UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d) of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **May 22, 2023**

DIAMEDICA THERAPEUTICS INC.

(Exact name of registrant as specified in its charter)

British Columbia	**001-36291**	**Not Applicable**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

301 Carlson Parkway, Suite 210 **Minneapolis, Minnesota** (Address of principal executive offices)	**55305** (Zip Code)

(763) 312-6755
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:
☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Voting common shares, no par value per share	DMAC	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 7.01 Regulation FD Disclosure.

On May 22, 2023, DiaMedica Therapeutics Inc. (the "Company") announced that the Company filed on May 19, 2023 a complete clinical hold response with the U.S. Food and Drug Administration (the "FDA") requesting that the clinical hold imposed on the Company's pivotal Phase 2/3 clinical trial of DM199 for acute ischemic stroke ("AIS"), or ReMEDy2 study, be lifted. Included in the response is a protocol amendment designed to incorporate a reduced dose for the intravenous administration of DM199 and incorporate certain additional measures to reduce the risk of severe hypotension in study participants.

Also, on May 22, 2023, the Company made available an investor presentation regarding the status of the ReMEDy2 study that the Company intends to use in connection with presentations at conferences and meetings (the "Investor Presentation"). The Investor Presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K, and the information set forth therein is incorporated herein by reference and constitutes a part of this Item 7.01. Representatives of the Company intend to make presentations at investor conferences and in other forums and these presentations may include the information contained in the Investor Presentation. The Company intends to disclose the information contained in the Investor Presentation, in whole or in part, and with updates and possibly modifications, in connection with presentations to investors, analysts and others and on its corporate website.

The information contained in Item 7.01 of this report and Exhibit 99.1 to this report shall not be deemed to be "filed" with the United States Securities and Exchange Commission for purposes of Section 18 of the United States Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, and shall not be deemed incorporated by reference into any filings made by the Company under the Securities Act of 1933, as amended, or the Exchange Act, except as may be expressly set forth by specific reference in such filing.

The information contained in this Current Report on Form 8-K and the exhibit hereto is summary information that is intended to be considered in the context of the Company's United States Securities and Exchange Commission (the "SEC") filings and other public announcements that the Company may make, by press release or otherwise, from time to time. The Company undertakes no duty or obligation to publicly update or revise the information contained in this report and the exhibit hereto, although it may do so from time to time as its management believes is warranted. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases or through other public disclosure. By filing this report and furnishing this information, the Company makes no admission as to the materiality of any information contained in this report, including the exhibit hereto.

Item 8.01 Other Events.

As described under Item 7.01 above, on May 19, 2023, the Company filed a complete clinical hold response with the U.S. Food and Drug Administration (the "FDA") requesting that the clinical hold imposed on the Company's pivotal Phase 2/3 clinical trial of DM199 for acute ischemic stroke ("AIS"), or ReMEDy2 study, be lifted. Included in the response is a protocol amendment designed to incorporate a reduced dose for the intravenous administration of DM199 and incorporate certain additional measures to reduce the risk of severe hypotension in study participants.

Item 9.01 Financial Statements and Exhibits.

(d) *Exhibits*.

Exhibit No.	Description
99.1	Investor Presentation issued by DiaMedica Therapeutics, Inc. in connection with the filing of a complete clinical hold response with the FDA regarding ReMEDy2 trial for acute ischemic stroke (furnished herewith)
104	The Cover Page from this Current Report on Form 8-K, Formatted in Inline XBRL

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

DIAMEDICA THERAPEUTICS INC.

By: /s/ Scott Kellen
Scott Kellen
Chief Financial Officer and Secretary

Date: May 22, 2023

ReMEDy2 Update

May 22, 2023

Cautionary Note Regarding Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and forward-looking information that are based on the beliefs of management and reflect management's current expectations. When used in this presentation, the words "estimate," "believe," "anticipate," "intend," "expect," "plan," "continue," "potential," "will," "may" or "should," the negative of these words or such variations thereon or comparable terminology and the use of future dates are intended to identify forward-looking statements and information.

