Celgene Corporation and bluebird bio Announce Results from Ongoing Multicenter Phase 1 Study of bb2121 anti-BCMA CAR T Cell Therapy in Patients with Multiple Myeloma Published in New England Journal of Medicine

SUMMIT, NJ and CAMBRIDGE, MA (May 1, 2019)—Celgene Corporation (Nasdaq: CELG) and bluebird bio, Inc. (Nasdaq: BLUE) today announced that the New England Journal of Medicine (NEJM) has published interim results from CRB-401, the ongoing phase 1 study of bb2121, the companies’ lead investigational BCMA-targeted chimeric antigen receptor (CAR) T-cell therapy candidate for patients with relapsed and refractory multiple myeloma.

The manuscript, “Anti-BCMA CAR T Cell Therapy bb2121 in Relapsed/Refractory Multiple Myeloma”, published in NEJM includes key safety and efficacy results from the dose escalation and first expansion cohort, including a minimum of six months follow up on all subjects. As of the data cut-off date of April 30, 2018, manageable safety and deep and durable responses were reported in the first 33 patients infused with bb2121 BCMA-targeted CAR T-cells. Patients in the study were heavily pre-treated, with a median of seven prior multiple myeloma treatment regimens (range, 3 to 23), which included prior treatment with immunomodulatory drugs, proteasome inhibitors and daratumumab in the majority of patients. All but one patient had previously received an autologous stem cell transplant.

“CAR T-cell therapy is an important area of research for relapsed/refractory multiple myeloma patients where there remains a need for new options. We are encouraged by the expansion and persistence of the CAR T-cells, as well as the deep and durable responses with a manageable safety profile we’ve seen for bb2121 to date,” said senior author and principal investigator James N. Kochenderfer, M.D., Experimental Transplantation and Immunology Branch, National Cancer Institute Center for Cancer Research.

For the first 33 patients, the most common grade ≥3 events were hematologic toxicities, including neutropenia (85%), leukopenia (58%), anemia (45%) and thrombocytopenia (45%). Neurotoxicity all-grades occurred in 14 (42%) patients; 13 (39%) were grade ≤2 and one patient (3%) had grade 4 neurotoxicity which resolved within one month. Twenty-five (76%) patients experienced cytokine release syndrome; 23 (70%) were grade ≤2 events and two (6%) were grade 3 events; all events were reversible. Infection occurred in 14 (42%) patients; two were grade 3 (6%) and there were no grade 4 events. Peak CAR T cell expansion was higher in patients with cytokine release syndrome and CAR T-cells remained detectable in the blood in 57% of patients at six months following infusion.

Treatment with bb2121 resulted in an 85% objective response rate (ORR) with 45% of patients achieving a complete response (CR) (n=15) and an additional 27% of patients (n=9) achieving a very good partial response (VGPR) to yield a ≥ VGPR rate of 73%. Sixteen responding patients were evaluable for assessment of minimal residual disease (MRD) and all tested MRD negative at one or more time points.

Responses to bb2121 CAR T-cell infusion occurred early, with a median time to first partial response or better of 1.0 month (range, 0.5 to 3.0), and responses were durable, with a median duration of response of 10.9 months (95% CI, 7.2 to not estimable). Researchers observed that greater CAR T-cell expansion
occurred in responding patients. Responses were observed independent of tumor or serum BCMA levels. Median progression-free survival among all 33 patients was 11.8 months (95% CI, 6.2–17.8).

“These data from CRB-401 demonstrate that BCMA is a promising target in the treatment of patients with multiple myeloma. We continue to be encouraged by the potential of bb2121 as a first-in-class BCMA-targeted CAR T-cell therapy,” said Alise Reicin, M.D., President, Global Clinical Development for Celgene. “The compelling data in these heavily pre-treated relapsed/refractory patients has provided important insights in the development of bb2121 as we continue the follow up of patients in our recently fully enrolled pivotal KarMMa trial. We are also evaluating the potential for bb2121 in earlier lines of multiple myeloma treatment in the other KarMMa trials.”

