Viridian Announces Positive Data from Ongoing Phase 1/2 Trial Evaluating VRDN-001 in Patients with Thyroid Eye Disease (TED)

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- Significant and rapid improvement in both signs and symptoms of TED after two infusions of 20 mg/kg VRDN-001, generally consistent with 10 mg/kg results at week 6 -

- Global Phase 3 THRIVE clinical program initiated -

- Across all VRDN-001 treated patients to date: 75% were proptosis responders, 75% were overall responders, 58% achieved a Clinical Activity Score (CAS) of 0 or 1, and 75% had complete resolution of their diplopia -

- Safety profile favorable at 20 mg/kg dose, with no reported SAEs, no drug-related hyperglycemia, no hearing impairment, and no infusion reactions -

- Low volume SC programs on track for proof-of-concept data in 2H23; final Phase 1 data for VRDN-002 demonstrates half-life up to 43 days -

- Company well capitalized with cash, cash equivalents, and short-term investments of $431M, providing cash runway into 2H25 -

WALTHAM, Mass., Nov. 14, 2022 (GLOBE NEWSWIRE) -- Viridian Therapeutics, Inc. (NASDAQ: VRDN), a biotechnology company advancing new treatments for patients suffering from serious diseases underserved by current therapies, today announced positive topline clinical data from the first two cohorts in its ongoing Phase 1/2 clinical trial of VRDN-001, an anti-IGF-1R antibody, in patients with active thyroid eye disease (TED). TED is a rare autoimmune disease in which the body's own immune system attacks the tissues around and behind the eyes causing inflammation, swelling, and damage that develops into debilitating signs and symptoms including double vision, bulging eyes, and ocular pain.

"These additional Phase 1/2 clinical data continue to support the potential for VRDN-001 to be a new treatment option for patients suffering from TED," said Raymond Douglas, M.D., Ph.D., director of the Orbital and Thyroid Eye Disease Program, Cedars-Sinai Medical Center and an investigator on the VRDN-001 trial. "The data show that a majority of patients experienced meaningful improvements in proptosis and clinical activity score, and complete resolution of diplopia after only two infusions of VRDN-001, with initial data suggesting a prolonged duration of benefit. This profile could offer substantial benefits to patients."

VRDN-001 – Phase 1/2 proof-of-concept trial
The double-blind, placebo-controlled Phase 1/2 trial is evaluating two infusions of VRDN-001 administered intravenously, three weeks apart, with efficacy measured six weeks after the first dose. Each dose is evaluated in a cohort of eight patients, with six patients randomized to receive VRDN-001 and two patients randomized to receive placebo. The inclusion and exclusion criteria and the baseline patient characteristics for this trial are in line with prior TED clinical trials. Efficacy measurements include proptosis (bulging eyes), Clinical Activity Score (CAS), and diplopia (double vision), which are the same endpoints as measured in the clinical development of Tepezza®, the only approved therapy targeting IGF-1R in patients with TED. The first cohort of the Phase 1/2 study evaluated a dose of 10 mg/kg, with initial positive clinical data reported on August 15, 2022, and with additional 12-week data announced today. The second cohort evaluated a dose of 20 mg/kg with 6-week data announced today. In addition, the Company plans to report results from the third cohort evaluating a dose of 3 mg/kg in early January 2023.

VRDN-001 – Safety data
VRDN-001 was well-tolerated by all patients treated at the 20 mg/kg dose, with safety data consistent with the 10 mg/kg dose. There were no reported serious adverse events (SAEs), no patient discontinuations, no hearing impairment, no drug-related hyperglycemia, and no infusion reactions as of November 8, 2022, the most recent cut-off date for follow-up observation.

