Latest DB-OTO Results Demonstrate Clinically Meaningful Hearing Improvements in Nearly All Children with Profound Genetic Hearing Loss in CHORD Trial

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As presented at ARO, 10 of 11 children with at least one post-treatment assessment showed notable improvements in hearing

Speech and development progress followed dramatic improvements in hearing in first child treated in the trial

TARRYTOWN, N.Y., Feb. 24, 2025 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced updated data for the investigational gene therapy DB-OTO from the Phase 1/2 CHORD trial in 12 children who have profound genetic hearing loss due to variants of the otoferlin (*OTOF*) gene. These include 72-week results showing speech and development progress in the first child dosed at 10 months of age, as well as initial results in 11 children (aged 10 months to 16 years old) – three of whom received DB-OTO bilaterally (in both ears). The latest results were presented in an oral presentation at the Association for Research in Otolaryngology's (ARO) 48 th Annual MidWinter Meeting.

"Sound is a significant part of the human experience that connects us to each other and our environment," said Jay T. Rubinstein, M.D., Ph.D., Virginia Merrill Bloedel Professor of Otolaryngology and Bioengineering and Director, Bloedel Hearing Research Center, University of Washington School of Medicine, and a CHORD clinical trial investigator. "A year after treatment in one ear with DB-OTO, a child born profoundly deaf was able to enjoy music, engage in imaginative play and participate in bedtime reading when the cochlear implant on their other ear was removed. These seemingly small interactions are life-changing for these children as well as their families and these results continue to underscore the revolutionary promise of DB-OTO as a potential treatment for otoferlin-related hearing loss."

In the trial, 12 participants have received DB-OTO to date – of whom nine were administered an intracochlear injection in one ear and three received it bilaterally. The surgical procedure to administer DB-OTO leverages an approach similar to cochlear implantation, which enables use in young infants.

As presented at ARO, 48-week results from the first participant dosed in the trial showed improvement of hearing to near-normal levels across key speech frequencies. This included hearing thresholds that were within normal limits (0.25-2.0 kHz) in most speech-relevant frequencies and corroborated with positive auditory brainstem responses (ABRs). Particularly encouraging were results from formal speech perception tests in which the child demonstrated improvement from week 48 to week 72 and correctly identified words – such as mommy, cookies and airplane – that were presented at a conversational level without any visual cues.

Among the 11 participants with at least one post-treatment assessment, 10 demonstrated a notable response, with improved hearing at various decibel hearing levels (dBHL). Additionally, among five participants with 24-week assessments, three experienced improvements in average hearing thresholds to "nearly normal" (n=1; ≤40 dBHL) or normal (n=2; ≤25 dBHL) hearing levels. All ABR responses were corroborated by hearing improvements assessed by pure tone audiometry (PTA). One participant has not experienced a change from their baseline hearing at 24 weeks post-dosing.

Across all 12 participants, both the surgical procedure and DB-OTO were well tolerated, and there were no adverse events or serious adverse events considered related to DB-OTO. Five of 12 participants experienced transient post-surgical vestibular adverse events (e.g., nystagmus, nausea, dizziness, vomiting), which resolved within 6 days of dosing.

DB-OTO received Orphan Drug, Rare Pediatric Disease, Fast Track and Regenerative Medicine Advanced Therapy designations from the U.S. Food and Drug Administration and Orphan Drug Designation was granted by the European Medicines Agency. The potential use of DB-OTO for otoferlin-related hearing loss is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

About Otoferlin-related Hearing Loss
Congenital deafness (hearing loss present at birth) is a significant unmet medical need that affects approximately 1.7 out of every 1,000 children born in the U.S. and approximately half of these cases have genetic causes. However, otoferlin-related hearing loss is ultra-rare. This specific condition is caused by variants in the *OTOF* gene, which leads to a lack of a functional otoferlin protein that is critical for the communication between the sensory cells of the inner ear and the auditory nerve.

About the CHORD Trial
The CHORD trial is an ongoing, Phase 1/2 first-in-human, multicenter, open-label trial to evaluate the safety, tolerability and preliminary efficacy of DB-OTO in infants, children and adolescents with otoferlin variants.

Currently enrolling children across sites in the U.S., United Kingdom and Spain (<18 years of age), CHORD is being conducted in two parts. In the initial dose-escalation cohort (Part A), participants receive a single intracochlear injection of DB-OTO in one ear, and in the expansion cohort (Part B), participants receive simultaneous single intracochlear injections of DB-OTO in both ears at the selected dose from Part A.

Hearing improvements were assessed by PTA and ABR. PTA is considered by auditory experts to be the gold standard measurement of hearing and is measured through behavioral responses to sound (e.g., turning head towards sound) that is emitted at different intensity levels and measured in decibels (dB). ABR corroborates these behavioral responses, serving as an objective confirmation of hearing function, and is measured through electrical brainstem responses to sound emitted at different dBs. At baseline, all participants had no behavioral (PTA) or electrophysiological (ABR) responses at maximum sound levels (≥100 dB).

Additional information about the trial, including enrollment, can be obtained by contacting clinicaltrials@regeneron.com.

About DB-OTO and the Regeneron Auditory Program
DB-OTO is an investigational cell-selective, dual adeno-associated virus (AAV) vector gene therapy designed to provide durable, physiological hearing to individuals with profound, congenital hearing loss caused by variants of the *OTOF* gene. The treatment aims to deliver a working copy to replace the faulty *OTOF* gene using a modified, non-pathogenic virus that is delivered via an injection into the cochlea under general anesthesia (similar to the procedure used for cochlear implantation). In this gene therapy, the newly introduced *OTOF* gene is under the control of a proprietary cell-specific Myo15 promoter, which is intended to restrict expression only to inner hair cells that normally express otoferlin.

In addition to *OTOF*, Regeneron is committed to investigating several other targets for genetic forms of hearing loss, including *GJB2*.

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.

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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 the investigational gene therapy DB-OTO; 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 DB-OTO for the treatment of otoferlin-related hearing loss; 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 DB-OTO); the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators or licensees (including the studies discussed or referenced in this press release) may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; 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 DB-OTO) 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; 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. 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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