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

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- VRDN-001 data demonstrated clinically meaningful and rapid improvement in signs and symptoms of chronic TED at week 6 after receiving two infusions of VRDN-001 10 mg/kg or 3 mg/kg –

- Ongoing THRIVE Phase 3 trial in patients with active TED amended to reflect Viridian's confidence in 5-dose regimen and key stakeholder feedback on evolving TED treatment paradigm -

- THRIVE-2 Phase 3 trial in patients with chronic TED expected to start in third quarter 2023 –

- 3 mg/kg data support low-volume subcutaneous (SC) dosing profile for Company's SC candidates in TED -

- Viridian plans to select lead SC program candidate by year-end 2023; VRDN-001 SC IND amendment and VRDN-003 IND submitted to the FDA –

- Conference call and webcast to be held today, Monday, July 10th at 5:00 p.m. ET -

WALTHAM, Mass.--(BUSINESS WIRE)--Jul. 10, 2023-- 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 preliminary data from its ongoing Phase 1/2 clinical trial of VRDN-001, an investigational full antagonist antibody to the insulin-like growth factor 1 receptor (IGF-1R), in patients with chronic thyroid eye disease (TED). The Company also announced an amendment to its ongoing THRIVE Phase 3 trial design and provided an update on recent progress of its SC program candidates in TED.

"It is quite impressive that patients in the 10 mg/kg and 3 mg/kg dose cohorts experienced reductions in proptosis as well as improvements in their clinical activity scores after receiving just two infusions of VRDN-001," said Kimberly Cockerham, M.D., an Oculoplastic Surgeon specializing in neuro-ophthalmology, orbital oncology and oculofacial restoration at the SENTA Clinic in San Diego, California, and an investigator on the VRDN-001 clinical trial. "Importantly, VRDN-001 was generally well tolerated among all treated patients, who will continue to be evaluated for safety and durability of response. Thus far, these data suggest that VRDN-001 has the potential to become an important new treatment option for managing the signs and symptoms of TED."

VRDN-001 – Phase 1/2 proof-of-concept trial in chronic TED

The proof-of-concept portion of the double-masked, placebo-controlled Phase 1/2 trial evaluated two infusions of VRDN-001 administered intravenously (IV), three weeks apart, with clinical activity endpoints measured six weeks after the first infusion. VRDN-001 was evaluated at doses of 10 and 3 mg/kg, with each cohort designed to include six patients randomized to drug, and two patients randomized to placebo.

Participant eligibility criteria included: chronic TED with documented evidence of ocular symptoms or signs that began more than one year prior to screening (mean duration of 7.8 years), and proptosis of ≥3 mm above normal values for gender and race. Any clinical activity score (CAS, 0 – 7) was allowed for randomization (mean CAS was 3.3).

VRDN-001 – Safety data

VRDN-001 was generally well tolerated by all drug treated patients in both dose cohorts. There were no reported serious adverse events (SAEs), including no hearing impairment or hyperglycemia events, in patients with chronic TED treated with VRDN-001 as of May 30, 2023, the most recent cutoff date for follow-up observation. The safety and tolerability profile was generally consistent with previously reported results in patients with active TED treated with VRDN-001.

VRDN-001 – Clinical activity data in chronic TED

Patients in the 10 mg/kg (n=6) and 3 mg/kg (n=6) cohorts who were treated with two doses of VRDN-001 were evaluated for changes in proptosis, CAS, and diplopia at week 6. Proptosis changes from baseline were measured both by exophthalmometry and magnetic resonance imaging (MRI, an exploratory measure). We believe exophthalmometry and MRI together provide a robust assessment of changes in proptosis. The following activity was observed in the 10 mg/kg cohort (n=6), 3mg/kg cohort (n=6), and across both dose groups (n=12):

Proptosis:

- Patients treated with VRDN-001 had lower mean proptosis at baseline when compared with placebo (25.0 mm).

	VRDN-001 10 mg/kg cohort (n = 6)	VRDN-001 3 mg/kg cohort (n = 6)	VRDN-001 combined 10 and 3 mg/kg (n = 12)
Mean baseline proptosis	21.1 mm	23.4 mm	22.2 mm
Mean reduction in proptosis from baseline (measured by exophthalmometry)	-1.8 mm	-1.5 mm	-1.6 mm
Mean reduction in proptosis from baseline (measured by MRI*)	-1.5 mm	-2.6 mm	-2.0 mm
Proptosis responder rate	50%	33%	42%

**Masked, centrally reviewed MRI; MRI data is preliminary, MRI data available for 4 of 6 VRDN-001 10 mg/kg treated patients, 4 of 6 VRDN-001 3*

mg/kg treated patients, and 5 of 5 placebo-treated patients (mean reduction in proptosis by MRI = -0.2 mm for placebo).

