miRagen Announces Encouraging Preclinical Safety and Efficacy Data for its Next-generation miR-29 Replacement Product Candidate Intended for the Treatment of Idiopathic Pulmonary Fibrosis

June 22, 2020

Key Opinion Leader call on IPF scheduled for 11 a.m. ET on Tuesday, June 23rd

BOULDER, Colo., June 22, 2020 (GLOBE NEWSWIRE) -- miRagen Therapeutics, Inc. (NASDAQ: MGEN), a clinical-stage biopharmaceutical company focused on the discovery and development of RNA-targeted therapies, today announced preclinical safety and efficacy data for MRG-229, a next-generation miR-29 mimic intended for systemic administration and targeted delivery, in Idiopathic Pulmonary Fibrosis (IPF).

"MRG-229 has demonstrated mechanistic biomarker regulation and antifibrotic activity *in vitro* using human model systems. In addition, subcutaneous administration of the product candidate induced the reversal of pathologic fibrotic gene expression and resulted in a significant reduction of fibrosis in the most commonly employed pre-clinical animal model of pulmonary fibrosis. Finally, high doses of MRG-229 in preclinical toxicology studies in rats showed no clinically significant toxicity," stated William S. Marshall, Ph.D., President and Chief Executive Officer of miRagen Therapeutics. "We believe this body of evidence supports further development of MRG-229 as a potentially differentiated approach for the treatment of IPF."

"In our recently published analysis of fibrosis progression in the human lung, miR-29 emerged as a key regulator of fibrotic pathways in IPF," said Naftali Kaminski, M.D., Boehringer-Ingelheim Endowed Professor of Internal Medicine, Chief of Pulmonary, Critical Care and Sleep Medicine at Yale School of Medicine, and the principle investigator on NIH-NHLBI CADET grant focusing on mir-29 therapeutics in pulmonary fibrosis. "The most recent data, generated as part of our collaboration with miRagen and supported by an NIH CADET grant, is encouraging and suggests that miR-29 replacement may represent a novel paradigm in the treatment of IPF."

A summary of the latest preclinical observations:

- miR-29 expression was reduced in lungs of IPF patients compared to controls and circulating miR-29 correlates with survival.
- Next-generation targeted miR-29 mimics demonstrated target pathway down-regulation assessed by fibrotic gene signatures in normal human lung fibroblasts *in vitro*. These anti-fibrotic effects extended to collagen secretion, assessed from the cell extract, from diseased lung fibroblasts *in vitro*, highlighting functional activity in addition to molecular readouts.
- Next-generation targeted miR-29 mimics demonstrated efficacy in *ex vivo* in profibrotic--induced human precision cut lung slices as assessed by histopathology.
- Next-generation miR-29 mimics blocked fibrosis in a therapeutic dosing-regimen of mouse bleomycin-induced pulmonary fibrosis with increased potency compared to first generation miR-29 mimics. Anti-fibrotic activity of next-generation miR-29 mimics in mouse bleomycin-induced pulmonary fibrosis was observed for both intravenous and subcutaneous routes of administration.
- Potential biomarkers identified in bronchoalveolar lavage fluid and serum for miR-29 antifibrotic activity that could be relevant in future studies.
- Preliminary toxicity studies in rats and mice showed MRG-229 showed no clear test article related adverse effects on organ histology, hematology, clinical chemistries, coagulation, or urinalysis when dosed up to 30 mg/kg twice a week for up to 4 weeks. Company believes these data support advancing into Non-Human Primate toxicology studies, which are currently initiating.

Conference Call Details:

miRagen Therapeutics is scheduled to host a key opinion leader (KOL) conference call and webcast at 11:00 a.m. ET tomorrow, June 23rd, to discuss the current and increasing unmet medical needs in treating patients with IPF, as well as the encouraging new preclinical safety and efficacy data for MRG-229 announced today. The call will feature KOLs Fernando J. Martinez, MD, Weill Cornell Medicine, Teresa Barnes, Coalition for Pulmonary Fibrosis, and Naftali Kaminski, MD, Yale School of Medicine, joined by Dr. Montgomery who will provide a presentation of the MRG-229 development program in IPF.

