Regeneron's BCMAxCD3 Bispecific Antibody (REGN5458) Shows Deep and Durable Responses in Patients with Heavily-pretreated Multiple Myeloma in Phase 1

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63% response rate in patients treated with the highest reported dose

Among all patients responding to treatment, 95% experienced a very good partial response or better; among responding patients with ≥6 months of follow-up, 83% have ongoing responses for up to 13 months at the time of analysis

Potentially registrational Phase 2 portion of the trial has been initiated and is enrolling patients

Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced updated data for REGN5458, a BCMAxCD3 bispecific antibody, from the Phase 1 portion of a Phase 1/2 trial in patients with relapsed or refractory (R/R) multiple myeloma. The results were shared in an oral presentation at the virtual 2020 American Society of Hematology (ASH) Annual Meeting. BCMA (B-cell maturation antigen) is a protein that is typically over-expressed on multiple myeloma cells. REGN5458 is designed to bind to BCMA on multiple myeloma cells and the CD3 receptor on T-cells in order to bridge them together and activate T-cells to kill the cancer cells.

"REGN5458 continues to show early, deep and durable anti-tumor responses in patients with relapsed and refractory multiple myeloma across all dose levels. This is particularly encouraging given that a majority of patients were heavily pretreated and had few options remaining. All patients were triple-refractory, with 57% being penta-refractory," said Deepu Madduri, M.D., Assistant Professor of Medicine at the Icahn School of Medicine at Mount Sinai in New York and a trial investigator. "As these data continue to mature, we look forward to assessing whether responses will further deepen and remain durable with ongoing REGN5458 treatment."

In the trial, the 49 patients evaluated had a median of five prior lines of therapy (range: 2-17) with 100% being triple-refractory and 57% being penta-refractory; all patients were refractory to anti-CD38 therapy. With a median follow up of 2.6 months (range: 1-13), responses generally occurred by week 4 and deepened over time. Exploratory analyses suggest that patient-reported global health status/quality of life (per EORTC QLQ-C30) also improved meaningfully at week 4 and was maintained through week 24, with assessment ongoing.

Efficacy results, a secondary endpoint, by dose level were as follows:

% (n)	Dose Levels 1, 2, 3 (3, 6, 12 mg; n=24)	Dose Levels 4, 5 (24, 48 mg; n=17)	Dose Level 6 (96 mg; n=8)
Median follow-up (range)	3 months (1-13 months)	3 months (1-9 months)	2 months (1-6 months)
Overall response rate (ORR)	29% (7)	41% (7)	63% (5)
Complete response (CR) or stringent CR (sCR)	21% (5)	18% (3)	0% (0)*
Very good partial response (VGPR)	4% (1)	24% (4)	63% (5)
Partial response (PR)	4% (1)	0% (0)	0% (0)

*As of data cut-off, dose level 6 patients had been followed for a median of 2 months, and responses may deepen over time.

Among all patients who responded to treatment (n=19) as of data cut-off:

- 95% (n=18) achieved a VGPR or better
- 42% (n=8) had a CR or sCR
- 57% of evaluable patients (4 of 7 patients) were minimal residual disease (MRD) negative
- Tumor response was not correlated with BCMA expression as assessed by immunohistochemistry

In assessing durability among patients who responded to treatment and with data continuing to mature at the time of analysis:

- Among responding patients with ≥6 months of follow-up, 83% (10 of 12 patients) have ongoing responses for up to 13 months at the time of analysis
- 74% of responders (n=14) remain on treatment
- The observed median duration of response was 6 months (range: 1-13)

The most common adverse events (AEs) were cytokine release syndrome (CRS; 39%; n=19), anemia (37%; n=18), fatigue (35%; n=17), nausea (31%; n=15), pyrexia (31%; n=15) and back pain (27%; n=13). Grade ≥3 AEs occurred in 69% (n=34) of patients with the most common being anemia (22%; n=11), neutropenia (14%; n=7) and lymphopenia (12%; n=6). There were no reports of Grade ≥3 CRS or neurotoxicity. Dose-limiting toxicity was reported in 2 patients with 1 patient experiencing acute kidney injury and 1 patient experiencing elevated alanine aminotransferase (ALT)/raised aspartate aminotransferase (AST). Both cases were resolved with supportive care, and the patient that experienced elevated ALT/AST remains on REGN5458 and has since achieved a VGPR.

"REGN5458 is the second CD3 bispecific in our oncology portfolio to show clinically meaningful results. Alongside our CD20xCD3 bispecific odronextamab, REGN5458 offers additional evidence to support the potential of our bispecific platform to transform the treatment of diverse blood cancers for patients," said L. Andres Sirulnik, M.D., Ph.D., Senior Vice President, Translational & Clinical Sciences, Hematology at Regeneron. "Regeneron continues to drive increasing momentum across our oncology and non-oncology hematology programs. We are currently enrolling patients in a potentially registrational Phase 2 portion of this REGN5458 trial. We are also expanding our odronextamab program with multiple pivotal trials in 2021."

In addition to the REGN5458 data, updated results from the Phase 1 odronextamab trial in R/R follicular lymphoma, diffuse large B-cell lymphoma and other B-cell non-Hodgkin lymphomas will also be shared in an oral presentation (Abstract 400) at ASH and will include patient follow-up data of up to 3 years.

