Regeneron Genetics Center Publication in New England Journal of Medicine Links ANGPTL4 Inhibition and Risk of Coronary Artery Disease

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TARRYTOWN, N.Y., March 2, 2016 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN), working in collaboration with Geisinger Health System, today announced that the *New England Journal of Medicine* has published a paper showing that inactivating mutations of the angiopoeitin-like 4 (ANGPTL4) gene are associated with a significantly reduced risk of coronary artery disease (CAD) in humans.

"This is the first of what we hope will be many notable peer-reviewed publications with our collaborators, and one example of how the Regeneron Genetics Center and Geisinger link genetic mutations with real-world health outcomes to make actionable discoveries," said Alan Shuldiner, M.D., a lead author of the publication and Vice President and Co-Head of the Regeneron Genetics Center LLC (RGC), a wholly-owned subsidiary of Regeneron. "In aggregate, the RGC has sequenced de-identified DNA samples from approximately one hundred thousand consented volunteers in less than two years, and many of our findings are already being used to inform Regeneron's robust and integrated R&D programs, with the ultimate goal of developing safe and effective treatments for patients in need."

ANGPTL4 inhibits lipoprotein lipase (LPL), an enzyme that helps break down triglycerides, a form of fat derived from food. Previous studies have found that activation of LPL leads to the reduction of circulating triglycerides, increased levels of which are thought to be an independent risk factor for ischemic cardiovascular disease. It was hypothesized, therefore, that genetic mutations inactivating ANGPTL4 would lead to activation of LPL, low levels of circulating triglycerides and reduced risk of cardiovascular disease.

In this study, scientists at the RGC sequenced the exomes of individuals in the DiscovEHR cohort, comprised of de-identified Geisinger Health System patients who consented to participate in the MyCode Community Health Initiative. Analyses revealed that individuals with one or two copies of the p.E40K mutation, which was previously known to inactivate ANGPTL4, had about 19 percent lower CAD risk. People with one of 13 other ANGPTL4 "loss-of-function" mutations newly-identified by the researchers had an almost 45 percent reduction in CAD risk.

"The ability to link exome sequence data to longitudinal electronic health records of MyCode volunteers provides a unique opportunity to find genetic variants that impact important health-related traits. One of Geisinger's long-term goals is to use such information to improve health and medical care for patients, which is a key pillar of the concept of Precision Medicine," said David J. Carey, Ph.D., Associate Chief Research Officer at Geisinger, and one of the lead Geisinger investigators working with Regeneron on the DiscovEHR collaboration.

"This paper highlights how we incorporate large-scale sequencing into our discovery and pipeline approaches," said Aris Baras, M.D., publication author and Vice President and Co-Head of the RGC. "It also demonstrates the advantages of our unique combination of technologies. Using our proprietary *VelociGene*® technology, we developed animal models that corroborated the human genetics findings. The *VelocImmune*® platform was leveraged to create a fully human monoclonal antibody inhibitor of ANGPTL4 that reduced triglyceride levels in mice and non-human primates."

Further evaluation is needed to characterize the potential efficacy and safety of ANGPTL4 inhibition in humans.

Regeneron currently has an angiopoeitin-like 3 (ANGPTL3) antibody, known as evinacumab or REGN1500, in clinical development. ANGPTL4 and ANGPTL3 are thought to be related inhibitors of LPL.

About DiscovEHR
The DiscovEHR human genetics study population for this analysis includes 42,930 Geisinger Health System patients who consented to participate in the MyCode Community Health Initiative. MyCode volunteers have given informed consent to allow sharing of de-identified electronic health records, provide samples that can be linked to their health records for broad research, and permit re-contact for additional studies. Electronic health records for this group are available for a median of 15 years of clinical care.

About the Regeneron Genetics Center
The RGC is a fully integrated genomics program that spans early gene discovery and functional genomics and facilitates drug development. The primary goal of the RGC is to improve patient outcomes by identifying novel drug targets, clinical indications for development programs, and genomic biomarkers for pharmacogenomic applications. The RGC is tackling various sequencing (exomes, targeted sequencing, etc.) and analytical approaches and has established numerous collaborations with leading human genetics researchers. To enable this large-scale sequencing and analysis program, the RGC utilizes fully-automated sample preparation and data processing, as well as cutting-edge cloud-based informatics. Through these efforts, the RGC is currently sequencing de-identified samples from patient volunteers at a rate of more than 80,000 unique exomes per year.

About Regeneron Pharmaceuticals, Inc.
Regeneron is a leading science-based biopharmaceutical company based in Tarrytown, New York that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. Regeneron commercializes medicines for eye diseases, high LDL-cholesterol, and a rare inflammatory condition and has product candidates in development in other areas of high unmet medical need, including oncology, rheumatoid arthritis, asthma, atopic dermatitis, pain, and infectious diseases. For additional information about the company, please visit www.regeneron.com or follow @Regeneron on Twitter.

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 translational research and functional biology capabilities and use of human genetics in Regeneron's research process; the extent to which the results from Regeneron's research programs or preclinical testing may lead to advancement of product candidates to clinical trials or therapeutic applications; unforeseen safety issues resulting from the administration of products and product candidates in patients, including serious complications or side effects in connection with the use of Regeneron's product candidates in clinical trials; the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's product candidates (such as evinacumab (REGN1500)) and new indications for 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; 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; coverage and reimbursement determinations by third-party payers, including Medicare and Medicaid; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its sales or other 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 and Bayer HealthCare LLC, 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. 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 fiscal year ended December 31, 2015. 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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