November 14, 2023

Trevena Reports Third Quarter 2023 Results and Provides Business Update

Company previously announced statistically significant topline TRV045 data from two proof-of-concept studies evaluating S1PR mechanism of action and CNS target engagement

Company reported favorable safety and tolerability data from TRV045 POC studies

Three abstracts for OLINVYK presented at American Society of Anesthesiologists (ASA) Conference

$15 million tranche from ex-US royalty-based financing agreement received in September

Company to host conference call today, November 14, 2023 at 8:00 a.m. ET

CHESTERBROOK, Pa., Nov. 14, 2023 (GLOBE NEWSWIRE) -- Trevena, Inc. (Nasdaq: TRVN), a biopharmaceutical company focused on the development and commercialization of novel medicines for patients with central nervous system (CNS) disorders, today reported its financial results for the third quarter ended September 30, 2023 and provided an overview of its recent operational highlights.

“The third quarter was exciting for Trevena as we reported promising proof-of-concept data for our two TRV045 studies, including favorable safety and tolerability topline data, and strengthened our balance sheet with the receipt of the $15 million dollar R-Bridge tranche,” said Carrie Bourdow, President and CEO of Trevena. “There is a significant need for safe and effective non-opioid therapies in pain, and for novel mechanisms for the treatment of epilepsy. By the end of the year we anticipate receipt of topline data for TRV045 from the NIH nonclinical seizure prevention study, and we look forward to updating you on the next steps of our plan to advance TRV045, on our own or with a strategic partner, for potential treatment of neuropathic pain, epilepsy and other CNS disorders.”

Third Quarter 2023 and Recent Corporate Highlights

- **TRV045 demonstrates CNS target engagement and encouraging overall results in two proof-of-concept studies.** TRV045 is a novel S1P modulator selective for the S1P receptor subtype 1. The Company previously announced preliminary topline data from two Phase 1 proof-of-concept studies evaluating S1PR mechanism of action and CNS target engagement. Data from both studies demonstrated CNS penetration and target engagement, as well as plasma exposures in the anticipated active dose range, supporting the therapeutic potential of TRV045. In a validated capsaicin-induced neuropathic pain model, TRV045 showed a statistically significant, dose-dependent treatment effect. In the transcranial magnetic stimulation (TMS) proof-of-concept study, TRV045 demonstrated statistically significant changes in the power spectral density in several EEG bands associated with alertness and higher order cognitive function.

In these studies, TRV045 showed an overall favorable safety and tolerability profile with no drug-related adverse events, no serious adverse events and no study drug-related discontinuations reported. The Company is encouraged by the totality of the data from the POC studies and expects to be in a position in the near future to announce next steps in the clinical development program for TRV045.

Subjects in both studies were enrolled outside of the United States, and the studies were not conducted under the Investigational New Drug Application for TRV045.

- **Three OLINVYK abstracts presented at ASA .**The Company announced the completion of the initial analysis of respiratory data from the 200 patient VOLITION study that was generated at Cleveland Clinic and Wake Forest Baptist Health. The results were presented at the recent ASA meeting. The VOLITION study, a real-world, open-label, multi-site study, assessed the potential impact of OLINVYK on respiratory, gastrointestinal (GI), and cognitive function outcomes in the postoperative setting. In addition, data from the ARTEMIS study, an EMR-based outcomes analysis was presented that demonstrated 1.4 hospital days saved when using OLINVYK. Finally, an invited, oral presentation of the cognitive function study results was presented.

- **Company receives $15 million tranche from ex-US royalty-based financing.**The Company previously announced receipt of a $15 million tranche under its non-dilutive ex-US royalty-based financing (the R-Bridge Financing). This tranche of funding was triggered by the first commercial sale of OLINVYK in China by Jiangsu Nhwa, the Company's licensee in China. As previously announced, OLINVYK has been approved in China for use in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate. As part of the R-Bridge Financing, Trevena may receive an additional $10 million upon achievement of either a commercial or financing milestone.

Financial Results for Third Quarter 2023
For the third quarter of 2023, the Company reported a net loss attributable to common stockholders of $7.9 million, or $0.57 per share, compared to $15.3 million, or $2.24 per share in the third quarter of 2022.

Cash and cash equivalents were $35.0 million as of September 30, 2023, which the Company believes will be sufficient to fund the Company's operating expenses and capital expenditure requirements into the third quarter of 2024.