"The data published in NEJM from CRB-401 provide the foundation for advancing the development of bb2121, which is currently being assessed in multiple clinical studies across different patient populations within multiple myeloma,” said Dave Davidson, M.D., chief medical officer, bluebird bio. “We hope that this potentially first-in-class BCMA-targeted CAR T-cell therapy may provide a new treatment option for patients living with multiple myeloma.”

In November 2017, bb2121 was granted Breakthrough Therapy Designation (BTD) by the U.S. Food and Drug Administration and PRIority Medicines (PRIME) eligibility by the European Medicines Agency based on preliminary clinical data from the phase 1 CRB-401 study.

bb2121 is being developed as part of a Co-Development, Co-Promote and Profit Share Agreement between Celgene and bluebird bio.

Potential approval of bb2121 in the U.S. is anticipated in the second half of 2020. bb2121 is an investigational therapy; safety and efficacy have not yet been established. bb2121 has not been approved for use by any health authority.

About CRB-401
The open-label phase 1 CRB-401 study (NCT02658929) is evaluating the preliminary safety and efficacy of bb2121 BCMA-targeted CAR T-cell therapy in patients with relapsed/refractory multiple myeloma. The primary endpoint of the study is safety. The first portion of the study included a dose-escalation phase in which cohorts of patients received ascending doses of bb2121 to determine the maximum tolerated dose; these findings established the recommended dose of the phase 2 KarMMa trial. The second portion of the study was a dose expansion phase where patients received bb2121 to further evaluate the safety, tolerability and clinical activity at the recommended phase 2 dose. All patients have been treated in the study and follow-up is ongoing. Complete data from the additional expansion cohorts will be published at a later date.

Patients in the dose escalation cohort and first expansion cohort of the study were heavily pre-treated, with a median of seven prior multiple myeloma treatment regimens (range: 3-14) in the dose escalation cohort (n=21) and eight prior regimens (range: 3-23) in the dose expansion cohort (n=12). Patients in the dose escalation phase had received at least three previous lines of therapy, including a proteasome inhibitor and an immunomodulatory agent, or were refractory to both drug classes. In addition, patients in the expansion cohorts had received a CD38 antibody and were refractory to their last regimen. All but one patient had previously received an autologous stem cell transplant. As of the data cut-off, patients had at least six months of follow-up or had disease progression, and there was one patient death unrelated to study treatment.

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.

Patients were enrolled and dosed in either the dose-escalation cohort of the study, at four target dose levels (50 x 10^6, 150 x 10^6, 450 x 10^6 and 800 x 10^6 CAR+ T cells), or in the dose expansion cohort in a target dose range between 150-450 x 10^6 CAR+ T cells.

**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](https://www.celgene.com), Pinterest, LinkedIn, Facebook and YouTube.

**About bluebird bio, Inc.**
bluebird bio is pioneering gene therapy with purpose. From our Cambridge, Mass., headquarters, we’re developing gene 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 by researching cerebral adrenoleukodystrophy, sickle cell disease, transfusion-dependent 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](https://bluebirdbio.com), LinkedIn, Instagram and YouTube.

**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; 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, 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 and includes risk factors related to the proposed transaction between Bristol-Myers Squibb and Celgene, such as, but not limited to, the risks that: Celgene’s management’s time and attention is diverted on transaction related issues; disruption from the transaction makes it more difficult for Celgene to maintain business, contractual and operational relationships; and Bristol-Myers Squibb, Celgene or the combined company is unable to retain key personnel. 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.

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

For Celgene:  
Investors:  
+1-908-673-9628  
ir@celgene.com  
or  
Media:  
+1-908-673-2275  
media@celgene.com

For bluebird bio  
Investors:  
Elizabeth Pingpank, 617-914-8736  
epingpank@bluebirdbio.com  
or  
Media:  
Catherine Falcetti, 617-583-3411  
cfalcetti@bluebirdbio.com