PALM Ebola Clinical Trial Stopped Early as Regeneron's REGN-EB3 Therapy Shows Superiority to ZMapp in Preventing Ebola Deaths

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TARRYTOWN, N.Y., Aug. 12, 2019 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) today announced that the Company was informed by study investigators that a randomized, controlled trial evaluating four investigational therapies for Ebola virus infection was stopped early because REGN-EB3 was superior to ZMapp in preventing death. ZMapp served as the control arm of the trial because it was considered the standard-of-care based on the previous PREVAIL II clinical trial. The protocol specified that the PALM trial would only be stopped early for a highly statistically significant result. The independent data safety monitoring board decided to stop the trial after reviewing interim mortality data from 499 patients. The trial was conducted in the Democratic Republic of Congo (DRC), where the current outbreak is ongoing.

The trial was first initiated in 2018 with three treatment arms: mAb114, remdesivir and ZMapp. The trial protocol was amended after the World Health Organization (WHO) held an Ad-Hoc Expert Consultation to assess all preclinical and clinical data on available investigational products, and recommended the addition of REGN-EB3 as a fourth treatment arm.

"The Regeneron team worked tirelessly to discover, develop and produce REGN-EB3 in record time utilizing our *VelocImmune*®-based technologies," said Neil Stahl, Ph.D., Executive Vice President of Research and Development at Regeneron. "We are moved to know our therapy is helping save the lives of people facing this deadly infectious disease. We look forward to reviewing the trial data and are working with governments and other collaborators, including BARDA, to make REGN-EB3 available for the current outbreak and future use."

"This trial was conducted in difficult circumstances during a public health emergency, and we appreciate the efforts of the WHO and other experts to add REGN-EB3 to the trial," said Sumathi Sivapalasingam, M.D., Senior Director, Early Clinical Development and Experimental Sciences at Regeneron. "This trial is a remarkable advance in the decades-long struggle to respond to Ebola and we appreciate the tremendous efforts of the many governmental and non-governmental organizations who made it possible."

REGN-EB3 (also known as REGN3470-3471-3479) was invented by Regeneron using its *VelociSuite*® technologies; the therapy combines three fully-human monoclonal antibodies. REGN-EB3 has received orphan drug designation from both the U.S. Food and Drug Administration and the European Medicines Agency. REGN-EB3 is being developed, tested and manufactured as part of an agreement established in 2015 with the Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response at the U.S. Department of Health and Human Services (HHS). REGN-EB3 is currently under clinical development and its safety and efficacy have not been fully evaluated by any regulatory authority.

"REGN-EB3 is a three-antibody cocktail designed with the goal of enhancing efficacy, reducing the development of viral sequences that lead to resistance, and increasing potential utility in future outbreaks as viruses continually evolve," said Christos Kyratsous, Ph.D., Vice President of Research, Infectious Diseases and Viral Vector Technologies at Regeneron. "The Regeneron rapid response infectious disease platform has the opportunity to accelerate our response to future epidemics and pandemics, and we continue to work on additional diseases that may pose a threat to public health."

About the PALM Trial
The PAmoja TuLinde Maisha (PALM [together save lives]) clinical trial was a randomized, multicenter, controlled trial to evaluate the safety and efficacy of four investigational agents for the treatment of patients with Ebola virus infection – including three antibody-based therapies, REGN-EB3, ZMapp and mAb114 (a single monoclonal antibody); and one small molecule antiviral, remdesivir. The primary objective of the trial was to compare mortality in patients with Ebola who received either REGN-EB3, mAb114 or remdesivir to those who received ZMapp in the control arm. The National Institutes of Health (NIH) and the Institut National de Recherche Biomédicale (INRB) in the DRC jointly sponsored and served as co-principal investigators.

By August 2019, the trial had enrolled nearly 700 participants across four Ebola Treatment Centers in the DRC. With the preliminary findings in 499 trial participants, REGN-EB3 and mAb114 will be the two investigational treatments given as part of an Extension Phase to further evaluate safety until final results of the clinical trial are known, after which an Expanded Access Phase will be initiated using the lead therapeutics from the trial.

Regeneron and BARDA have several ongoing research collaborations in addition to the Ebola program, including a collaboration to develop treatments for Middle East Respiratory Syndrome (MERS) and a collaboration for the discovery, research, development and manufacturing of a portfolio of antibodies targeting up to 10 pathogens that pose significant risk to public health.

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 seven 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 disease, 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 produces optimized fully-human antibodies, and 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 nature, timing, and possible success and therapeutic applications of Regeneron's products, product candidates, and research and clinical programs now underway or planned, including without limitation Regeneron's potential antibody therapies for the treatment of Ebola (REGN-EB3 or REGN3470-3471-3479) and Middle East Respiratory Syndrome (MERS); the extent to which the results from the research and development programs conducted by Regeneron or its collaborators may be replicated in later studies and lead to therapeutic applications; unforeseen safety issues and possible liability resulting from the administration of products and product candidates in patients, including without limitation Regeneron's potential antibody therapies for the treatment of Ebola and MERS; serious complications or side effects in connection with the use of Regeneron's products and product candidates (such as Regeneron's potential antibody therapies for the treatment of Ebola and MERS) in clinical trials; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates and new indications for marketed products; the availability and extent of reimbursement of the Company'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; ongoing regulatory obligations and oversight impacting Regeneron's marketed products, research and clinical programs, and business, including those relating to patient privacy; 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, such as Regeneron's potential antibody therapies for the treatment of Ebola and MERS; competing drugs and product candidates that may be superior to Regeneron's products and product candidates; 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) on the commercial success of Regeneron's products and product candidates; 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 or collaboration agreement, including Regeneron's agreements with Sanofi, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), as well as the agreements with the Biomedical Advanced Research and Development Authority of the U.S. Department of Health and Human Services referenced in this press release, to be cancelled or terminated without any further product success; 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) Injection, and Praluent® (alirocumab) Injection, the ultimate outcome of any such proceedings, 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 United States Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2018 and its Form 10-Q for the quarterly period ended June 30, 2019. 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 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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