Viridian Announces Positive Data from Ongoing Phase 1/2 Trial Evaluating Low Dose 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 3 mg/kg, generally consistent with prior 10 and 20 mg/kg results –

- Among 3 mg/kg VRDN-001 treated patients, 67% were proptosis responders, 56% were overall responders, 67% achieved a Clinical Activity Score (CAS) of 0 or 1, and 20% had complete resolution of their diplopia –

- Across all 21 VRDN-001 treated patients to date, 71% were proptosis responders, 67% were overall responders, 62% achieved a CAS of 0 or 1, and 54% had complete resolution of their diplopia, with a favorable safety profile seen across all dose levels –

- 3 mg/kg data support planned once-monthly low-volume subcutaneous dosing profile for VRDN-002 and VRDN-003 –

WALTHAM, Mass., Jan. 08, 2023 (GLOBE NEWSWIRE) -- Viridian Therapeutics, Inc. (NASDAQ: VRDN), a biopharmaceutical company focused on discovering and developing potential best-in-class medicines for serious and rare diseases, today announced positive topline clinical data from the third, low dose cohort in its ongoing Phase 1/2 clinical trial of VRDN-001, an anti-insulin-like growth factor 1 receptor (IGF-1R) antibody, in patients with active thyroid eye disease (TED). The Company believes this data further validate the differentiated and potentially best-in-class clinical activity of VRDN-001. The data also support the planned dosing interval for Viridian's VRDN-002 and VRDN-003 subcutaneous programs of up to once monthly.

"The rapid and meaningful improvements in signs and symptoms of TED observed with a low dose of VRDN-001 reinforce previously reported findings in this trial, and suggest that VRDN-001 may offer a differentiated efficacy profile," said Roger Turbin, M.D., Professor of Ophthalmology and Visual Science within the Department of Ophthalmology of Rutgers New Jersey Medical School, and an investigator on the VRDN-001 trial. "The data also support development of VRDN-001 as a patient-friendly low volume subcutaneous injection, which could reduce the burden of care for patients suffering from TED."

VRDN-001 – Phase 1/2 proof-of-concept trial
The proof-of-concept portion of this double-blind, placebo-controlled Phase 1/2 trial evaluated two infusions of VRDN-001 administered intravenously, three weeks apart, with efficacy measured six weeks after the first dose. VRDN-001 was evaluated at doses of 3, 10, and 20 mg/kg, with each cohort designed to include six patients randomized to drug, and two patients randomized to placebo. The Company previously announced positive results from the first two dose cohorts, which demonstrated a favorable safety profile. The third cohort evaluated a VRDN-001 dose of 3 mg/kg with 6-week data announced today. In the 3 mg/kg dose cohort, nine patients were randomized to receive VRDN-001 to enable all consented patients who were eligible following screening to participate in the trial, and two patients were randomized to receive placebo. One patient receiving placebo discontinued in the trial prior to the 6-week evaluation.

VRDN-001 – Safety data
VRDN-001 was generally safe and well-tolerated by all patients treated in the three dose cohorts. There were no reported serious adverse events (SAEs), no discontinuations, and no infusion reactions in patients treated with VRDN-001 as of December 19, 2022, the most recent cut-off date for follow-up observation. The safety and tolerability profile at the 3 mg/kg dose level was generally consistent with previously reported results.

VRDN-001 – Clinical activity data
All VRDN-001 treated patients (n=21) in the 3 mg/kg (n=9), 10 mg/kg (n=6) and 20 mg/kg (n=6) cohorts were treated for two full cycles and were evaluated for changes in proptosis, clinical activity score (CAS) and diplopia. Improvement in proptosis and CAS was generally consistent across the three cohorts. A preliminary analysis of systemic IGF-1 levels, a biomarker for target engagement, shows a similar increase was also observed across the three cohorts. The following activity was observed in the 3mg/kg cohort (n=9) and across all three dose groups (n=21) at week 6:

Proptosis

- Proptosis responder rate, defined as a ≥2-millimeter (mm) reduction in proptosis from baseline as measured by exophthalmometry
  - 67% in the 3mg/kg cohort
  - 71% across all three dose groups
- Mean reduction in proptosis from baseline as measured by exophthalmometry
  - 2.7 mm in the 3mg/kg cohort
  - 2.3 mm across all three dose groups
- Mean reduction in proptosis from baseline as measured by blinded, centrally reviewed magnetic resonance imaging (MRI)
  - 2.8 mm in the 3mg/kg cohort (MRI available for 7 patients)
  - 2.76 mm across all three dose groups (MRI available for 16 patients)

Clinical Activity Score (CAS)

- Mean reduction in CAS from baseline on a 7-point measure of signs and symptoms of TED
  - 4.2-points in the 3mg/kg cohort

    - 4.1-points across all three dose groups
- Maximal or near-maximal therapeutic effect on CAS, defined as reaching a CAS of 0 or 1 on the 7-point composite measure of signs and symptoms of TED
    - 67% in the 3mg/kg cohort
    - 62% across all three dose groups

Overall response

- Overall responder rate, defined as a ≥2 mm reduction in proptosis and a ≥2 point reduction in CAS
    - 56% in the 3mg/kg cohort
    - 67% across all three dose groups

Diplopia

- Complete resolution of diplopia, defined as patients with baseline diplopia who achieved a score of 0 on the Gorman subjective diplopia scale
    - 20% in the 3mg/kg cohort (5 patients with diplopia at baseline)
    - 54% across all three dose groups (13 patients with diplopia at baseline)

“Data from this low dose cohort expand our overall data set to 21 drug-treated patients and build additional confidence in our ongoing Phase 3 ‘THRIVE’ trial evaluating VRDN-001 in patients with active TED.” said Barrett Katz, MD, MBA, Chief Medical Officer at Viridian. “This low dose data also increases our confidence in our planned subcutaneous program, which we are advancing as a convenient, self-administered pen.”

