MeiraGTx Announces Poster Presentation on a Potential Treatment for MC4R Genetic Deficiency at the 2024 Society for Neuroscience Conference

October 09, 2024

Results indicate a potent and effective locally delivered AAV-BDNF gene therapy for the treatment of obesity caused by MC4R deficiency

LONDON and NEW YORK, Oct. 09, 2024 (GLOBE NEWSWIRE) -- MeiraGTx Holdings plc (Nasdaq: MGTX), a vertically integrated, clinical stage genetic medicine company, today announced a poster presentation at the 2024 Society for Neuroscience Conference (SfN), which is being held from October 5-9, 2024, in Chicago, IL.

“We are pleased to share data at this year’s Society for Neuroscience Conference on the remarkable efficacy of our AAV-BDNF treatment in diet-induced obesity animal models,” said Alexandria Forbes, Ph.D., president and chief executive officer of MeiraGTx. “We leveraged our proprietary vector design platform to create a highly potent construct with the potential to treat children with severe early-onset obesity caused by *MC4R* genetic deficiency via the local delivery of a small dose of AAV-BDNF to a specific site in the ventromedial hypothalamus. This represents a powerful mechanism to treat these severely affected patients with no current treatment options available.”

The poster is available on the Posters and Publications page of the Company’s website on October 9, 2024.

The details of the poster presentation are as follows:

Poster Number: 5090
Abstract Title: *A CNS-targeted gene therapy for the treatment of severe pediatric obesity*
Date: October 9, 2024
Time: 1pm CT

In the ventromedial hypothalamus, the leptin-proopiomelanocortin pathway interprets energy signals from the periphery to initiate feeding or fasting through two opposing neuronal populations. In a fed state, elevated leptin signals a decrease in food intake via the release of brain derived neurotrophic factor (BDNF) from Melanocortin 4 receptor (MC4R) expressing neurons. Loss-of-function mutations along this pathway, including in MC4R or BDNF, cause severe obesity in humans. MC4R deficiency leads to a severe form of early-onset pediatric obesity that is characterized by an increased drive to eat and impaired satiety. Hyperphagia and food-related distress have been reported in patients as young as 8 months old. Current therapeutic approaches such as bariatric surgery and glucagon-like peptide 1 (GLP1) agonists do not result in significant, durable treatment for persons with MC4R deficiency. MC4R agonists are being developed, but this approach will not benefit patients with homozygous mutations. Therefore, there remains a need to develop a therapeutic that results in healthy weight loss that can be maintained throughout life. With this aim, we developed an adeno-associated virus (AAV)-based gene therapy to deliver BDNF to the ventromedial hypothalamus to treat patients with MC4R deficiency. Here, we show that our optimized BDNF gene therapy, designed by altering various cis-regulatory components, achieves significantly higher expression compared to a previously published construct. In head-to-head comparisons in primary mouse cortical neurons and various immortalized neural cell lines, the optimized vector achieved 4-fold greater expression. As a demonstration of our synthetic promoter, expression of a fluorescent protein was as strong as the CAG promoter while off-target expression in the liver and heart was much lower, highlighting the specificity of our promoter. Furthermore, AAV-mediated delivery of our optimized BDNF gene therapy to the hypothalamus caused significant weight loss in a diet-induced obesity (DIO) mouse model within 21 days. Our BDNF gene therapy expresses 143-fold greater than basal levels of BDNF *in vivo*, which is in excess of the 10-fold increase required to prevent weight gain in the DIO model. By designing a highly expressing BDNF gene therapy, we can drive efficacy at lower viral vector doses and potentially lower immune responses and decrease safety risks. Taken together, these results indicate a potent and effective gene therapy for the treatment of patients with MC4R deficiency.

About MeiraGTx

MeiraGTx (Nasdaq: MGTX) is a vertically integrated, clinical-stage genetic medicine company with a broad pipeline of late-stage clinical programs supported by end-to-end manufacturing capabilities. MeiraGTx has an internally developed manufacturing platform process, internal plasmid production for GMP, two GMP viral vector production facilities as well as an in-house Quality Control hub for stability and release, all fit for IND through commercial supply. MeiraGTx has core capabilities in viral vector design and optimization and a potentially transformative riboswitch gene regulation platform technology that allows for the precise, dose-responsive control of gene expression by oral small molecules. MeiraGTx is focusing the riboswitch platform on delivery of metabolic peptides including GLP-1, GIP, Glucagon and PYY using oral small molecules, as well as cell therapy for oncology and autoimmune diseases. Although initially focusing on the eye, central nervous system, and salivary gland, MeiraGTx has developed the technology to apply genetic medicine to more common diseases, increasing efficacy, addressing novel targets, and expanding access in some of the largest disease areas where the unmet need remains great.

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 anticipated milestones regarding our pre-clinical and clinical data, reporting of such data and the timing of results of data and regulatory matters, 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, repay our debt obligations, 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, 2024, 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.

Contacts

Investors:
MeiraGTx
Investors@meiragtx.com

or

Media:
Jason Braco, Ph.D.
LifeSci Communications
jbraco@lifescicomms.com