



Regeneron Shares Preliminary Results Showing Gene Therapy Improves Auditory Responses in Child with Profound Genetic Hearing Loss

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Global Phase 1/2 CHORD trial investigating otoferlin gene therapy (DB-OTO) represents Regeneron's first auditory program and is currently enrolling patients

DB-OTO is part of a growing pipeline of genetic medicines for hearing loss and other therapeutic areas that are being advanced by the company

TARRYTOWN, N.Y., Oct. 26, 2023 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced preliminary, positive safety and efficacy results from the first patient (<2 years of age) dosed in the Phase 1/2 CHORD trial investigating otoferlin gene therapy (DB-OTO) in children with profound genetic hearing loss due to mutations of the otoferlin gene.

"The children who are being enrolled in CHORD are often born with profound hearing loss due to mutations in a single gene, otoferlin, which essentially turns off their auditory circuits," said Professor Manohar Bance, M.B., an ear surgeon and principal trial investigator at Cambridge University Hospitals NHS Foundation Trust in the United Kingdom. "Cochlear implants are the current standard of care but are unable to replicate the full complexity and range of sound. With these very preliminary DB-OTO results, we now have encouraging evidence that this gene therapy may be able to help turn these auditory circuits back on. We look forward to following this child and others further to determine if DB-OTO gene therapy can restore clinically meaningful hearing as they are learning to interact with the world."

In the trial, the child received an intracochlear injection of DB-OTO in one ear. At planned follow-ups, the child experienced improvements in auditory responses through week 6 compared to baseline, per auditory brainstem response (ABR) and behavioral (pure tone) audiometry. ABR, a clinically accepted physiologic measure of hearing sensitivity, is often absent in those with classic otoferlin-related hearing loss and was absent in both ears of the child at baseline. There were no concerning safety signals through week 6 following treatment.

Congenital hearing loss (hearing loss present at birth) is a significant unmet medical need with no approved pharmacologic treatment options that affects approximately 1.7 out of every 1,000 children born in the U.S. While hearing loss caused by mutations of the otoferlin gene is ultra-rare, the majority of permanent, congenital hearing loss cases diagnosed in developed countries are sensorineural and result from a single gene defect, making them suitable targets for gene therapy.

"These preliminary DB-OTO results provide early and encouraging proof-of-concept for the treatment of otoferlin-related hearing loss, as well as our pipeline of gene therapies to address more common forms of genetic hearing loss and other therapeutic areas," said Christos Kyratsous, Ph.D., Senior Vice President of Research and co-head of Genetic Medicines at Regeneron. "The ongoing CHORD trial is our first clinical-stage auditory program, and we are incredibly grateful to the investigators and the family of this child for embarking on this breakthrough trial. We remain committed to advancing this research and hope these results mean that children with genetic hearing loss will eventually be able to benefit from the revolutionary promise of gene therapies like DB-OTO."

DB-OTO was originally developed under a collaboration between Regeneron and Decibel Therapeutics that was initially established in [2017](#), with an extension announced in [2021](#). In [September 2023](#), Regeneron acquired Decibel Therapeutics, cementing this long-standing collaboration. In addition to the DB-OTO development program, other clinical efforts include AAV.103 for people with GJB2-related hearing loss and AAV.104 for people with stereocilin (STRC)-related hearing loss.

The potential use of DB-OTO for otoferlin-related hearing loss is currently under clinical development, and its safety and efficacy have not been evaluated by any regulatory authority.

About the CHORD Trial

The CHORD trial ([NCT# 05788536](#)) is a Phase 1/2 first-in-human, multicenter, open-label trial to evaluate the safety, tolerability, and preliminary efficacy of DB-OTO in pediatric patients with otoferlin mutations.

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

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

1-617-370-8701.

About DB-OTO

DB-OTO is an investigational cell-selective, adeno-associated virus (AAV) gene therapy designed to provide durable, physiological hearing to individuals with profound, congenital hearing loss caused by mutations of the otoferlin gene. The treatment aims to deliver a working copy of the faulty otoferlin 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 introduced otoferlin gene is under the control of a proprietary cell-specific Myo15 promoter, which is intended to restrict expression only to the cells that normally express otoferlin.

DB-OTO received Orphan Drug and Rare Pediatric Disease designations from the U.S. Food and Drug Administration in 2021. In the European Union, Orphan Drug Designation was granted by the European Medicines Agency in 2023.

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 for 35 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to numerous FDA-approved treatments and product candidates in development, almost all of which were homegrown in our laboratories. Regeneron's medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, hematologic conditions, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through its 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 additional information about Regeneron, please visit www.regeneron.com or follow Regeneron on [LinkedIn](#).

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 the investigational gene therapy DB-OTO discussed in this press release as well as Regeneron's other genetic medicine programs for hearing loss and other therapeutic areas referenced in this press release; 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 in children with genetic hearing loss due to mutations of the otoferlin gene; the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators or licensees (including the preliminary data discussed in this press release) may be further replicated and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; 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 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; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and Regeneron's Product Candidates; 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 (such as the COVID-19 pandemic) on Regeneron's business; 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 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 and its Form 10-Q for the quarterly period ended June 30, 2023. 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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