Akouos Receives FDA Clearance of its IND Application for AK-OTOF, a Gene Therapy Intended for the Treatment of OTOF-mediated Hearing Loss

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-The IND for AK-OTOF is the first to receive FDA clearance for a genetic form of hearing loss and the first for an AAV vector therapy with the potential to treat an inner ear condition

-Akouos plans to initiate a pediatric Phase 1/2 clinical trial, including children as young as two years of age in the dose-escalation phase (Part A), to evaluate AK-OTOF for the treatment of OTOF*-mediated hearing loss*

-Based on auditory brainstem response data from nonclinical studies, a one-time administration of AK-OTOF has the potential to deliver durable restoration of auditory function

BOSTON, Sept. 13, 2022 (GLOBE NEWSWIRE) -- Akouos, Inc. (NASDAQ: AKUS), a precision genetic medicine company dedicated to developing potential gene therapies for individuals living with disabling hearing loss worldwide, today announced that it has received clearance from the U.S. Food and Drug Administration (FDA) for its Investigational New Drug (IND) application to initiate a Phase 1/2, first in human, pediatric clinical trial of AK-OTOF, a gene therapy intended for the treatment of patients with otoferlin gene (*OTOF*)-mediated hearing loss. Currently, there are no approved pharmacologic treatment options for individuals with *OTOF*-mediated hearing loss, a form of sensorineural hearing loss caused by mutations in the *OTOF* gene.

"The AK-OTOF IND clearance from FDA is an important step toward achieving our mission of making healthy hearing available to all," said Manny Simons, Ph.D., M.B.A., co-founder, president, and chief executive officer of Akouos. "This first in human clinical trial for AK-OTOF is groundbreaking and highlights Akouos's leadership in the field -- we expect this to be the first clinical trial for a genetic inner ear condition, the first in which an AAV gene therapy is administered to the inner ear, and the first for any inner ear condition to begin in a pediatric population."

"We are excited to advance AK-OTOF into clinical development. There is a significant unmet need in *OTOF*-mediated hearing loss, as individuals typically have Severe to Profound sensorineural hearing loss from birth, and there are currently no approved pharmacologic options," said Jen Wellman, chief operating officer of Akouos. "This clinical trial is designed not only to evaluate the safety and potential benefit of AK-OTOF for individuals with *OTOF*-mediated hearing loss, but also to help us demonstrate the applicability of our novel delivery approach to a broad range of inner ear conditions. We look forward to sharing what we learn from this pioneering work."

OTOF-mediated hearing loss is a form of sensorineural hearing loss caused by mutations in the otoferlin gene, which encodes otoferlin, a protein that enables the inner hair cells of the cochlea to release neurotransmitter vesicles in response to stimulation by sound to activate auditory neurons. Individuals with *OTOF*-mediated hearing loss have bilateral hearing loss that is typically Severe to Profound and congenital, exhibiting absent or highly abnormal auditory brainstem response (ABR) from birth. Approximately 20,000 individuals are affected in the United States and Europe. In April 2021, FDA granted both Orphan Drug Designation and Rare Pediatric Disease Designation for AK-OTOF.

AK-OTOF is a dual adeno-associated viral (AAV) vector-based gene therapy intended to treat patients with *OTOF*-mediated hearing loss by delivering transgenes encoding *OTOF* to the inner hair cells (IHCs) of the cochlea. A one-time, unilateral intracochlear administration of AK-OTOF is intended to result in the expression of normal full-length functional otoferlin protein in the IHCs, which has the potential to lead to recovery of auditory function.

The advancement of AK-OTOF into clinical development is supported by nonclinical data demonstrating administration of AK-OTOF in *Otof* knockout mice results in durable expression of human otoferlin protein sufficient for sustained restoration of auditory function, as assessed by translationally relevant ABR assessments. In both mice and non-human primates, AK-OTOF was systemically and locally well tolerated, and no adverse effects were observed in clinical pathology, otic pathology, systemic histopathology, or auditory or cochlear function.

The Phase 1/2 clinical trial is designed to evaluate the safety and tolerability of escalating doses of AK-OTOF administered unilaterally to trial participants with *OTOF*-mediated hearing loss; it is also designed to assess efficacy through clinical measures such as ABR, which is an objective, clinically accepted endpoint. Given both the early onset of serious manifestations, as well as the need for timely intervention due to anatomical considerations and developmental considerations, eligible participants for the clinical trial will be pediatric. Based on interactions with FDA during the 30-day IND review period, the Company expects the first two participants will be as young as seven years of age, and that subsequent participants will be as young as two years of age at the time of administration.

The Company plans to provide an update on clinical trial initiation activities for AK-OTOF later this year.

About Akouos
Akouos is a precision genetic medicine company dedicated to developing gene therapies with the potential to restore, improve, and preserve high-acuity physiologic hearing for individuals living with disabling hearing loss worldwide. Leveraging its precision genetic medicine platform that incorporates a proprietary adeno-associated viral (AAV) vector library and a novel delivery approach, Akouos is focused on developing precision therapies for forms of sensorineural hearing loss. Headquartered in Boston, Akouos was founded in 2016 by leaders in the fields of neurotology, genetics, inner ear drug delivery, and AAV gene therapy.

Forward-Looking Statements
Statements in this press release about future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute "forward-looking statements" within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements relating to the initiation, plans, timing of our future clinical trials for AK-OTOF, and the potential benefit of AK-OTOF. The words "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "might," "may," "plan,"

“potential,” “predict,” “project,” “should,” “target,” “will,” “would,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: our limited operating history; uncertainties inherent in the development of product candidates, including the initiation and completion of nonclinical studies and clinical trials; whether results from nonclinical studies will be predictive of results or success of clinical trials; the timing of and our ability to submit applications for, and obtain and maintain regulatory approvals for, our product candidates; our expectations regarding our regulatory strategy; our ability to fund our operating expenses and capital expenditure requirements with our cash, cash equivalents, and marketable securities; the potential advantages of our product candidates; the rate and degree of market acceptance and clinical utility of our product candidates; our estimates regarding the potential addressable patient population for our product candidates; our commercialization, marketing, and manufacturing capabilities and strategy; our ability to obtain and maintain intellectual property protection for our product candidates; our ability to identify additional products, product candidates, or technologies with significant commercial potential that are consistent with our commercial objectives; the impact of government laws and regulations and any changes in such laws and regulations; risks related to competitive programs; the potential that our internal manufacturing capabilities and/or external manufacturing supply may experience delays; the impact of the COVID-19 pandemic on our business, results of operations, and financial condition; our ability to maintain and establish collaborations or obtain additional funding; and other factors discussed in the “Risk Factors” included in the Company’s Quarterly Report on Form 10-Q for the quarter ended June 30, 2022, filed with the Securities and Exchange Commission on August 15, 2022, and in other filings that the Company makes with the Securities and Exchange Commission in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and the Company expressly disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

Contacts

Media:
Katie Engleman, 1AB
katie@1abmedia.com

Investors:
Courtney Turiano, Stern Investor Relations
Courtney.Turiano@sternir.com