Akouos Presents Nonclinical Data Demonstrating Potential Applicability of Precision Genetic Medicine Platform for a Broad Range of Inner Ear Conditions at the Association for Research in Otolaryngology 45th Annual Mid-Winter Meeting

February 7, 2022

- Data from two nonclinical studies evaluating protein expression and tolerability support future clinical development of AK-antiVEGF for the treatment of vestibular schwannoma

- AAVAnc80 and a supporting cell selective promoter can drive widespread GJB2 *expression in supporting cells, while limiting expression in, and loss of, hair cells in mice*

- AAV-mediated RNAi gene silencing and CRISPR/Cas9 gene editing methods demonstrate a promising reduction of gene of interest protein expression, which expands Akouos's genetic medicine platform capabilities

BOSTON, Feb. 07, 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 Association for Research in Otolaryngology (ARO) 45th Annual Mid-Winter Meeting that support future development of gene therapies targeting inner ear conditions. The company shared the data in two podium presentations and one poster.

"We are pleased to present these data, which further demonstrate the potential of our precision genetic medicine platform of proprietary ancestral adeno-associated viral (AAV) vectors, novel delivery approach, and multiple vector-mediated modalities to address a broad range of inner ear conditions, including those that are monogenic and of complex etiology," said Manny Simons, Ph.D., founder, president, and chief executive officer of Akouos. "As we progress toward planned IND submissions for AK-OTOF in H1 2022 and AK-antiVEGF in 2022, we also continue to advance preclinical development of 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."

Demonstration of Secreted Protein Expression Levels Following Intracochlear Delivery of AK-antiVEGF (AAVAnc80-antiVEGF Vector) Across Multiple Doses in Non-human Primates
Presenting Author: Michelle D. Valero, Ph.D.
Podium Session: 11

AK-antiVEGF is a gene therapy candidate in preclinical development for the potential treatment of patients with vestibular schwannomas (VS). Data published from previous clinical trials of systemic VEGF inhibitor therapy show reduction of VS tumor volume and improvement in hearing in some participants with VS due to mutations in the *NF2* gene. However, associated toxicity can limit long-term systemic administration of VEGF inhibitors as a viable treatment option for VS. Local expression of anti-VEGF protein following intracochlear administration of AK-antiVEGF is robust and well tolerated in non-human primates (NHPs), an anatomically relevant model for evaluating delivery parameters. Data from two nonclinical studies evaluating multiple doses demonstrate that systemic exposure to anti-VEGF protein is limited. Computational modelling supports the potential for diffusion of reported biologically active anti-VEGF protein levels to the typical location of early VS tumors. Together, these data support the future clinical development of AK-antiVEGF for the potential treatment of VS.

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

Tailoring Regulatory Elements in Gene Therapies for Hearing Loss
Presenting Author: Danielle R. Lenz, Ph.D.
Podium Session: 11

Ubiquitous promoters can drive safe expression of multiple transgenes and are used in commercially approved and development-stage gene therapies. In mice and NHPs, AAVAnc80-hOTOF with a ubiquitous promoter enabled robust and well-tolerated expression of hOTOF.FLAG. However, depending on the gene of interest, a tailored regulation of expression pattern may be preferred. Inclusion of a selective promoter was evaluated in the case of *GJB2*, where expression in hair cells is not well tolerated. Akouos developed a method to guide customization of regulatory elements based on bioinformatic efforts; regulatory elements to drive various differential expression patterns were identified and supporting cell-selective promoters were evaluated in mice in vivo. Nonclinical data demonstrate that a combination of AAVAnc80 and a supporting cell selective promoter can drive widespread *GJB2* expression in supporting cells, while limiting expression in, and loss of, hair cells in mature cochleae in wild-type mice. Future work will include customization of regulatory elements where this may be beneficial.

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

In Vitro Characterization of Gene Silencing Methods with the Potential to Treat Autosomal Dominant Hearing Loss
Presenting Author: Katherine D. Gribble, Ph.D.
Poster Number: 574

The development of AAV vectors as an intracochlear drug delivery platform presents a unique opportunity to treat genetic forms of hearing loss, including autosomal dominant hearing loss (ADHL), by developing precision medicines that are selectively designed to target affected genes. To address affected genes, one genetic medicine-based approach is to reduce expression levels of both alleles and simultaneously deliver a functional copy of the gene. Both AAV vector-mediated RNAi biallelic gene silencing and CRISPR/Cas9 biallelic gene editing were evaluated, with simultaneous add-back of a functional copy of the gene of interest. Engineered microRNA constructs and CRISPR/Cas9 constructs were evaluated for efficacy in

target gene reduction. With both microRNA and CRISPR/Cas9 constructs, a promising reduction of protein expression for the target ADHL gene was observed. The data show no measurable decrease in the protein product of a codon-modified add-back target gene, suggesting that the microRNA and CRISPR/Cas9 constructs are selective for the intended endogenous sequence. The results build foundational platform capabilities which may be used to develop potential AAV vector-mediated therapies for many types of ADHL and other inner ear conditions.

The digital poster 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.

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