VRDN-001 – Clinical activity data
All 12 VRDN-001 treated patients in the 10 mg/kg (n=6) and 20 mg/kg (n=6) cohorts were treated for two full cycles and were evaluated for proptosis, clinical activity score (CAS), and diplopia. Improvement in proptosis, CAS, and diplopia was generally consistent across the two cohorts. A similar IGF-1 response, a biomarker for target engagement, was also observed across the two cohorts. The following activity was observed across all patients at week 6:

Proptosis

- 75% proptosis responder rate (83% at 10 mg/kg and 67% at 20 mg/kg), defined as a ≥2mm reduction in proptosis from baseline as measured by exophthalmometry
- 2.04mm mean reduction in proptosis from baseline (-2.4mm at 10 mg/kg and -1.7mm at 20 mg/kg) as measured by exophthalmometry
- 2.75mm mean reduction in proptosis from baseline when measured by blinded, centrally reviewed MRI

Clinical Activity Score (CAS)

- 4.0 point mean reduction in CAS from baseline on a 7-point measure of signs and symptoms of TED (4.3 points at 10 mg/kg and 3.7 points at 20 mg/kg reduction)
- 58% of patients achieved maximal or near-maximal therapeutic effect on CAS (83% at 10 mg/kg and 33% at 20 mg/kg), defined as reaching a CAS of 0 or 1 on the 7-point composite measure of signs and symptoms of TED

Overall response

- 75% overall responder rate (83% at 10 mg/kg and 67% at 20 mg/kg), defined as a ≥2mm reduction in proptosis and a ≥2 point reduction in CAS

Diplopia

- 75% complete resolution of diplopia, defined as patients with baseline diplopia who achieved a score of 0 on the Gorman subjective diplopia scale (75% at 10 mg/kg and 75% at 20 mg/kg)

The Company also reported 12-week data from the 10 mg/kg cohort, showing that after two infusions, VRDN-001 maintained efficacy for six additional weeks through week 12. This data further supports the potential for a shorter course of treatment via a 5-infusion schedule being studied alongside the standard 8 infusion arm in the Company's Phase 3 THRIVE program.

"We are delighted to deliver robust data from a second cohort of TED patients, showing rapid, clinically meaningful improvements in every measure of the signs and symptoms of TED. We were also pleased with our recent Type C meeting with the U.S. Food and Drug Administration (FDA) and two European Union (EU) scientific advice meetings and now have initiated our global Phase 3 THRIVE clinical trial in active TED patients," said Barrett Katz, MD, MBA, Chief Medical Officer at Viridian.

VRDN-001 – Upcoming milestones

- Topline data from 3 mg/kg cohort of active TED patients expected in early January 2023
- First patient expected to be enrolled in chronic TED proof-of-concept study in December 2022 with preliminary data expected in the first half of 2023; patient screening underway in November 2022
- First patient expected to be enrolled in Phase 3 THRIVE study in active TED in December, with results expected in mid-2024; patient screening underway in November 2022

SC Programs: VRDN-002 and VRDN-003
Earlier this year, Viridian initiated a first-in-human Phase 1 clinical trial of VRDN-002, a novel monoclonal antibody that incorporates half-life extension technology and is designed to support administration as a convenient, low-volume, subcutaneous (SC) injection for the treatment of TED patients. This single ascending dose trial explored safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of intravenously administered VRDN-002 at doses of 3, 10, and 20mg/kg in 12 healthy volunteers. In August 2022, interim VRDN-002 half-life data in healthy volunteers was reported suggesting a potential half-life of 30-40 days, which would support Q2W or Q4W dosing. Today, the Company is reporting updated PK/PD data from the complete dataset in healthy volunteers.

The following VRDN-002 healthy volunteers results were observed:

- The data confirmed an extended half-life up to 43 days, approximately four times the half-life of VRDN-001 and teprotumumab, and an improvement over the interim results announced in August 2022
- After a single IV dose of VRDN-002, plasma IGF-1 levels increased approximately 2.5-fold and were sustained throughout the measurement period of 84 days
- VRDN-002 was well tolerated with no reported serious adverse events, hearing impairment, hyperglycemia, muscle spasms, or infusion reactions reported

The Company is on track to deliver topline SC proof of concept data for VRDN-002 in TED patients in the second half of 2023; this trial will evaluate subcutaneous injections of 2mL 300mg dosed Q2W or Q4W.

