Stephanie C. Bovee
United States Federal Trade Commission
Bureau of Competition
600 Pennsylvania Avenue, NW
Washington, DC 20580
Via: sbovee@ftc.gov

February 16, 2018

Dear Stephanie C. Bovee;

Thank you for the meeting on February 14, 2017, where KEI registered our opposition to Celgene's acquisition of Juno Therapeutics. This letter elaborates on our objections.

1. **The Celgene-Juno acquisition will reduce potential competition in the market for B-cell maturation antigen (BCMA) chimeric antigen receptor T-cell (CAR T) technologies for the treatment of multiple myeloma.**

The Celgene acquisition of Juno Therapeutics would give Celgene control over two competing candidates for the treatment of multiple myeloma that use B-cell maturation antigen (BCMA) CAR T technologies. We ask that the FTC either block the acquisition, or require Celgene to divest one of the two competing BCMA technologies to an independent third party.

The Bluebird BCMA CAR T MM candidates

Celgene has a previously established agreement with Bluebird Bio on the development and commercialization of bb2121 and bb21217.

As described in its 2017 Q3 10Q filing with the SEC, on February 10, 2016, Celgene exercised its option to obtain an exclusive worldwide license to develop and commercialize bb2121 and on September 22, 2017, Celgene exercised its option to obtain an exclusive worldwide license to develop and commercialize bb21217.

Celgene has an additional option to co-develop and co-promote bb21217.

There is an Amended Collaboration Agreement between Bluebird and Celgene relating to the BCMA technologies.

Bluebird has benefited from licenses from the National Institutes of Health (NIH) on patented inventions on BCMA CAR T, and NIH Cooperative Research and Development Agreements (CRADAs). The NIH CRADA (C-008-2016/0) is for a Phase 1 Study of bb2121 in BCMA-Expressing multiple myeloma. The abstract for the NIH CRADA reads as follows:

> Under a Cooperative Research and Development Agreement (CRADA), NCI and bluebird bio, Inc. will collaborate on the Phase I clinical testing of bluebird bio's proprietary anti-BCMA (B cell maturation antigen) chimeric antigen receptor (CAR) bb2121 in autologous T cell therapy in patients with multiple myeloma.

The NIH-owned inventions licensed by the NIH to Bluebird Bio include the inventions listed in this 2014 Federal Register notice (79 FR 41700, link here) for an exclusive license to Bluebird Bio.

According to 35 USC § 209(a)(4), the NIH is required to ensure that "granting the license will not tend to substantially lessen competition or create or maintain a violation of the Federal antitrust laws."

On November 16, 2017, Celgene and Bluebird Bio issued a joint press release to "Announce bb2121 Anti-BCMA CAR-T Cell Therapy Has Been Granted Breakthrough Therapy Designation from FDA and Prime Eligibility from EMA for Relapsed and Refractory Multiple Myeloma." According to the press release, the designations were "based on preliminary clinical data from ongoing phase I study of bb2121 in heavily pre-treated multiple myeloma."

The Juno BCMA CAR T MM candidates

The Juno BCMA CAR T candidate is JCARH125.

Table 1 lists the BCMA CAR T trials listed in ClinicalTrials.Gov for which Juno is either a Sponsor or a Collaborator.

Table 1: Juno Therapeutics BCMA CAR T trials

NCT number and official title	Summary	Sponsors and Collaborators
NCT03070327: A Phase I Trial of B-cell Maturation Antigen (BCMA) Targeted EGFRt/BCMA-41BBz Chimeric Antigen Receptor (CAR) Modified T Cells With or Without Lenalidomide for the Treatment of Multiple Myeloma (MM)	The purpose of this phase I clinical trial is to test the safety of these CAR T cells in patients with myeloma.	Sponsor: Memorial Sloan Kettering Cancer Center, Collaborators: Juno Therapeutics, Inc.

