MeiraGTx Announces the Presentation of Two Novel Inherited Retinal Disease (IRD) Programs and Riboswitch Gene Regulation Platform at the European Society of Gene and Cell Therapy (ESGCT) 2021 Annual Congress

October 19, 2021

Three Poster Presentations Highlight Versatility and Novelty of MeiraGTx's Gene Therapy Development Platforms

Novel Synthetic Riboswitch Platform Reversibly Regulates Gene Expression to High Dynamic Range and Drives Precise Dose Responsive Activation of Transgene Expression In Vivo

LONDON and NEW YORK, Oct. 19, 2021 (GLOBE NEWSWIRE) -- MeiraGTx Holdings plc (Nasdaq: MGTX), a vertically integrated, clinical stage gene therapy company, today announced three poster presentations at the European Society of Gene and Cell Therapy (ESGCT) 2021 Annual Congress. Two pre-clinical programs addressing Inherited Retinal Diseases (IRDs) caused by mutations in *KCNV2* and *GUCY2D* are presented with data supporting the development of these viral vectors as gene therapies.

A third presentation outlines MeiraGTx's proprietary gene regulation platform demonstrating tight regulation of gene expression to high dynamic range in mammalian cells and precise regulation *in vivo* in response to dosing of an oral small molecule.

"We're pleased to present data illustrating the depth and versatility of our scientific platform, including early data on optimized viral vectors for two Inherited Retinal Diseases, as well initial data from our novel gene regulation platform," said Alexandria Forbes, Ph.D., President and Chief Executive Officer of MeiraGTx. "Since our formation more than six years ago, in addition to developing novel vectors for gene replacement therapies in inherited diseases such as IRDs, we have aimed to develop gene regulation technology that may be applied to larger more common diseases. The Company's synthetic riboswitch gene regulation system provides an unprecedented platform for spatial and temporal control of gene therapy with broad implications for the applicability of genetic medicines for treating a wide range of potential disorders not limited to inherited diseases. We look forward to discussing our riboswitch gene regulation platform in more detail at an R&D Day later this year."

MeiraGTx continues to anticipate up to two new INDs for novel viral vectors addressing IRDs in 2022.

The Company will hold a research and development day in December 2021 in which further data on its synthetic riboswitch gene regulation platform as well as the Company's proprietary promoter platforms will be presented.

ESGCT 2021 Presentations and Data Summaries:

Title: Novel riboswitches regulate AAV delivered transgene expression in mammals via small molecule inducers
Poster ID: P164
Presenter: A. J. Forbes
Date and Time: Tuesday, October 19, 8:00 am CEST (2:00 am ET)
Session: Gene Targeting

As the field of gene therapy has progressed, multiple elements of viral vectors have been optimized to increase potency, specificity and safety of these therapies including the development of engineered promoters and transcriptional regulatory elements. However, until now the development of tight temporal control of gene therapies using oral small molecules has remained elusive, and protein-based switches have proved of little use due to low dynamic range, low levels of expression, and potential for immunogenicity.

MeiraGTx presents a potent gene regulation platform based on rationally designed synthetic riboswitches built in mammalian cells. These riboswitches drive a splicing-based expression platform engineered to create an 'on' switch in the presence of specific aptamer small molecule binding. Small molecule binding results in hairpin stabilization sequestering a splice site of an alternative exon. This platform regulates protein expression with high dynamic range and allows precise control of transgene expression levels. The extremely high dynamic range of this switch has allowed us to screen, identify and modify novel aptamers that bind and respond to novel small molecules. This platform is modular and adjustable and is optimized for each transgene to achieve the required expression level and dynamic range. This regulation platform has been demonstrated to work in multiple genes, multiple cell types *in vitro* and *in vivo.* When delivered through an AAV vector in mice, the engineered riboswitches reversibly regulate transgene expression via an orally delivered small molecule inducer, providing precise control of transgene expression. MeiraGTx's potent gene regulation system provides a platform for using unique aptamer-ligand pairs to regulate genes in mammals.

- Rationally designed synthetic riboswitches activate transgene expression via a splicing based expression platform cassette
- Novel synthetic riboswitches are highly dynamic in regulating gene expression in mammalian cells allowing precise activation of gene expression with small molecule inducers
- Aptamers are interchangeable within the switch and multiple novel synthetic aptamer and novel small molecule pairs have been generated
- Multiple transgenes have been regulated in multiple cell types *in vitro* and *in vivo*
- AAV delivered transgene expression is precisely regulated in a dose-dependent fashion *in vivo* via orally available small molecule inducer

This platform enables precise temporal and spatial control of gene expression, expanding the range of possibilities for using gene-based vectors as therapies.

