Regeneron Announces Positive Phase 3 Trial in Adults with Ultra-Rare Genetic Disorder Fibrodysplasia Ossificans Progressiva (FOP), Demonstrating that Garetosmab Prevents Greater than 99% of Abnormal Bone Formation

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FOP is a disease in which muscles, tendons and ligaments are progressively replaced by bone, leading to eventual incapacitation

Garetosmab is the first and only treatment to demonstrate a dramatic reduction in both number and volume of abnormal bone lesions (heterotopic ossification, or HO lesions) in adults with FOP

Primary endpoint was met, showing a 90% or greater reduction in new HO lesions at 56 weeks, and garetosmab also led to a greater than 99% reduction in the total volume of new HO lesions

Based on these data and the safety profile, the Independent Data Monitoring Committee (IDMC) recommended those receiving placebo be transitioned to garetosmab as soon as possible; U.S. regulatory submission of garetosmab in adults planned for year-end 2025

TARRYTOWN, N.Y., Sept. 17, 2025 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced the primary endpoint was met in the Phase 3 OPTIMA trial investigating garetosmab in adults with fibrodysplasia ossificans progressiva (FOP). At 56 weeks, both doses of garetosmab, 3 mg/kg and 10 mg/kg, were highly efficacious in reducing the number of new bone lesions (heterotopic ossification, or HO lesions) as compared to placebo, demonstrating a 94% and 90% reduction, respectively. Garetosmab is a monoclonal antibody that neutralizes the Activin A protein, which Regeneron scientists discovered to be a critical protein in the development of HO lesions in people with FOP.

“Heterotopic ossification is a hallmark of FOP, a horrific disease in which muscles, tendons and ligaments are progressively replaced by bone, gradually incapacitating patients,” said Professor Richard Keen, Director of the Metabolic Bone Disease Centre, Royal National Orthopaedic Hospital, London, and global primary investigator of the OPTIMA trial. “The OPTIMA trial results clearly illustrate the potential of garetosmab to alter the disease and reduce new lesions that define this condition. Notably, garetosmab is the first and only investigational therapy to demonstrate a dramatic reduction in both the number and volume of abnormal bone lesions."

OPTIMA, a global, multi-center, randomized, double-blind, placebo-controlled trial, enrolled 63 people with FOP aged 18 years and older. Trial participants were randomized to intravenously receive either placebo, 3 mg/kg garetosmab, or 10 mg/kg garetosmab once every four weeks. Following this, participants could elect to extend their treatment through at least 84 weeks or discontinue treatment and enter into an observation-only arm.

In OPTIMA, the primary and key secondary endpoints were assessed at 56 weeks. As seen in the table below, the total number of new HO lesions was significantly reduced, which was further reaffirmed by the reduction in total new lesion volume.

Endpoints	placebo (n=21)	garetosmab 3 mg/kg (n=19)	garetosmab 10 mg/kg (n=23)
Patients completing treatment (%)	20 (95%)	19 (100%)	23 (100%)
Primary endpoint: Total number of new HO lesions in total treated population† and reduction compared to placebo	19 lesions	1 lesion 94% reduction (p=0.0274)	2 lesions 90% reduction (p=0.0260)
Key secondary endpoint: Total number of clinician-assessed flare-ups and reduction compared to placebo	70 flare-ups	53 flare-ups 20% reduction (p=0.7125)	9 flare-ups 89% reduction (p=0.0007)
Post-hoc analysis: Mean total volume (cm^3) and reduction in mean total volume of new HO lesions compared to placebo‡	10.45 cm^3	0.01 cm^3 99.9% reduction (95% CI: 98.3% to 100%; p=0.0013§)	0.02 cm^3 99.8% reduction (95% CI: 96.4% to 100%; p=0.0005§)

† As assessed by computed tomography (CT) scan

‡ A supportive parametric post-hoc analysis was performed using a statistical model that utilized the actual total lesion volume

§ Nominal p-value

At 56 weeks, there were no discontinuations among the garetosmab treatment arms, and there was one discontinuation in the placebo arm due to an ovarian cyst. There was a dose-dependent increase in skin and soft tissue infections (n=7, n=9, n=15 for the placebo, 3 mg/kg garetosmab, and 10 mg/kg garetosmab arms, respectively). There was no dose-dependent increase in epistaxis (n=5, n=10, n=4 for the placebo, 3 mg/kg garetosmab, and 10 mg/kg garetosmab arms, respectively); and there were no serious bleeding events. There was a decrease in musculoskeletal pain-related adverse events, similar in both garetosmab arms (n=14, n=6, n=4 for the placebo, 3 mg/kg garetosmab and 10 mg/kg garetosmab arms, respectively). Serious treatment-emergent adverse events occurred in 2 patients treated with placebo, 1 patient treated with 3 mg/kg garetosmab, and 2 patients treated with 10 mg/kg garetosmab. No deaths were reported in the trial.