The forward-looking reflect management's current plans, objectives, estimates, expectations and intentions, involve assumptions that may never materialize of may prove to be incorrect and inherently involve significant risks and uncertainties, including factors beyond DiaMedica's control that could cause actual results, performance or achievements, or other future events, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Applicable risks and uncertainties include, among others, the risk that the Company may not know the cause of the hypotension events or that its plan to resolve the issues and prevent future events may not be successful; the risk that the Company may not be able to address successfully the concerns identified in the clinical hold letter or may require the Company to collect additional data or information beyond what it has submitted to the FDA; the risk that the Company may not be able to lift the clinical hold or do so in a timely manner; uncertainties relating to regulatory applications and related filing and approval timelines, including the risk that FDA may not remove the clinical hold on the ReMEDy2 trial; the possibility of additional future adverse events associated with or unfavorable results from the ReMEDy2 trial; the risk that existing preclinical and clinical data may not be predictive of the results of ongoing or later clinical trials; DiaMedica's plans to develop, obtain regulatory approval for and commercialize its DM199 product candidate for the treatment of acute ischemic stroke (AIS) or chronic kidney disease (CKD) and its expectations regarding the benefits of DM199; DiaMedica's ability to conduct successful clinical testing of DM199 and within its anticipated parameters, enrollment numbers, costs and timeframes; the adaptive design of the ReMEDy2 trial and the possibility that the targeted enrollment and other aspects of the trial could change depending upon certain factors, including additional input from the FDA and the blinded interim analysis; the potential direct or indirect impact of COVID-19, hospital and medical facility staffing shortages, and worldwide global supply chain shortages on DiaMedica's business and clinical trials, including its ability to meet its site activation and enrollment goals; DiaMedica's reliance on collaboration with third parties to conduct clinical trials; DiaMedica's ability to continue to obtain funding for its operations, including funding necessary to complete planned clinical trials and obtain regulatory approvals for DM199 for AIS or CKD, and the risks identified under the heading "Risk Factors" in DiaMedica's annual report on Form 10-K for the fiscal year ended December 31, 2022, quarterly report on Form 10-Q for the quarter ended March 31, 2023 and subsequent U.S. Securities and Exchange Commission filings.

Other risk and uncertainties of which DiaMedica is not currently aware may also affect the Company's forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. All forward-looking statements contained in this presentation speak only as of the date on which they were made and are based on management's assumptions and estimates as of such date. DiaMedica undertakes no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

Background

- **Human urinary-derived kallikrein (HUK) is approved to treat acute ischemic stroke (AIS) in China; ~600,000 patients treated in 2022**
  - HUK is administered daily by intravenous (IV) infusion over three weeks
    - ~1.5-hour drug half-life with IV dosing results in substantial daily pharmacokinetics (PK) fluctuations
  - HUK not available in subcutaneous (SC) form; we believe this is due to residual citric acid and excipients required for urine extraction of the protein which prevents bolus injection (severe injection pain)
- **DM199 IV dosing regimen was informed by the PK profile of HUK and further optimized by DM199's ability to be dosed SC**
  - Dose 1: IV dose of DM199 closely matches the PK curve of HUK and allows for rapid DM199 administration in AIS
  - Doses 2 – 8 (over 3 weeks): SC doses of DM199 every three days more consistently maintain PK near DM199 peak concentration (Cmax)
- **DiaMedica dosed 46 patients with DM199 in its ReMEDy1 Phase 2 AIS trial based on this regimen; no hypotensive events observed**
  - 10 of the 46 patients were on ACE inhibitors (ACEi) with the last dose received either the day before or, for one subject, the same day as receiving the IV dose of DM199. No significant blood pressure decrease was seen in any of these 10 AIS patients.
- **Three unexpected severe hypotensive events occurred in the ReMEDy2 Phase 2/3 trial causing DiaMedica to halt enrollment and unblind the three patients**
  - All three patients had received DM199 and were on ACEi prior to enrollment
    - Note one received first-time administration of ACEi prior to enrollment
  - Decreases in blood pressure were transient and resolved within a few minutes after IV infusion halted
  - After reporting to the FDA, the ReMEDy2 trial placed on clinical hold
- **After a thorough investigation DiaMedica identified that the change in IV bag from polyolefin, used in the ReMEDy1 trial, to PVC bags, used in the ReMEDy2 trial, was the primary cause of the hypotensive events**