NCT03338972: A Phase I Study of Adoptive Immunotherapy for Advanced B-Cell Maturation Antigen (BCMA)+ Multiple Myeloma With Autologous CD4+ and CD8+ T Cells Engineered to Express a BCMA-Specific Chimeric Antigen Receptor	This phase I trial studies the side effects and best dose of BCMA CAR-T cells in treating patients with BCMA positive multiple myeloma that has come back or does not respond to treatment. T cells are a type of white blood cell and a major component of the immune system. T-cells that have been genetically modified in the laboratory express BCMA and may kill cancer cells with the protein BCMA on their surface. Giving chemotherapy before BCMA CAR-T cells may reduce the amount of disease and to cause a low lymphocyte (white blood cell) count in the blood, which may help the infused BCMA CAR-T cells survive and expand.	Sponsor: Fred Hutchinson Cancer Research Center Collaborators: Juno Therapeutics, Inc. National Cancer Institute (NCI)
NCT03430011: Protocol H125001: An Open-Label Phase 1/2 Study of JCARH125, BCMA-targeted Chimeric Antigen Receptor (CAR) T Cells, in Subjects With Relapsed or Refractory Multiple Myeloma	This is an open-label, multicenter, Phase 1/2 study to determine the safety and efficacy of JCARH125, a CAR T-cell product that targets B-cell maturation antigen (BCMA), in adult subjects with relapsed or refractory multiple myeloma. The study will include a Phase 1 part to determine the recommended dose of JCARH125 in subjects with relapsed or refractory multiple myeloma, followed by a Phase 2 part to further evaluate the safety and efficacy of JCARH125 at the recommended dose.	Sponsor: Juno Therapeutics, Inc

Analysts have expressed positive views on the prospects of JCARH125 as a treatment for multiple myeloma. In its January 22, 2018 press release on the proposed acquisition of Juno, Celgene identified JCARH125 as “a key target in multiple myeloma,” and one of only two technologies in the pipeline specifically identified as a “strategic rationale for acquiring Juno.” [See: http://ir.celgene.com/releasedetail.cfm?releaseid=1054833]

Other BCMA CAR T MM candidates

Other companies are also investigating BCMA CAR T treatments for multiple myeloma. **Table A1** (attached below) identifies the names of companies listed as sponsors or collaborators on 24 trials listed on ClinicalTrials.Gov for BCMA CAR T treatments. Some of the 24 trials have not yet begun, and some companies (like Juno and Bluebird) are involved in multiple trials. It is not known how many of the candidates will be successful. Treatments that have entered a second trial are generally more likely than other candidates to succeed.

In the publication, "Clinical Development Success Rates, 2006-2015" by BIO, Biomedtracker, and Amplion, the likelihood of approval for a new hematologic **drug** for oncology was 8.1 percent for products entering Phase 1 trials, with the odds improving as products move through each successive phase.

CAR T treatments are procedures, and not drugs, and the FDA is just beginning approve these technologies. The first two CAR T treatments, targeting CD19, were approved in expedited procedures, based upon very few patients. It is reasonable to anticipate that both the Bluebird and the Juno CAR T treatments have a good chance of approval. Some of the other candidates are more speculative.

For a number of important innovative therapies, such as trastuzumab and adalimumab, rival therapies have been slow to emerge, and this lack of competition has been associated with aggressive monopoly pricing. In other cases, the entrance of new treatments has led to significant price competition.

2. **The current prices for CAR T treatments are excessive, and competition is needed to moderate excessive prices and expand access.**

The first two CAR T treatments were based upon NIH funded research, but were priced extremely high. The Novartis Kymriah treatment has a price of at least $475,000, which is several multiples of the average per capita income or the average life savings of individuals. Gilead's Yescarta was also very expensive, and both treatments are considerably more expensive than the value of the average single family home sold in the United States, a purchase that normally takes a family 30 years to pay off.

In our experience, high prices on products create financial stress for patients, drive up premiums for everyone, and result in access restricting formularies.

When Gilead registered new innovative treatments for the treatment of HCV, the price of Harvoni, a two drug sofosbuvir based combination, was $95,000. When AbbVie developed a successful alternative HCV treatment that did not require sofosbuvir, competition among the two

companies drove prices below $30,000 in the United States and below $7,000 in some other high income countries.

KEI is of the opinion that potential competition between the Bluebird and Juno BCMA-targeted CAR T treatments for multiple myeloma will be important, and moreover, that Celgene is seeking to avoid such price competition, and the desire to protect the price for the Bluebird candidates was a primary motivation for the merger.

3. **The relevant market is BCMA-targeted CAR T treatment for multiple myeloma.**

Investors and scientists consider BCMA-targeted CAR T technologies as a unique treatment that is itself a market relevant for antitrust review.

