Pozelimab (C5 Antibody) BLA for Treatment of Children and Adults with Ultra-rare CHAPLE Disease Accepted for FDA Priority Review

February 21, 2023 at 7:00 AM EST

If approved, pozelimab would be the first and only treatment for those living with CHAPLE

CHAPLE is an ultra-rare hereditary immune disease that causes overactivation of the complement system, leading to potentially life-threatening abdominal and cardiovascular symptoms

TARRYTOWN, N.Y., Feb. 21, 2023 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced the U.S. Food and Drug Administration (FDA) has accepted for Priority Review the Biologics License Application (BLA) for pozelimab as a treatment for adults and children as young as 1 year of age with CHAPLE disease (also known as CD55 deficiency with Hyperactivation of complement, Angiopathic thrombosis and Protein Losing Enteropathy or CD55-deficient protein-losing enteropathy). There are currently no approved treatments for CHAPLE, an ultra-rare and life-threatening hereditary immune disease driven by an overactivation of the complement system. Pozelimab is an investigational fully human monoclonal antibody designed to block the activity of complement factor C5, a protein involved in complement system activation. The target action date for the FDA decision is August 20, 2023.

Those living with CHAPLE are unable to regulate complement activity due to mutations in the CD55 gene, a protein regulating the body's complement system which is a mechanism for destroying microbes. Without proper CD55 regulation, the complement system may attack normal cells, causing damage to blood and lymph vessels along the upper digestive tract and leading to the loss of proteins and to blood cells. In most patients, this process results in a range of potentially life-threatening symptoms beginning in infancy, including abdominal pain, bloody diarrhea, vomiting, malnutrition, slow growth, swelling in the legs (edema), recurrent infections, and blood clots. There are fewer than 100 patients worldwide who are known to have CHAPLE.

The BLA is supported by results from a Phase 2/3 open-label trial that investigated the efficacy and safety of pozelimab in 10 patients aged 1 year or older. Patients were given a single loading dose of pozelimab 30 mg/kg intravenously on day 1, followed by subcutaneous weekly weight-based doses of pozelimab. At 24 weeks, the co-primary endpoints were achieved with 100% of patients experiencing rapid and sustained normalization of serum albumin (a disease biomarker) and improvement or no worsening of clinical symptoms. Clinical symptoms evaluated, included abdominal pain, number of bowel movements per day, and investigator-assessed facial and peripheral edema. Analyses of secondary endpoints also demonstrated marked reductions in hospitalization days and total number of albumin transfusions, as well as clinically meaningful increases in body weight for age and stature for age. Adverse events (AEs), which occurred in 7 of 10 patients, were limited to those of mild or moderate severity with the most common being iron deficiency, pyrexia, rhinitis, urticaria and vomiting (n=2 each). No AEs led to treatment discontinuation.

Life-threatening meningococcal infections have occurred in patients treated with complement protein C5 inhibitors and may become rapidly life-threatening or fatal if not recognized and treated early. Recommended guidance indicates patients with complement deficiencies should be vaccinated at least 2 weeks prior to receiving a C5 inhibitor. Vaccination reduces, but does not eliminate, the risk of meningococcal infections. All patients in the pozelimab trial received vaccination for meningococcal infection prior to treatment with pozelimab.

The FDA designated pozelimab for treatment of CHAPLE as a drug for a "rare pediatric disease" in April 2020, with the opportunity for Regeneron to receive a rare pediatric disease priority review voucher should pozelimab be approved for CHAPLE. Orphan Drug Designation was granted at the same time, which is given to investigational medicines intended for the treatment of rare diseases that affect fewer than 200,000 people in the U.S. Pozelimab was also granted Fast Track designation in September 2022, which is designed to expedite the FDA's review of innovative new drugs that demonstrate the potential to address an unmet medical need. Pozelimab is currently under clinical development for CHAPLE, and its safety and efficacy have not been evaluated by any regulatory authority.

About Pozelimab

Pozelimab was invented using Regeneron's proprietary *VelocImmune*® technology and is an investigational, fully human, monoclonal antibody designed to block the activity of complement factor C5 and prevent diseases mediated by the complement pathway. It is an IgG4 antibody that binds with high affinity to wild-type and variant human C5.

As part of its ongoing development program, pozelimab is also being evaluated in combination with Alnylam's cemdisiran (siRNAi C5 inhibitor) as an investigational combination therapy for the treatment of other complement-mediated disorders including paroxysmal nocturnal hemoglobinuria (PNH) and myasthenia gravis (MG). This combination 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 currently available. This includes REGEN-COV® (casirivimab and imdevimab), Dupixent® (dupilumab), Libtayo® (cemiplimab-rwlc), Praluent® (alirocumab), Kevzara® (sarilumab), Evkeeza® (evinacumab-dgnb) and Inmazeb™ (atoltivimab, maftivimab and odesivimab-ebgn).

About Regeneron
Regeneron is a leading biotechnology company that invents, develops and commercializes life-transforming medicines for people with serious diseases. Founded and led for 35 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to nine FDA-approved treatments and numerous product candidates in development, almost 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, pain, hematologic conditions, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite* technologies, such as *VelocImmune*, which uses unique genetically-humanized mice 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 more information, 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 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 or licensees (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of 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 pozelimab; 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 pozelimab for the treatment of adults and children as young as 1 year of age with CHAPLE disease (including potential approval by the U.S. Food and Drug Administration based on the Biologics License Application discussed in this press release) as well as pozelimab in combination with cemdisiran (a siRNA C5 inhibitor being developed by Alnylam Pharmaceuticals, Inc.) for the treatment of other complement-mediated disorders, including paroxysmal nocturnal hemoglobinuria and myasthenia gravis; 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 pozelimab); 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; safety issues resulting from the administration of Regeneron's Products and Regeneron's Product Candidates (such as pozelimab) 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 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 Regeneron's Product Candidates; 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; 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, Praluent® (alirocumab), and REGEN-COV® (casirivimab and imdevimab)), 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, 2022. 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).

Contacts:

Media Relations
Taylor Ramsey
Tel: +1 914-409-2381
taylor.ramsey@regeneron.com

Investor Relations
Vesna Tosic
Tel: +1 914-847-5443
vesna.tosic@regeneron.com

REGENERON

Source: Regeneron Pharmaceuticals, Inc.