CAS:

- Observed a 50% to 72% reduction in mean CAS at week 6 compared with mean baseline levels in patients treated with VRDN-001.

	VRDN-001 10 mg/kg cohort (n = 6)	VRDN-001 3 mg/kg cohort (n = 6)	VRDN-001 combined 10 and 3 mg/kg (n = 12)
Mean baseline CAS	2.5	4.0	3.3
Mean reduction in CAS from baseline, all patients (7-point measure)	-1.8	-2.0	-1.9
Mean reduction in CAS from baseline, patients CAS>0 at baseline*	-2.8	-2.0	-2.3

**2 patients from the VRDN-001 10 mg/kg cohort with CAS of 0 at baseline excluded from calculation.*

Diplopia:

- Five out of the twelve VRDN-001 treated patients across both dose cohorts had diplopia (double vision) at baseline. None of the patients treated with VRDN-001 achieved complete resolution of diplopia at week 6, defined as patients with baseline diplopia who achieved a score of 0 on the Gorman subjective diplopia scale.

"We continue to be enthusiastic over the clinical trial data we're compiling on VRDN-001," said Barrett Katz, M.D., M.B.A., Chief Medical Officer at Viridian. "As shown previously in our proof-of-concept study in patients with active TED, and now in those with chronic disease, VRDN-001 appears to be generally well tolerated and shows clinically meaningful changes, making it a promising lead candidate in our mission to develop therapies to improve the lives of those with TED."

THRIVE Phase 3 trials in TED

Following recent discussions with the US Food and Drug Administration (FDA) regarding Viridian's proposal to amend the THRIVE Phase 3 trial design, THRIVE will now include the VRDN-001 5-dose treatment regimen and placebo arms only. The trial design amendment reflects Viridian's confidence in the 5-dose treatment regimen of VRDN-001 and takes into consideration key stakeholder feedback from the TED community expressing preference for a shortened treatment regimen compared to an 8-dose treatment regimen.

The primary efficacy endpoint for THRIVE, proptosis responder rate, will be evaluated at week 15. The Company expects to announce topline results from the THRIVE Phase 3 trial in the middle of 2024.

Viridian plans to initiate the THRIVE-2 Phase 3 trial to evaluate the safety and efficacy of VRDN-001 in patients with chronic TED in the third quarter of 2023. The Company expects to announce topline results from the THRIVE-2 trial by year-end 2024.

Subcutaneous (SC) programs in TED

Viridian believes that data from the 3 mg/kg dose cohorts of VRDN-001 in patients with active or chronic TED validate a low-volume, SC product profile for the Company's three SC candidates. The Company's recent progress and upcoming priorities for its SC programs, include:

- Completed the SC formulation work for all three SC programs, allowing for a concentration of 150 mg/mL for administration of a 300 mg/2 mL dose in its SC clinical trials.
- Filed an investigational new drug (IND) application for VRDN-003 and an IND amendment for VRDN-001 SC with the FDA in June 2023. Following clearance of the submissions, Viridian plans to initiate Phase 1 trials of VRDN-003 and VRDN-001 SC in healthy volunteers in the third quarter of 2023, with initial data expected in the fourth quarter of 2023.
- Completed enrollment of the Phase 1 healthy volunteer trial of VRDN-002 single IV and single SC dose cohorts.
- Initiation of a pen device supply agreement with an experienced drug delivery device manufacturer in the second half of 2023.

Viridian expects to select its lead subcutaneous program by year-end 2023 and to advance the program into a pivotal Phase 2/3 trial in the middle of 2024.

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

Conference call and webcast information

The Company will host a conference call today at 5:00 p.m. ET to discuss the topline data and program updates in TED. The dial-in number for the conference call is 1-888-330-3622 for domestic participants and 1-646-960-0662 for international participants. The conference ID is 3961606.

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'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 Phase 2 portion of the ongoing trial established clinical proof-of-concept for VRDN-001 in patients with active and chronic TED. VRDN-001 was generally well tolerated in the trial.

The THRIVE Phase 3 trial in patients with active TED is ongoing. The Company is currently planning to start its second Phase 3 trial, called THRIVE-2, in patients with chronic TED.

The Company is also advancing three candidates (VRDN-001 SC, VRDN-002, and VRDN-003) designed for administration as convenient, low-volume, SC injection for the treatment of TED.

Viridian's goal is to bring a best-in-class IV therapy followed by a first- and best-in-class SC therapy to the market for the treatment of the TED.

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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. In addition to its intravenously administered VRDN-001 program, the Company is advancing three 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 in patients with chronic Thyroid Eye Disease 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; the Company's ability to develop an SC formulation; the Company's plans regarding a lead SC program candidate 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; and potential addressable market size,, including those risks set forth under the caption "Risk Factors" in the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 10, 2023 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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