VRDN-003, which is VRDN-001 enhanced with the same half-life extension as VRDN-002, is on track for an IND filing in the second quarter of 2023, with non-human primate PK indicating a half-life at least as long as VRDN-002. The Company continues to expect to deliver topline PK/PD data from a healthy volunteer study in the fourth quarter of 2023, and to select either VRDN-002 or VRDN-003 to advance to a pivotal Phase 3 trial in early 2024.

"The TED market, projected to exceed $4 billion globally, offers a rare opportunity for a differentiated entrant to quickly capture market share. Thus far, our VRDN-001 clinical data is remarkable and bolsters our confidence in our TED programs. We are developing a complete global portfolio, including best-in-class IV and SC IGF-1R therapies for TED, designed to maximize the benefits we can deliver for patients," said Jonathan Violin, Ph.D., President and CEO of Viridian Therapeutics.

Conference call and webcast
The Company will host a conference call today at 8:00 a.m. ET to discuss the topline data for VRDN-001 and VRDN-002. The dial-in number for the conference call is 1-877-407-0789 for domestic participants and 1-201-689-8562 for international participants. The conference ID is 13732927. A live webcast of the conference call can be accessed through the "Events" page in the Investors section of the Viridian Therapeutics website. Following the live webcast, an archived version of the call will also be available on the website.

About Viridian Therapeutics
Viridian Therapeutics is a biotechnology company advancing new treatments for patients suffering from serious diseases underserved by current therapies. Viridian's most advanced program, VRDN-001, is a differentiated monoclonal antibody targeting insulin-like growth factor-1 receptor (IGF-1R), a clinically and commercially validated target for the treatment of thyroid eye disease (TED). VRDN-002 is a distinct anti-IGF-1R antibody and incorporates half-life extension technology. VRDN-003 is an extended half-life version of VRDN-001. Both VRDN-002 and VRDN-003 are designed for administration as convenient, low-volume, subcutaneous injections. TED is a debilitating autoimmune disease that causes inflammation and fibrosis within the orbit of the eye which can cause double vision, pain, and potential blindness. Viridian is based in Waltham, Massachusetts.

Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of words such as, but not limited to, "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "will," or "would" or other similar terms or expressions that concern the Company's expectations, plans and intentions. Forward-looking statements include, without limitation, statements regarding the Company's expectations, strategies, plans and intentions. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on the Company's current beliefs, expectations, and assumptions. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. Such forward-looking statements are subject to a number of material risks and uncertainties including but not limited to: the potential efficacy and safety of VRDN-001 and VRDN-002 for the treatment of TED; the relationship between the results from the positive data from the ongoing Phase 1/2 clinical trial of VRDN-001 and the first-in-human Phase 1 clinical trial of VRDN-002 and results of ongoing and future clinical trials; the timing, progress and plans for the Company's ongoing and future research and clinical development programs; trial protocols for ongoing clinical trials, including the clinical trials for VRDN-001 and VRDN-002; expectations regarding the timing for data, including the expected timing of additional data from the ongoing Phase 1/2 clinical trial of VRDN-001 and the first-in-human Phase 1 clinical trial of VRDN-002 and VRDN-003; uncertainty and potential delays related to clinical drug development; the duration and impact of regulatory delays in the Company's clinical programs; manufacturing risks; competition from other therapies or products; other matters that could affect the sufficiency of existing cash, cash equivalents and short-term investments to fund operations; the Company's financial position and its projected cash runway; the Company's future operating results and financial performance; the timing of pre-clinical and clinical trial activities and reporting results from same; potential addressable market size; the effects from the COVID-19 pandemic on the Company's research, development and business activities and operating results, including those risks set forth under the caption "Risk Factors" in the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on March 11, 2022 and other subsequent disclosure documents filed with the SEC. Any forward-looking statement speaks only as of the date on which it was made. Neither the Company, nor its affiliates, advisors, or representatives, undertake any obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date hereof.

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