Akouos Presents Nonclinical Data Supporting the Planned Clinical Development of AK-OTOF and Strategies for Regulated Gene Expression in the Inner Ear at the American Society of Gene and Cell Therapy 25th Annual Meeting

May 19, 2022

- Nonclinical data demonstrate that a single intracochlear administration of an AAVAnc80 vector led to durable restoration of auditory function and was well tolerated, supporting planned clinical development of AK-OTOF for the treatment of OTOF*-mediated hearing loss*

- MicroRNA target site (miR-TS)-incorporation in AAV vectors is shown to have potential benefits for de-targeting transgene expression in the inner ear, supporting future
development of gene therapies targeting a broad range of inner ear conditions

BOSTON, May 19, 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, presented nonclinical data at the American Society of Gene and Cell Therapy (ASGCT) 25th Annual Meeting. The company gave two nonclinical presentations at the meeting: one that supports the planned clinical development of AK-OTOF, a gene therapy intended for the treatment of *OTOF*-mediated hearing loss; and another that supports the potential use of microRNA target site (miR-TS) in adeno-associated viral (AAV) vectors for regulated gene expression in the inner ear.

"We are excited to present these nonclinical data, which highlight our precision genetic medicine platform and the potential of genetic medicines to address a broad range of inner ear conditions, to the gene and cell therapy community. The AK-OTOF nonclinical data demonstrate durable restoration of auditory function and show that the product candidate was systemically and locally well tolerated in two translationally relevant animal species," said Manny Simons, Ph.D., founder, president, and chief executive officer of Akouos. "As we continue to progress toward planned IND submissions for AK-OTOF in the first half of 2022 and AK-antiVEGF in 2022, we are encouraged by the growing body of evidence supporting these filings, as well as by our efforts to advance preclinical development of other potential gene therapies for inner ear conditions, such as *GJB2*-mediated hearing loss, and to develop platform capabilities that can be applied to regenerative medicine approaches in the inner ear."

Nonclinical* In Vivo *Expression, Durability of Effect, Biodistribution/Shedding, and Safety Evaluations Support Clinical Development of AK-OTOF (AAVAnc80-hOTOF Vector) for* OTOF*-mediated Hearing Loss
Presenting Author: Ann E. Hickox, Ph.D.
Session Title and Room: Ophthalmic and Auditory Diseases; Salon G

AK-OTOF is an AAV vector-based gene therapy intended for the treatment of patients with otoferlin gene (*OTOF*)-mediated hearing loss by delivering transgenes encoding *OTOF* to inner hair cells (IHCs). Following intracochlear delivery, and subsequent co-transduction of IHCs by each component vector, the two transgene products recombine to generate a full-length otoferlin mRNA transcript and subsequently a full-length otoferlin protein. Results from this presentation show:

- Intracochlear administration of AK-OTOF in otoferlin knockout (Otof -/-) mice, or its tagged version (AAVAnc80-FLAG.hOTOF) in non-human primates (NHPs), leads to full-length human otoferlin protein expression only in the target IHCs; human otoferlin expression in IHCs of Ofof -/- mice restores auditory function as early as two weeks post-administration and restoration was durable through at least six months.
- AK-OTOF was systemically and locally well tolerated in both mice and NHPs, and no adverse effects were observed in clinical pathology, otic pathology, systemic histopathology, or auditory or cochlear function.
- Limited systemic exposure of AK-OTOF following intracochlear administration was observed, and no otoferlin protein expression was detected in any non-target tissue types evaluated, including those with detectable levels of vector sequences and otoferlin mRNA expression.

Together, these nonclinical studies further support the planned clinical development of AK-OTOF for the treatment of *OTOF*-mediated hearing loss.

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

Evaluating miR-Target Sites as a Strategy to Allow AAV Vector-based De-targeting of Gene Expression in the Inner Ear
Presenting Author: Richard M. Churchill Jr.
Poster Board Number: Tu-37

In the development of AAV gene therapy vectors, a goal is to generate safe and effective product candidates that deliver targeted transgene expression. Ubiquitous promoters can drive strong widespread expression in the inner ear in mice and NHPs. This expression can be well tolerated across the inner ear, as is the case for Akouos's first two programs, AK-OTOF and AK-antiVEGF. Addition of selective cis-regulatory elements may be needed for some transgenes, such as *GJB2*, where expression in a portion of nontarget cells is not well tolerated. This nonclinical study explored the potential use of miR-TS incorporation in AAV vectors for de-targeting transgene expression in different cell types of the cochlea. Using an *in vitro* model, expression of transgene mRNA and protein in the presence or absence of the target sites was evaluated. Akouos identified multiple microRNA target sites to drive various differential expression patterns demonstrating that a combination of AAVAnc80 and miR-TS can drive expression in supporting cells, while limiting expression in hair cells in cochlear explants. Future work will focus on evaluating miR-TS regulation *in vivo* and identifying combinations of different miR-TSs to enhance de-targeting in specific cell types where, for example, expression driven by ubiquitous promoters is not well tolerated.

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.

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, and the timing of our IND submissions for AK-OTOF and AK-antiVEGF. 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 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" section of our Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, which is on file with the Securities and Exchange Commission, and in other filings that Akouos may make with the Securities and Exchange Commission. 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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