"The success of the OPTIMA trial is a direct result of Regeneron's relentless pursuit of science and use of proprietary technologies to improve the lives of people with debilitating and life-threatening diseases, no matter their prevalence," said George D. Yancopoulos, M.D., Ph.D., Board co-Chair, President and Chief Scientific Officer at Regeneron. "Our research in FOP began decades ago – leading to the discovery of the role Activin A plays in driving this devastating disease, and now, a medicine with the potential to prevent the uncontrolled formation of new bone. We are thankful to the many patients, healthcare providers, and others who have been active partners on this journey, and we look forward to submitting garetosmab for evaluation by regulatory authorities as soon as possible."

Based on these data and the safety profile, the Independent Data Monitoring Committee (IDMC) recommended those receiving placebo be transitioned to garetosmab as soon as possible. A U.S. regulatory submission for garetosmab to treat FOP is planned for year-end 2025, with global regulatory submissions slated for 2026. These data are also planned for future presentation and publication. A Phase 3 trial of garetosmab in adolescents and children with FOP, OPTIMA 2, is intended to begin next year.

The potential use of garetosmab for the treatment of FOP is investigational and has not been approved by any regulatory authority.

About the OPTIMA Clinical Trial

OPTIMA is a Phase 3, multi-center, multinational trial to assess the efficacy of garetosmab on the reduction of heterotopic bone formation, as well as its safety, tolerability, and pharmacokinetics, in patients with active fibrodysplasia ossificans progressiva (FOP).

The trial enrolled 63 patients aged 18 years and older who have any FOP-causing variant of type I Activin A receptor (ACVR1), exhibited FOP disease activity or progression of heterotopic ossification (HO) lesions, and had a cumulative analogue joint involvement (CAJIS) score at screening of ≤19. CAJIS is a clinician-assessed tool, with higher scores representing greater disease severity (scale: 0 to 30). Eligible participants were randomized to intravenously receive 3 mg/kg garetosmab, 10 mg/kg garetosmab, or placebo once every four weeks for 56 weeks. Following this, participants could elect to extend their treatment for at least 84 weeks or discontinue treatment and enter into an observation-only arm.

During the treatment period, efficacy was evaluated through whole body computed tomography (CT) scans for HO lesions; physician and patient assessment of flare-ups; utilization of the CAJIS scale to rate joint functionality; and observances of change in disease severity. Safety assessment includes reports of adverse events, measurement of vital signs, physical examination, and coagulation testing.

A Phase 3 trial of garetosmab in adolescents and children with FOP, OPTIMA 2, is planned to begin next year. For more information, visit the Regeneron clinical trials website, contact clinicaltrials@regeneron.com, or call +1 844-734-6643.

About Fibrodysplasia Ossificans Progressiva (FOP)

Fibrodysplasia ossificans progressiva (FOP) is a relentless, progressive, ultra-rare genetic disorder in which muscles, tendons and ligaments are progressively replaced by bone, a process known as heterotopic ossification (HO). Approximately 900 people are diagnosed with FOP worldwide, with many others thought to remain undiagnosed or misdiagnosed.

HO of the jaw, spine, hip and rib cage can make it difficult to speak, eat, walk or breathe, leading to weight loss and escalating loss of mobility and skeletal deformity. People with FOP also experience episodic, localized inflammation known as "flare-ups," although HO may occur both silently as well as in association with symptoms. Most people with FOP are wheelchair bound by 30 years old and the median age of survival is approximately 56 years. Death often results from complications, such as pneumonia, heart failure and aspiration stemming from HO and loss of mobility in the chest, neck and jaw.

About Garetosmab

Regeneron has been engaged in FOP research for decades and helped to provide fundamental insights in the biology and natural history of the disease. Regeneron scientists discovered that Activin A plays a key role in FOP by driving HO, the main pathology of FOP. Garetosmab is a *VelocImmune*-derived fully-human monoclonal antibody that binds and neutralizes Activin A, which is involved in the development of heterotopic bone in people with FOP.

