escalation study is to evaluate safety and efficacy of bb2121 and determine a recommended Phase 2 dose.

"Celgene has a longstanding commitment to patients with multiple myeloma through our extensive research efforts in this deadly blood cancer," said Nadim Ahmed, President, Hematology and Oncology for Celgene. "Looking ahead, we see BCMA as an important target in this disease and we believe bb2121 has the potential to create significant impact on the treatment approach and outcomes for these patients."

"The growing body of bb2121 clinical data are building a compelling story, further supporting the importance of the therapy's unique features," said Dave Davidson, M.D., chief medical officer, bluebird bio. "The responses achieved in this relapsed and refractory patient population, combined with the generally tolerable safety profile, reinforce the potential role of bb2121 as a groundbreaking CAR T therapy in multiple myeloma."

### **Durable clinical responses in heavily pretreated patients with relapsed/refractory multiple myeloma: Updated results from a multicenter study of bb2121 anti-BCMA CAR T cell therapy (Abstract #740)**

**Presenter:** James Kochenderfer, M.D., the Center for Cancer Research at the National Cancer Institute in Bethesda, Maryland

**Date:** Monday, December 11, 3:00 pm (Oral presentation)

**Location:** Hall C1 (Georgia World Congress Center)

**Session Title:** Myeloma: Therapy, excluding Transplantation I

The open-label Phase 1 CRB-401 study (NCT02658929) is evaluating the preliminary safety and efficacy of bb2121 anti-BCMA CAR T cell in patients with relapsed and/or refractory multiple myeloma. The study also evaluated the recommended dose of bb2121 for future studies.

Patients on study were heavily pre-treated, with a median of 7 prior therapies (range: 3 - 14):

- | 100% previously treated with lenalidomide and bortezomib
- | 91% previously treated with pomalidomide and carfilzomib
- | 71% previously treated with daratumumab
- | 29% of patients were penta-refractory (bortezomib, lenalidomide, carfilzomib, pomalidomide, daratumumab)

- | All patients had at least one prior autologous stem cell transplant (ASCT)

As of the October 2, 2017 data cut-off, 21 patients had been enrolled and dosed in the dose-escalation phase of the study, in four dose cohorts:  $50 \times 10^6$ ,  $150 \times 10^6$ ,  $450 \times 10^6$  and  $800 \times 10^6$  CAR+ T cells. This multi-center study has enrolled patients at nine sites in the U.S. with central manufacturing performed at Celgene.

Patients received a conditioning regimen of cyclophosphamide and fludarabine, 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.

**Results in the active dose cohorts ( $150 \times 10^6$ ,  $450 \times 10^6$  and  $800 \times 10^6$  CAR+ T cells; N=18) were:**

- | Median follow-up was 40 weeks (range: 6.6-69)
- | 17/18 (94%) patients achieved an objective response
- | 16/18 (89%) patients achieved at least a very good partial response (VGPR)
- | 10/18 (56%) patients achieved a complete response (CR, N = 7), or unconfirmed complete response (N = 3)
- | 9 of 10 patients who were evaluable for MRD status were found to be MRD-negative
- | Median PFS has not been reached in the active dose cohorts. The PFS at 6 months and 9 months was 81% and 71%, respectively
- | Three patients in the dose-escalation who responded to therapy subsequently experienced disease progression

In the dose-escalation phase, 15/21 (71%) of patients had cytokine release syndrome (CRS), mostly Grade 1 & 2, with 2 patients experiencing Grade 3 CRS (9%). Four patients received tocilizumab, 1 (Grade 2 CRS) received steroids and in each case the CRS resolved within 24 hours. The most common treatment-emergent Grade 3-4 AEs in 21 infused patients were cytopenias commonly associated with lymphodepleting chemotherapy including neutropenia (86%), anemia (57%) and thrombocytopenia (43%). There were two deaths in the active cohorts at 22 and 69 weeks following infusion, respectively. The first was due to cardiac arrest and the second was due to myelodysplastic syndrome; both subjects were in a myeloma CR at their last study assessment prior to death. Based on the findings during dose escalation, a dose expansion phase of 12 subjects has started testing doses between  $150$ - $450 \times 10^6$  CAR+ T cells. In the dose expansion phase, one patient treated at the  $450 \times 10^6$  CAR+ T cells dose experienced Grade 4 neurotoxicity including focal cerebral edema and subarachnoid hemorrhage. This patient had a high tumor burden, and a history of subarachnoid hemorrhage. The event was successfully managed, and the patient remains in the response group. No other Grade 3/4 neurotoxicity was observed in the escalation or expansion cohort.

"To see these types of responses after one treatment with bb2121 in a heavily pre-treated patient population is very promising, and we are hopeful that CAR T therapy with bb2121 may become an important therapy in the fight against multiple myeloma, which remains an insidious and incurable disease," said James Kochenderfer, M.D., the Center for Cancer Research at the National Cancer Institute in Bethesda, Maryland and a primary investigator in the study.

bb2121 is an investigational compound that is not approved for any use in any country. bb2121 recently received Breakthrough Therapy Designation from the U.S. FDA and PRIME eligibility from the EMA. Celgene has also sponsored an open-label, single-arm phase 2 study (KarMMa), which is open to recruitment, to evaluate bb2121 further in patients with relapsed/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](http://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 its Lenti-D™ product candidate, currently in a Phase 2/3 study, called the Starbeam

Study, for the treatment of cerebral adrenoleukodystrophy, and its LentiGlobin® product candidate, currently in five clinical studies for the treatment of transfusion-dependent  $\beta$ -thalassemia, also known as  $\beta$ -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. bb2121 and bb21217 are each currently being studied in Phase 1 trials for the treatment of relapsed/refractory multiple myeloma. bluebird bio also has discovery research programs utilizing megaTALs/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 Europe.

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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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For Celgene:

Investors:

Patrick Flanigan, 908-673-9969

[pflanigan@celgene.com](mailto:pflanigan@celgene.com)

or

Media:

Greg Geissman, 908-673-9854

[ggeissman@celgene.com](mailto:ggeissman@celgene.com)

or

For bluebird bio

Investors & Media

Elizabeth Pingpank, 617-914-8736

[epingpank@bluebirdbio.com](mailto:epingpank@bluebirdbio.com)

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