To access the call, please dial 877-407-0789 (domestic) or 201-689-8562 (international) and provide the passcode 13705048. A live webcast of the call will be available at (Click Here) or visit the Events section of miRagen's website: www.investors.miragen.com/events. A replay of this conference call will be available approximately one hour after its completion at (Click Here) or visit the Events section of miRagen's website: www.investors.miragen.com/events.

About MRG-229

MRG-229 is a second-generation mimic of miR-29, a microRNA that is found at abnormally low levels in a number of pathologic fibrotic conditions, including idiopathic pulmonary fibrosis (IPF). miR-29 is believed to play a role in the regulation of certain processes that contribute to fibrosis, including the initiation and maintenance of fibrosis through transforming growth factor beta, or TGF-β, signaling and the deposition of the components that make up fibrotic tissue, including collagen and extracellular matrix proteins. The company believes that increasing the levels of miR-29 by administration of MRG-229 could be beneficial in the treatment of patients who suffer from IPF. This program was recently awarded additional funds from an NIH/NHLBI CADET grant and Yale University.

About miRagen Therapeutics

miRagen Therapeutics, Inc. is a clinical-stage biopharmaceutical company discovering and developing proprietary RNA-targeted therapies with a specific focus on microRNAs and their role in diseases where there is a high unmet medical need. miRagen has three clinical stage product candidates, cobomarsen, remlarsen, and MRG-110. miRagen's clinical product candidate for the treatment of certain cancers, cobomarsen, is an inhibitor of miR-155, which is found at abnormally high levels in malignant cells of several blood cancers. miRagen's clinical product candidate for the treatment of pathological fibrosis, remlarsen, is a replacement for miR-29, which is found at abnormally low levels in a number of pathological fibrotic conditions, including cutaneous, cardiac, renal, hepatic, pulmonary and ocular fibrosis, as well as in systemic sclerosis. MRG-110, an inhibitor of miR-92, is miRagen's product candidate for the treatment of heart failure and other ischemic disease. In addition to these programs, miRagen is developing a pipeline of preclinical product candidates. The goal of miRagen's translational medicine strategy is to progress rapidly to first-in-human studies once it has established the pharmacokinetics, pharmacodynamic, safety, and manufacturability of the product candidate in preclinical studies. For more information, please visit www.miragen.com. For information on clinical trials, please visit www.clinicaltrials.gov.

Note Regarding Forward-Looking Statements

This press release may contain forward-looking statements that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. All statements contained in this press release other than statements of historical fact, including statements regarding miRagen's strategy, anticipated clinical development milestones, prospects, plans and objectives of management are forward-looking statements. The words "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "plan," "expect," "predict," "potential," "opportunity," "goals," or "should," and similar expressions are intended to identify forward-looking statements. Such statements are based on management's current expectations and involve risks and uncertainties. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors, including, without limitation: that miRagen has incurred losses since its inception, and anticipates that it will continue to incur significant losses for the foreseeable future; future financing activities may cause miRagen to restrict its operations or require it to relinquish rights; miRagen may fail to demonstrate safety and efficacy of its product candidates; miRagen's product candidates are unproven and may never lead to marketable products; miRagen's product candidates are based on a relatively novel technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all; miRagen's product candidates may cause undesirable side effects or have other properties that could delay or prevent the regulatory approval; and the results of miRagen's clinical trials to date are not sufficient to show safety and efficacy of miRagen's product candidates and may not be indicative of future clinical trial results.

miRagen has based these forward-looking statements largely on its current expectations and projections about future events and trends. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described under the heading "Risk Factors" in miRagen's Annual Report on Form 10-K and subsequent periodic and current reports filed with the Securities and Exchange Commission. Moreover, miRagen operates in a very competitive and rapidly changing environment. New risks emerge from time to time.

It is not possible for its management to predict all risks, nor can it assess the impact of all factors on its business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements it may make. In light of these risks, uncertainties and assumptions, the future events and trends discussed in this press release may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. miRagen undertakes no obligation to revise or publicly release the results of any revision to such forward-looking statements, except as required by law. Given these risks and uncertainties, readers are cautioned not to place undue reliance on such forward-looking statements. All forward-looking statements are qualified in their entirety by this cautionary statement.

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