Akouos Presents Nonclinical Data Supporting Future Clinical Development of AK-OTOF and AK-antiVEGF at the American Society of Gene and Cell Therapy 24th Annual Meeting

May 11, 2021

- Intracochlear delivery of a dual AAVAnc80 vector encoding human otoferlin results in full-length protein expression in inner hair cells of non-human primates and in durable protein expression sufficient for sustained restoration of auditory function in Otof *knockout mice*

- Multiple analyses demonstrate in vitro *transduction with dual AK-OTOF vector results in full-length otoferlin expression, with no detection of truncated proteins*

- Long-term, local expression of anti-VEGF protein is robust and well tolerated following intracochlear administration of AK-antiVEGF in non-human primates

- Akouos continues to progress towards planned IND submissions for AK-OTOF in the first half of 2022 and for AK-antiVEGF in 2022

BOSTON, May 11, 2021 (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 presented nonclinical data supporting the future clinical development of both AK-OTOF, a gene therapy intended for the treatment of otoferlin gene (*OTOF*)-mediated hearing loss, and AK-antiVEGF, a gene therapy intended for the treatment of vestibular schwannoma, in three digital presentation sessions at the virtual American Society of Gene and Cell Therapy (ASGCT) 24th Annual Meeting.

“We are excited to share new data that highlight the potential of genetic medicines for inner ear conditions with the broader gene therapy community,” said Manny Simons, Ph.D., M.B.A., co-founder, president, and chief executive officer of Akouos. “Inner ear conditions represent one of the largest areas of unmet need in medicine today, and one of the challenges in this area is the ability to efficiently address the broad range of conditions that collectively affect hundreds of millions of individuals worldwide. The nonclinical data presented today for the AK-OTOF and AK-antiVEGF programs demonstrate how we are leveraging our genetic medicines platform and multiple AAV-mediated modalities, including gene transfer and therapeutic protein expression, to begin to address that challenge.”

“Nonclinical data presented at ASGCT for AK-OTOF continue to support the potential to restore physiologic hearing and provide long-lasting benefit to individuals with *OTOF*-mediated hearing loss. In *Otof* knockout mice, AK-OTOF administration results in durable expression of human otoferlin protein sufficient for sustained restoration of auditory function. In addition, data presented indicate that expression of exogenous secreted protein at or above reported biologically active levels, driven by a ubiquitous promoter, is well tolerated in non-human primates following administration of AK-antiVEGF. These IND-enabling nonclinical studies are promising and support future clinical development. Our team continues to work towards submission of INDs for AK-OTOF and AK-antiVEGF expected in 2022,” said Greg Robinson, Ph.D., chief scientific officer of Akouos.

In Vitro *and* In Vivo *Analyses of Dual Vector Otoferlin Expression to Support the Clinical Development of AK-OTOF (AAVAnc80-hOTOF Vector)*

Presenting Author: Eva Andres-Mateos

Abstract Number: 355

Otoferlin plays a critical role in exocytosis of synaptic vesicles at the inner hair cell synapse, and mutations in *OTOF*, the gene encoding otoferlin, are associated with autosomal recessive sensorineural hearing loss. AK-OTOF is designed to deliver normal *OTOF* by utilizing a dual vector approach, which encodes the 5’ and the 3’ components of *OTOF*. Multiple analyses demonstrate *in vitro* transduction with dual AK-OTOF vector results in full-length human otoferlin (RNA and protein), with no detection of truncated proteins from either AK-OTOF or its component vectors (5’hOTOF and 3’hOTOF). A one-to-one ratio of the AK-OTOF component vectors appears to be optimal for efficient reconstitution of full-length human otoferlin. In cynomolgus macaques, full-length human otoferlin protein expression is detected in inner hair cells of non-human primate (NHP) cochleae by both immunohistochemistry and immunodetection one month following intracochlear administration of AAVAnc80-FLAG.hOTOF.

The digital presentation is located at https://akouos.com/gene-therapy-resources/.

Durable Recovery of Auditory Function Following Intracochlear Delivery of AK-OTOF (AAVAnc80-hOTOF Vector) in a Translationally Relevant Mouse Model of Otoferlin Gene (OTOF)-Mediated Hearing Loss

Presenting Author: Ann Hickox

Abstract Number: 569

Otoferlin gene (*OTOF*)-mediated hearing loss is caused by mutations in the *OTOF* gene and is typically characterized by a congenital, Severe to Profound sensorineural hearing loss. The physiologic deficiency resulting from *OTOF* mutations is localized; specifically, synaptic transmission between the inner hair cell and the auditory nerve is affected, as measured by an absent or abnormal auditory brain stem response (ABR). Gene therapy for *OTOF*-mediated hearing loss is expected to confer the greatest benefit when cochlear integrity is preserved, as represented by present otoacoustic emissions (OAEs). Individuals with *OTOF*-mediated hearing loss typically experience a decline in cochlear integrity within the first decade of life, indicated by initially present, then absent, OAEs. In an *Otof* knockout mouse model that recapitulates the human phenotype, administration of AK-OTOF, an adeno-associated viral gene therapy vector encoding human otoferlin under the control of a ubiquitous promoter, results in durable restoration of auditory function, as measured by ABRs, and may preserve OAEs.

The digital presentation is located at https://akouos.com/gene-therapy-resources/.

Demonstration of Tolerability of a Novel Delivery Approach and Secreted Protein Expression Following Intracochlear Delivery of AK-antiVEGF (AAVAnc80-antiVEGF Vector) in Non-Human Primates

Presenting Author: John Connelly

Abstract Number: 358

Data published from previous clinical trials show that systemic VEGF inhibitor therapy can reduce vestibular schwannoma (VS) tumor volume and improve hearing in some participants with mutations in the *NF2* gene. However, toxicity limits the potential of this systemic delivery approach from being a viable treatment option for vestibular schwannoma. The exposure and tolerability of local expression of anti-VEGF protein following bilateral, intracochlear administration of AK-antiVEGF was evaluated through analyses of protein levels, as well as physiologic and histologic evaluations, in NHPs. Long-term, local expression of anti-VEGF protein, driven by a ubiquitous promoter, is robust and well tolerated in NHPs following intracochlear administration of AK-antiVEGF. Computational modelling supports the potential for diffusion of anti-VEGF protein at or above reported biologically active levels to the site of the VS tumor.

The digital presentation is located at https://akouos.com/gene-therapy-resources/.

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.

Cautionary Note Regarding 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, and timing of our future clinical trials and our research and development programs, the timing of our IND submissions for AK-OTOF and AK-antiVEGF, our expectations regarding our manufacturing capabilities and timelines, and the period over which we believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our operating expenses. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “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; 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 Annual Report on Form 10-K for the year ended December 31, 2020 filed with the Securities and Exchange Commission, 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.

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