Subcutaneous program
The Company believes that data from the 3 mg/kg dose cohort of VRDN-001 validate a low volume, subcutaneous product profile for the Company’s next-generation half-life extended anti-IGF-1R antibodies VRDN-002 and VRDN-003.

VRDN-002 is a novel anti-IGF-1R monoclonal antibody that incorporates half-life extension technology. The Company previously reported that VRDN-002 demonstrated a half-life up to 43 days in healthy volunteers, supporting administration as a low-volume, subcutaneous injection up to once-monthly.

VRDN-003 is an anti-IGF-1R monoclonal antibody with the same amino acid sequence as VRDN-001, except for the addition of the half-life extension technology that is incorporated in VRDN-002.

The Company’s updated pharmacokinetic (PK) modeling support feasibility of ongoing development of a self-administered pen for subcutaneous administration, and a planned dosing interval of up to once-monthly for VRDN-002 and VRDN-003.

A presentation of the VRDN-001 3 mg/kg data is available under “Events and Presentations” on the Investors section of the Viridian website at viridiantherapeutics.com.

Upcoming corporate priorities

- Initial VRDN-001 results from a proof-of-concept study in patients with chronic TED are expected in the first half of 2023
- VRDN-003 IND filing with the US Food and Drug Administration is planned for the second quarter of 2023, with Phase 1 results in healthy volunteers expected in the fourth quarter of 2023.
- VRDN-002 results in patients with active TED are expected in the second half of 2023
- The Company expects to select either the VRDN-002 or VRDN-003 subcutaneous program to advance to a pivotal Phase 3 trial in early 2024.
- Patient enrollment in the global THRIVE Phase 3 trial in patients with active TED is ongoing and results are expected mid-2024

About Viridian’s Thyroid Eye Disease Pipeline (VRDN-001, -002, and -003)

Viridian’s lead product candidate, 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). In preclinical studies, VRDN-001 was shown to be a full antagonist of IGF-1R, with more complete receptor blockade than other anti-IGF-1R antibodies, including the only currently approved TED therapy. Data from the initial dose cohorts of the Phase 2 portion of the ongoing trial established clinical proof-of-concept for VRDN-001 in patients with active TED. Preliminary data from the ongoing trial showed treatment with VRDN-001 led to clinically meaningful reductions in proptosis, improvement in clinical activity score (CAS), and diplopia resolution. VRDN-001 was generally safe and well tolerated in the trial. The Company recently initiated its THRIVE Phase 3 trial in patients with active TED to support global marketing registration.

VRDN-001 is also being evaluated in Phase 2 trial cohorts in patients with chronic TED. Pending positive results, the Company plans to start its THRIVE-2 Phase 3 trial in patients with chronic TED.

The Company is advancing VRDN-002, a distinct anti-IGF-1R antibody incorporating half-life extension technology, and VRDN-003, a half-life extended version of VRDN-001. Both VRDN-002 and VRDN-003 are designed for administration as convenient, low-volume, subcutaneous injections.

VRDN-001, -002, and -003 are investigational therapies that are not approved for any use in any country.

About TED

TED is a serious and debilitating rare autoimmune disease that causes inflammation within the orbit of the eye that can cause double vision, pain, and potential blindness. TED is a progressive disease consisting of an initial active phase, followed by a transition to a secondary chronic phase. More than 50,000 and 200,000 people are estimated to suffer from active and chronic TED, respectively, in the United States and Europe.

About Viridian Therapeutics

Viridian Therapeutics is a biopharmaceutical company focused on engineering and developing potential best-in-class medicines for patients with serious and rare diseases. Viridian's expertise in antibody discovery and engineering enables it to develop differentiated therapeutic candidates for previously validated drug targets in commercially established disease areas.

Viridian is advancing multiple candidates in the clinic for the treatment of patients with thyroid eye disease (TED). The Company recently initiated its first global Phase 3 trial called 'THRIVE' to evaluate the safety and efficacy of VRDN-001 in patients with active TED. Viridian is also evaluating VRDN-001 in a Phase 2 proof-of-concept trial in patients with chronic TED. In addition to its intravenously administered VRDN-001 program, the Company is advancing two candidates for its subcutaneous strategy with the goal of providing a more conveniently administered therapy to patients with TED. Viridian is developing multiple preclinical assets in autoimmune and rare diseases.

Viridian is based in Waltham, Massachusetts. For more information, please visit https://www.viridiantherapeutics.com. Follow Viridian on LinkedIn.

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, VRDN-002 and VRDN-003 for the treatment of TED; the relationship between the results from the positive data from the Phase 1/2 clinical trial of VRDN-001 and the results of ongoing or future clinical trials; the timing, progress and plans for the Company's ongoing and future research and clinical development programs; trial protocols for ongoing or future clinical trials, including the clinical trials for VRDN-001, VRDN-002 and VRDN-003; expectations regarding the timing for data; uncertainty and potential delays related to clinical drug development; the duration and impact of regulatory delays in the Company's clinical programs; manufacturing risks; our ability to develop a subcutaneous formulation; 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.

Investor and Media Contact
Todd James
Viridian Therapeutics, Inc.
Senior Vice President, Corporate Affairs and Investor Relations
617-272-4691
IR@viridiantherapeutics.com

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