4. **Attrition rates should be considered when evaluating the expected competition.**

For small molecule and biologic drugs, there is a great deal of publicly available data on the attrition rates for products entering Phase 1, 2 and 3 clinical trials. Less is known regarding the newer CAR T treatments, but in any event, the odds of regulatory approval for treatments entering Phase 1 testing is certainly greater than 0 and less than 1.

It is possible, and we believe likely, that both the Bluebird and the Juno BCMA-targeted CAR T treatments will be approved for multiple myeloma, and if so, the merger will have eliminated an important opportunity for price competition. What is unknown is how many other products will succeed, but one can at least imagine some scenarios. Suppose that there are six potential candidates (moving past phase 1), and the probability of approval is .5 for each one. Then there would be 3 technologies approved. If Celgene controlled 2 of the 3, there would be a duopoly. If Celgene controlled just 1 of the 3 there would be considerably more competition. And, if the odds of approval are .33, then the expected number of approvals would be 2, and if Celgene controlled both, there would be a monopoly.

5. **There are many intellectual property barriers to competition.**

A proliferation of CAR T patents is making entry more and more challenging for CAR T treatments. Every significant CAR T company or even non-profit research institute has been sued or is suing over infringement of CAR T-related patents. This time consuming and expensive litigation carries considerable risks for developers and creates significant barriers to competition. Ironically, several of the recent lawsuits have involved NIH funded inventions, that are being used to block development by other NIH funded or subsidized entities. Policymakers have yet to acknowledge and address the current and expanding patent thickets in the CAR T field.

The cross licensing between entities also raises questions about the nature of competition between companies that are negotiating for rights to use patents controlled by rivals. Celgene,

like other companies, is directly or indirectly engaged in negotiations over patent rights controlled by Novartis, Gilead and other companies, and other companies have to negotiate with Juno, Bluebird or Celgene for certain patent rights.

We ask that the FTC request copies of and examine documents regarding the negotiations, litigation and licensing of relevant intellectual property rights in the CAR T space, and also to take note of the extensive collaborations among companies that otherwise are held out to be competitors.

For these reasons, KEI objects to the Celgene acquisition of Juno.

Celgene could remedy our concerns by divesting either the Bluebird or the Juno BCMA multiple myeloma assets. If Celgene refuses to divest either the Bluebird or the Juno BCMA multiple myeloma assets, it is clear that Celgene sees the control of both companies' BCMA multiple myeloma technologies as the motivation for the merger, and this confirms our view that this merger is designed to prevent price competition with the Celgene/Bluebird Bio multiple myeloma technologies.

Sincerely,

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Attachment

Table A1: Companies and institutions listed on ClinicalTrials.Gov as sponsors or collaborators of trials with keyword BCMA and multiple myeloma.

US/European companies and research institutions

Autolus Limited
Bluebird bio
Celgene
Fred Hutchinson Cancer Research Center
Gilead
GlaxoSmithKline
Janssen Research & Development, LLC
Juno Therapeutics, Inc.
Memorial Sloan Kettering Cancer Center
NIH/National Cancer Institute (NCI)/National Institutes of Health Clinical Center (CC)
Pfizer
Poseida Therapeutics, Inc.
Seattle Genetics, Inc.
University of Pennsylvania
Unum Therapeutics Inc.

Chinese companies and research institutions

Carsgen Therapeutics, Ltd.
Carsgen Therapeutics, Ltd.
First Affiliated Hospital of Wenzhou Medical University
Henan Cancer Hospital
Jiangsu Provincial People's Hospital
Jiao Tong University School of Medicine
Kang YU
Nanjing Legend Biotech Co.
Ruijin Hospital
Second Affiliated Hospital of Xi'an Jiaotong University
Shanghai Changzheng Hospital
Shenzhen Geno-Immune Medical Institute
Southwest Hospital, China
The First Affiliated Hospital of Soochow University
The Pregene (ShenZhen) Biotechnology Company, Ltd.
The Second Affiliated Hospital of Henan University of Traditional Chinese Medicine
Xinhua Hospital, Shanghai
Xinqiao Hospital of Chongqing

NIH CRADAs

A list of CAR T CRADAs is available here.