Title: KCNV2 retinal organoid disease model for KCNV2 AAV gene therapy development
Poster ID: P364
Presenter: S. Ferrara
Date and Time: Tuesday, October 19, 8:00 am CEST (2:00 am ET)
Session: Stem Cells & Regenerative Medicine

Assessment of potential AAV gene replacement therapies for *KCNV2* mutations demonstrates that AAV-KCNV2-mediated gene therapy is a promising approach to the treatment of patients with cone-dystrophy due to *KCNV2* mutations. CRISPR/Cas9 gene editing was used to generate human KCNV2 Knockout (KCNV2 KO) and isogenic human control retinal organoids. KCNV2 KO retinal organoids were used to screen eight AAV vectors containing expression cassettes coding for either WT or codon-optimized versions of *hKCNV2*, as driven by either constitutive (CAG) or photoreceptor-specific rhodopsin kinase (RK) promoters. Both AAV5 and AAV7m8 vectors were assessed for their ability to restore hKCNV2 RNA expression and Kv8.2 localization to the inner segment of rod and cone photoreceptor cells following transduction.

All vectors tested successfully delivered the *hKCNV2* gene to photoreceptors in retinal organoids following transduction, restoring protein expression in the correct subcellular location as well as native protein-to-protein interactions. Transcriptomic analyses (single-cell RNA) indicated disease correction at a deep transcriptional level, and that AAV-mediated *KCNV2* gene supplementation has the potential to benefit patients with cone dystrophies due to *KCNV2* mutations.

Title: GUCY2D retinal organoid disease model for AAV gene therapy development
Poster ID: P395
Presenter: A. Naeem
Date and Time: Tuesday, October 19, 8:00 am CEST (2:00 am ET)
Session: Stem Cells & Regenerative Medicine

Assessment of potential AAV gene replacement therapies for *GUCY2D* mutations demonstrates that AAV-GUCY2D gene therapy constitutes a promising treatment for patients with cone-rod dystrophy due to *GUCY2D* mutations. Four AAV vectors, packaged into 7m8 capsids, were designed to enable the restoration of GUCY2D-mediated signaling in photoreceptor outer segments via gene replacement. Transduction of GUCY2D Knockout (GUCY2D KO) human retinal organoids by all vectors improved quantitative expression levels of GUCY2D and PDE6β relative to non-transduced controls, and total cGMP levels in transduced GUCY2D KO human retinal organoids were restored to close to those observed in healthy human retinal organoids, demonstrating vector potency and transgene function. These results indicate that gene replacement in GUCY2D-deficient human retinal organoids restored protein expression and cGMP levels in transduced organoids. This provides support for the potential use of AAV-mediated *GUCY2D* gene supplementation as a treatment for patients with inherited retinal dystrophy caused by mutations in *GUCY2D*.

About MeiraGTx
MeiraGTx (Nasdaq: MGTX) is a vertically integrated, clinical stage gene therapy company with six programs in clinical development and a broad pipeline of preclinical and research programs. MeiraGTx has core capabilities in viral vector design and optimization and gene therapy manufacturing, as well as a potentially transformative gene regulation technology. Led by an experienced management team, MeiraGTx has taken a portfolio approach by licensing, acquiring, and developing technologies that give depth across both product candidates and indications. MeiraGTx's initial focus is on three distinct areas of unmet medical need: ocular, including inherited retinal diseases and large degenerative diseases, neurodegenerative diseases, and severe forms of xerostomia. Though initially focusing on the eye, central nervous system, and salivary gland, MeiraGTx intends to expand its focus in the future to develop additional gene therapy treatments for patients suffering from a range of serious diseases.

For more information, please visit www.meiragtx.com.

Forward Looking Statement
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding our product candidate development and our pre-clinical data and reporting of such data and the timing of results of data, including in light of the COVID-19 pandemic, as well as statements that include the words "expect," "will," "intend," "plan," "believe," "project," "forecast," "estimate," "may," "could," "should," "would," "continue," "anticipate" and similar statements of a future or forward-looking nature. These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, our incurrence of significant losses; any inability to achieve or maintain profitability, raise additional capital, identify additional and develop existing product candidates, successfully execute strategic priorities, bring product candidates to market, expansion of our manufacturing facilities and processes, successfully enroll patients in and complete clinical trials, accurately predict growth assumptions, recognize benefits of any orphan drug designations, retain key personnel or attract qualified employees, or incur expected levels of operating expenses; the impact of the COVID-19 pandemic on the status, enrollment, timing and results of our clinical trials and on our business, results of operations and financial condition; failure of early data to predict eventual outcomes; failure to obtain FDA or other regulatory approval for product candidates within expected time frames or at all; the novel nature and impact of negative public opinion of gene therapy; failure to comply with ongoing regulatory obligations; contamination or shortage of raw materials or other manufacturing issues; changes in healthcare laws; risks associated with our international operations; significant competition in the pharmaceutical and biotechnology industries; dependence on third parties; risks related to intellectual property; changes in tax policy or treatment; our ability to utilize our loss and tax credit carryforwards; litigation risks; and the other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, as such factors may be updated from time to time in our other filings with the SEC, which are accessible on the SEC's website at www.sec.gov. These and other important factors could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, unless required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. Thus, one should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

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