Overview of Testing and Analytical Procedures

Phase 1C Trial Corroborates Safety & Tolerability - No Hypotensive Events at 0.5 µg/kg Dose Level

- Based upon a variety of interactions with the FDA, the following testing and analytical procedures were performed to support our hypothesis that the cause of the hypotensive events was due to a change in IV bag materials
- All testing was conducted at independent, third-party laboratories and a contract research organization

	Overview of Procedures	Results
IV Bag Study	▪ Tested drug concentration levels remaining upon discharge from IV bag ▪ Comparison testing of polyolefin and PVC bag materials	Up to ~50% drug sticking to polyolefin bag (ReMEDy1) and no drug sticking to PVC bag (ReMEDy2)
In-Use Study: Part 1	▪ Tested drug concentration levels using complete system (bag, tubes, pump…) ▪ Comparison testing of polyolefin and PVC bag materials	Up to ~50% drug sticking to polyolefin bag (ReMEDy1) and no drug sticking to PVC bag (ReMEDy2)
In-Use Study: Part 2	▪ Evaluated worst case scenarios such as varying storage durations, temperature and light exposure	No special handling instructions required for the IV administration
Phase 1C SAD Study*	▪ Single ascending dose study of DM199 in health volunteers with PVC IV bags; 3 patients per dose (0.1, 0.25 and 0.5 µg/kg); objective was safety and to identify dose with similar KLK1 exposure of polyolefin bags (ReMEDy1)	No SAEs or hypotensive events, 0.5 µg/kg dose closely matched PK profile of 1.0 µg/kg dose used in ReMEDy1 trial (see slide 4)

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*not requested or required by FDA

DM199 Phase 1C Trial

0.5 µg/kg PVC Bag Well Tolerated With Similar Drug Exposure Levels to 1.0 µg/kg non-PVC Bag

IV Dose well tolerated in Recent Phase 1C study

PVC Materials @ 0.5 µg/kg (N=3)

	C_{max} (ng/mL)	AUC_{0-24} (h*ng/mL)
Mean	2.287	**11.081**

DM199 IV dosing in PVC bag (50 ml) dose of 0.5 µg/kg (N=3); 15 minute slow infusion followed by 35 minutes at the full infusion rate (50 minutes total).*

IV Dose well tolerated with efficacy signal in ReMEDy1

Non-PVC Materials (Polyolefin) @ 1.0 µg/kg (N=3)

	C_{max} (ng/mL)	AUC_{0-24} (h*ng/mL)
Mean	4.197	**13.340**

DM199 dosing in Polyolefin IV bag (50 ml) dose of 1 µg/kg (N=3) over 30 minutes).[1]

* Phase 1C initiated IV dose with 15 minute slow/reduced infusion rate to evaluate patient response. Slowing initial infusion rate reduces maximum blood concentration (Cmax) but does not significantly affect total exposure (AUC).

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1. Int J Clin Trials. 2017Nov;4(4):139-146

ReMedy2 Status

- **On May 19, 2023, DiaMedica submitted its complete response to the FDA, including:**
  - Description/analysis of the cause of the hypotensive events
    - Unintentional overdose caused by change from non-PVC to PVC IV bag such that downward dose adjustment should mitigate against severe hypotension risk going forward
  - Supporting data from in-use stability studies
    - Confirmed adsorption of DM199 by non-PVC materials resulted in less DM199 being administered then with PVC materials
  - Data from Phase 1C SAD study justifying the safety of the proposed 0.5 µg/kg IV dose
    - Similar PK profile to the previous IV dose (ReMEDy2) suggests toleration and potential for therapeutic efficacy
- **Response also included an updated protocol with the following modifications:**
  - Reduced IV dose from 1.0 µg/kg to 0.5 µg/kg, with continued use of PVC materials for IV administration
  - 24-hour wash-out period for patients on ACEi (approximately 2 to 4 half-lives depending on which ACEi is used)
  - IV administration initiated with 15-minute slow infusion rate for all patients to monitor for potential blood pressure irregularities
  - Ability to continue slow infusion rate over extended time period (up to 3 hours) if the physician observes blood pressure irregularities
  - Cap the maximum IV dose at 50 µg DM199