REGN5458 and odronextamab were invented using Regeneron's proprietary *VelocImmune*® technology and created using the company's *Veloci-Bi*® platform. These allow for the creation of bispecific antibodies that closely resemble natural human antibodies with no linkers or artificial sequences. Additionally, Regeneron bispecifics are manufactured using similar approaches used for human monoclonal antibody medicines, yielding similar properties and pharmacokinetics.

REGN5458 and odronextamab are currently under clinical development, and their safety and efficacy have not been evaluated by any regulatory authority.

About the Phase 1/2 Dose-escalation Trial
REGN5458 monotherapy is being investigated in an open-label, Phase 1/2 dose-escalation trial in patients with R/R multiple myeloma who are at least triple refractory to existing therapeutic options, including proteasome inhibitors, immunomodulatory drugs and CD38 antibody treatments. The Phase 1 portion of the trial is primarily assessing safety, tolerability, and dose-limiting toxicities of REGN5458, with efficacy as secondary endpoints. The Phase 2 portion is currently enrolling patients and will further assess REGN5458 anti-tumor activity and safety.

Among the patients being enrolled are those with heavily pre-treated, triple refractory and penta-exposed multiple myeloma, including those with extra-medullary (outside of the bone marrow) and non-secretory (do not secrete detectable myeloma proteins) disease.

About Multiple Myeloma
Multiple myeloma is the second most common blood cancer with approximately 30,192 and 168,765 new diagnoses in the U.S. and the world, respectively, in 2020. It is characterized by the proliferation of cancerous plasma cells (multiple myeloma cells) that crowd out healthy blood cells in the bone marrow, infiltrate other tissues and cause potentially life-threatening organ injury. Multiple myeloma is not curable despite treatment advances. While current treatments are able to slow progression of the cancer, most patients will ultimately experience cancer progression and require additional therapies.

About Regeneron Pharmaceuticals, Inc.
Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to eight FDA-approved treatments and numerous product candidates in development, all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, infectious diseases, pain and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*® technologies, such as *VelocImmune*, which uses a unique genetically-humanized mouse to produce optimized fully-human antibodies and bispecific antibodies, and through ambitious research initiatives such as the Regeneron Genetics Center, which is conducting one of the largest genetics sequencing efforts in the world.

For additional information about the company, please visit www.regeneron.com or follow @Regeneron on Twitter.

Regeneron Forward-Looking Statements and Use of Digital Media
This press release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("Regeneron" or the "Company"), and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's business and its employees, collaborators, and suppliers and other third parties on which Regeneron relies, Regeneron's and its collaborators' ability to continue to conduct research and clinical programs, Regeneron's ability to manage its supply chain, net

product sales of products marketed or otherwise commercialized by Regeneron and/or its collaborators (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of Regeneron's Products and Regeneron's product candidates and research and clinical programs now underway or planned, including without limitation REGN5458 (a BCMAxCD3 bispecific antibody) and odronextamab (a CD20xCD3 bispecific antibody); the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's product candidates and new indications for Regeneron's Products, such as REGN5458 in relapsed/refractory (R/R) multiple myeloma and other potential indications and odronextamab in R/R stages of follicular lymphoma, diffuse large B-cell lymphoma, other B-cell non-Hodgkin lymphomas, and other potential indications; uncertainty of market acceptance and commercial success of Regeneron's Products and product candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary), including the studies discussed in this press release, on the commercial success of Regeneron's Products and product candidates; safety issues resulting from the administration of Regeneron's Products and product candidates in patients, including serious complications or side effects in connection with the use of Regeneron's Products and product candidates in clinical trials; determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's ability to continue to develop or commercialize Regeneron's Products and product candidates; ongoing regulatory obligations and oversight impacting Regeneron's Products, research and clinical programs, and business, including those relating to patient privacy; the availability and extent of reimbursement of Regeneron's Products from third-party payers, including private payer healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicaid; coverage and reimbursement determinations by such payers and new policies and procedures adopted by such payers; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and product candidates; the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; the ability of Regeneron's collaborators, suppliers, or other third parties (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's Products and product candidates; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its financial projections or guidance and changes to the assumptions underlying those projections or guidance; the potential for any license, collaboration, or supply agreement, including Regeneron's agreements with Sanofi, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), to be cancelled or terminated; and risks associated with intellectual property of other parties and pending or future litigation relating thereto (including without limitation the patent litigation and other related proceedings relating to EYLEA® (aflibercept) Injection, Dupixent® (dupilumab), and Praluent® (alirocumab)), other litigation and other proceedings and government investigations relating to the Company and/or its operations, the ultimate outcome of any such proceedings and investigations, and the impact any of the foregoing may have on Regeneron's business, prospects, operating results, and financial condition. A more complete description of these and other material risks can be found in Regeneron's filings with the U.S. Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2019 and its Form 10-Q for the quarterly period ended September 30, 2020. Any forward-looking statements are made based on management's current beliefs and judgment, and the reader is cautioned not to rely on any forward-looking statements made by Regeneron. Regeneron does not undertake any obligation to update (publicly or otherwise) any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.

Regeneron uses its media and investor relations website and social media outlets to publish important information about the Company, including information that may be deemed material to investors. Financial and other information about Regeneron is routinely posted and is accessible on Regeneron's media and investor relations website (http://newsroom.regeneron.com) and its Twitter feed (http://twitter.com/regeneron).

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