In 2017, the U.S. Food and Drug Administration (FDA) granted Fast Track designation for garetosmab for the prevention of HO in patients with FOP. In the U.S. and European Union (EU), garetosmab has been granted Orphan Designation. Garetosmab is

currently under clinical development, and its safety and efficacy have not been evaluated by any regulatory authority.

About Regeneron's VelocImmune Technology
Regeneron's *VelocImmune* technology utilizes a proprietary genetically engineered mouse platform endowed with a genetically humanized immune system to produce optimized fully human antibodies. When Regeneron's co-Founder, President and Chief Scientific Officer George D. Yancopoulos was a graduate student with his mentor Frederick W. Alt in 1985, they were the first to envision making such a genetically humanized mouse, and Regeneron has spent decades inventing and developing *VelocImmune* and related *VelociSuite*® technologies. Dr. Yancopoulos and his team have used *VelocImmune* technology to create a substantial proportion of all original, FDA-approved fully human monoclonal antibodies. This includes Dupixent® (dupilumab), Libtayo® (cemiplimab-rwlc), Praluent® (alirocumab), Kevzara® (sarilumab), Evkeeza® (evinacumab-dgnb), Inmazeb® (atoltivimab, maftivimab and odesivimab-ebgn) and Veopoz® (pozelimab-bbfg). In addition, REGEN-COV® (casirivimab and imdevimab) had been authorized by the FDA during the COVID-19 pandemic until 2024. Garetosmab was also created using Regeneron's *VelocImmune* technology.

About Regeneron
Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents, develops and commercializes life-transforming medicines for people with serious diseases. Founded and led by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to numerous approved treatments and product candidates in development, most 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, neurological diseases, hematologic conditions, infectious diseases, and rare diseases.

Regeneron pushes the boundaries of scientific discovery and accelerates drug development using our proprietary technologies, such as *VelociSuite*, which produces optimized fully human antibodies and new classes of bispecific antibodies. We are shaping the next frontier of medicine with data-powered insights from the Regeneron Genetics Center® and pioneering genetic medicine platforms, enabling us to identify innovative targets and complementary approaches to potentially treat or cure diseases. For more information, please visit www.Regeneron.com or follow Regeneron on LinkedIn, Instagram, Facebook or X.

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 products marketed or otherwise commercialized by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Products") and product candidates being developed by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Product Candidates") and research and clinical programs now underway or planned, including without limitation garetosmab; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's Product Candidates and new indications for Regeneron's Products, including garetosmab for the treatment of adults with fibrodysplasia ossificans progressiva as discussed in this press release; uncertainty of the utilization, market acceptance, and commercial success of Regeneron's Products and Regeneron's Product Candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary), including the studies discussed or referenced in this press release, on any of the foregoing or any potential regulatory approval of Regeneron's Products and Regeneron's Product Candidates (such as garetosmab); the ability of Regeneron's collaborators, licensees, suppliers, or other third parties (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's Products and Regeneron's Product Candidates; the ability of Regeneron to manage supply chains for multiple products and product candidates and risks associated with tariffs and other trade restrictions; safety issues resulting from the administration of Regeneron's Products and Regeneron's Product Candidates (such as garetosmab) in patients, including serious complications or side effects in connection with the use of Regeneron's Products and Regeneron's 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 Regeneron's 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 or copay assistance for Regeneron's Products from third-party payors and other third parties, including private payor 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 payors and other third parties and new policies and procedures adopted by such payors and other third parties; changes in laws, regulations, and policies affecting the healthcare industry; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and Regeneron's Product Candidates (including biosimilar versions of Regeneron's Products); the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators or licensees may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; 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 and Bayer (or their respective affiliated companies, as applicable), to be cancelled or terminated; the impact of public health outbreaks, epidemics, or pandemics on Regeneron's business; and risks associated with litigation and other proceedings and government investigations relating to the

Company and/or its operations (including the pending civil proceedings initiated or joined by the U.S. Department of Justice and the U.S. Attorney's Office for the District of Massachusetts), 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), 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, 2024 and its Form 10-Q for the quarterly period ended June 30, 2025. 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 (https://investor.regeneron.com) and its LinkedIn page (https://www.linkedin.com/company/regeneron-pharmaceuticals).

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