Interim Results from Ongoing Phase 2 COURAGE Trial Confirm Potential to Improve the Quality of Semaglutide (GLP-1 receptor agonist)-induced Weight Loss by Preserving Lean Mass

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Trial demonstrated that approximately 35% of semaglutide-induced weight loss was due to loss of lean mass

Combining semaglutide with muscle-preserving antibodies protected lean mass – sparing approximately 50%-80% of the lean mass lost with semaglutide alone – while also increasing loss of fat mass

TARRYTOWN, N.Y., June 02, 2025 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced interim results from the ongoing Phase 2 COURAGE trial investigating novel combinations of semaglutide (GLP-1 receptor agonist) and trevogrumab (anti-GDF8/anti-myostatin) with or without garetosmab (anti-activin A) for the treatment of obesity. The trial demonstrated that approximately 35% of semaglutide-induced weight loss was due to loss of lean mass**,** and further demonstrated that combining semaglutide with trevogrumab with or without garetosmab helped preserve lean mass while increasing loss of fat mass. The interim analysis was conducted when 50% of patients reached week 26 in the trial. The combination of semaglutide with trevogrumab was generally well-tolerated; the triplet combination of semaglutide with both antibodies had a substantially higher rate of discontinuations due to tolerability issues and other adverse events, consistent with the safety profile previously seen with garetosmab alone.

“Recent advancements have resulted in patients being able to lose significant amounts of body weight. Unfortunately, this weight loss comes at the cost of muscle loss, and we know muscle is important to overall health,” said George D. Yancopoulos, M.D., Ph.D., Board Co-Chair, President and Chief Scientific Officer at Regeneron. “These early insights from the COURAGE trial are consistent with recently published pre-clinical data in rodents and non-human primates, and clearly establish the principle that blocking GDF8 with or without activin A can preserve muscle and further increase fat loss in patients being treated with GLP-1 therapy, thereby improving the quality of weight loss. The full data set will be available later this year and will provide further insights to help optimize the dosing regimens in future trials.”

COURAGE was designed to investigate the quality of weight loss in patients with obesity (BMI ≥30 kg/m^2). Treatment is divided into two 26-week periods comprised of a weight-loss phase and a weight-maintenance phase. The three primary efficacy endpoints were assessed in this interim analysis when 50% of patients reached week 26 (end of weight-loss phase), and included percent change from baseline at week 26 in lean mass, fat mass and body weight.

During the weight-loss phase, patients were randomized to receive semaglutide alone or in combination with two different doses of trevogrumab (lower- or higher-dose combo), or higher-dose trevogrumab plus garetosmab (triplet). At this interim analysis, 34.5% of semaglutide-induced weight loss was due to lean mass loss, while patients in all combination groups preserved more lean mass with greater fat loss from baseline compared to semaglutide alone. Detailed results at data cutoff of this interim analysis include:

	Semaglutide monotherapy (n=151)	**Lower-dose combo** (n=149)	**Higher-dose combo** (n=152)	**Triplet** (n=147)
Lean mass				
Change in lean mass (SE), in lbs (% of total weight loss)	-7.9 (0.64) lbs (-34.5%)	-3.7 (0.64) lbs*** (-17.0%)	-4.2 (0.66) lbs*** (-16.8%)	-2.0 (0.75) lbs*** (-6.6%)
% preservation of lean mass (compared to semaglutide monotherapy)	---	50.8%	51.3%	80.9%
Fat mass				
Change in fat mass (SE), in lbs (% of total weight loss)	-15.3 (0.90) lbs (-66.3%)	-16.9 (0.90) lbs (-78.1%)	-18.9 (0.93) lbs* (-76.3%)	-25.4 (1.06) lbs*** (-84.4%)

% increase in fat loss (compared to semaglutide monotherapy)	---	17.8%	15.1%	27.3%
Body weight				
Change in body weight (SE), in lbs (% change in body weight)	-23.0 (1.12) lbs (-10.4%)	-21.6 (1.15) lbs (-9.9%)	-24.8 (1.15) lbs (-11.3%)	-30.0 (1.26) lbs*** (-13.2%)

SE=Standard Error
NOTE: Lean mass and fat mass was calculated using dual-energy X-ray absorptiometry (DXA) scan, while body weight was measured using a scale; as a result, the lean and fat mass numbers may not exactly sum to body weight. Results are based on MMRM analysis using efficacy estimand that excludes data after the treatment discontinuation.
***p<0.001; *p<0.05; p-values are for the primary endpoints of % change from baseline at week 26 in each category, and were not corrected for multiplicity.

After 26 weeks, patients enter into the weight-maintenance phase in which they receive either higher-dose trevogrumab monotherapy or placebo through the end of the trial (week 52). Data from this phase are not yet available.

Available safety data at data cutoff across treatment groups at 26-weeks were as follows:

Participants with at least one:	**Semaglutide monotherapy** (n=151)	**Lower-dose combo** (n=148)	**Higher-dose combo** (n=151)	**Triplet** (n=149)
TEAE	64.9%	68.2%	68.2%	77.2%
Severe TEAE	2.0%	1.4%	3.3%	10.1%
TE-SAE	0.7%	0.7%	1.3%	6.7%
TEAE leading to treatment discontinuation	4.6%	4.1%	10.6%	28.3%
Treatment-related TEAE	47.0%	48.6%	56.3%	63.8%

NOTE: Two deaths occurred in the triplet group, one due to an undetermined cause in a patient with multiple cardiovascular risk factors and the second due to a cardiac arrest in a person with a history of cardiovascular disease. Regeneron has not identified a causal association between treatment and these events.
TEAE=Treatment emergent adverse events; SAE=Serious adverse events

The safety and efficacy of trevogrumab and garetosmab have not been evaluated by any regulatory authority.

About Regeneron in Obesity
Obesity is a complex, multifaceted disease and a growing public health concern that affects more than a billion people worldwide. Despite the revolutionary impact of GLP-1 receptor agonists (GLP-1RAs) on weight loss, the quality of this weight loss can be negatively impacted because these agents can cause profound muscle loss. Moreover, a high percentage of patients cycle on and off treatment – while off treatment they can regain almost all of the weight lost, but mostly in the form of fat, leaving them with negatively altered body composition.

At Regeneron, we are developing a pipeline focused on the quality of weight reduction. We have several independent approaches focused on promoting and preserving muscle during weight loss, so as to increase the amount of fat loss since adiposity is the principal driver of comorbidities and metabolic diseases associated with obesity. In addition, Regeneron has an extensive pipeline of agents to address some of these co-morbidities and metabolic diseases, which have the potential to be combined with GLP-1RAs. The combination of our science, pipeline, research and clinical innovation uniquely positions us to make a meaningful difference in obesity and obesity-related diseases.

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.

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 Regeneron's clinical program investigating novel combinations of semaglutide (GLP-1 receptor agonist) and high- or low-dose trevogrumab (anti-GDF8 /anti-myostatin) with or without garetosmab (anti-activin A) for the treatment of obesity 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 those referenced above); 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 those referenced above for the treatment of obesity; 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 those referenced above) 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; the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators or licensees (such as the interim results from the ongoing Phase 2 COURAGE trial discussed in this press release) may be replicated and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; 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); 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 March 31, 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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