Conference Call and Webcast Information

The Company will host a conference call and webcast with the investment community on November 14, 2023, at 8:00 a.m. Eastern Time featuring remarks by Carrie Bourdow, President and Chief Executive Officer, Patricia Drake, Chief Commercial Officer, Pattie Drake, Senior Vice President and Chief Commercial Officer, Mark Demitrack, M.D., Senior Vice President and Chief Medical Officer, and Barry Shin, Chief Financial Officer. In addition, Dan Clauw, M.D., Professor of Anesthesiology, Medicine (Rheumatology) and Psychiatry at the University of Michigan and Director of the Chronic Pain and Fatigue Research Center will join the call as well.

Title:	Trevena Third Quarter 2023 Financial Results Conference Call & Webcast
Date:	Tuesday, November 14, 2023
Time:	8:00 a.m. ET
Conference Call Details:	Toll-Free: 1-877-704-4453 International: 1-201-389-0920 Conference ID: 13741466

The conference call will be webcast live from the Company's website and will be available via the following links:

Webcast: https://viavid.webcasts.com/starthere.jsp?ei=1636100&tp_key=5e8700c550

The webcast should be accessed 15 minutes prior to the conference call start time. A replay of the webcast will be available following the conclusion of the live broadcast and will be accessible on the Company's website.

About OLINVYK® (oliceridine) injection

OLINVYK is a new chemical entity approved by the FDA in August 2020. OLINVYK contains oliceridine, an opioid, which is a Schedule II controlled substance with a high potential for abuse similar to other opioids. It is indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate. OLINVYK is available in 1 mg/1 mL and 2 mg/2 mL single-dose vials, and a 30 mg/30 mL single-patient-use vial for patient-controlled analgesia (PCA). Approved PCA doses are 0.35 mg and 0.5 mg and doses greater than 3 mg should not be administered. The cumulative daily dose should not exceed 27 mg. Please see Important Safety Information, including the BOXED WARNING, and full prescribing information at www.OLINVYK.com.

IMPORTANT SAFETY INFORMATION

WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; NEONATAL OPIOID WITHDRAWAL SYNDROME; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CENTRAL NERVOUS SYSTEM (CNS) DEPRESSANTS

ADDICTION, ABUSE, AND MISUSE – OLINVYK exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk before prescribing OLINVYK, and monitor all patients regularly for the development of behaviors or conditions.

LIFE-THREATENING RESPIRATORY DEPRESSION – Serious, life-threatening, or fatal respiratory depression may occur with use of OLINVYK. Monitor for respiratory depression, especially during initiation of OLINVYK or following a dose increase.

NEONATAL OPIOID WITHDRAWAL SYNDROME – Prolonged use of OLINVYK during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed

by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

RISK FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS – Concomitant use of opioids with benzodiazepines or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation.

INDICATIONS AND USAGE

OLINVYK is an opioid agonist indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate.

Limitations of Use

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve OLINVYK for use in patients for whom alternative treatment options [e.g., non-opioid analgesics or opioid combination products]:

- Have not been tolerated, or are not expected to be tolerated
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

The cumulative total daily dose should not exceed 27 mg, as total daily doses greater than 27 mg may increase the risk for QTc interval prolongation.

CONTRAINDICATIONS

OLINVYK is contraindicated in patients with:

- Significant respiratory depression
- Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment
- Known or suspected gastrointestinal obstruction, including paralytic ileus
- Known hypersensitivity to oliceridine (e.g., anaphylaxis)

WARNINGS AND PRECAUTIONS

- OLINVYK contains oliceridine, a Schedule II controlled substance, that exposes users to the risks of addiction, abuse, and misuse. Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed OLINVYK. Assess risk, counsel, and monitor all patients receiving opioids.
- Serious, life-threatening respiratory depression has been reported with the use of opioids, even when used as recommended, especially in patients with chronic pulmonary disease, or in elderly, cachectic and debilitated patients. The risk is greatest during initiation of OLINVYK therapy, following a dose increase, or when used with other drugs that depress respiration. Proper dosing of OLINVYK is essential, especially

when converting patients from another opioid product to avoid overdose. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status.

- Opioids can cause sleep-related breathing disorders including central sleep apnea (CSA) and sleep-related hypoxemia with risk increasing in a dose-dependent fashion. In patients who present with CSA, consider decreasing the dose of opioid using best practices for opioid taper.
- Prolonged use of opioids during pregnancy can result in withdrawal in the neonate that may be life-threatening. Observe newborns for signs of neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using OLINVYK for a prolonged period of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.
- Profound sedation, respiratory depression, coma, and death may result from the concomitant use of OLINVYK with benzodiazepines or other CNS depressants (e.g., non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, or alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate, prescribe the lowest effective dose, and minimize the duration.
- OLINVYK was shown to have mild QTc interval prolongation in thorough QT studies where patients were dosed up to 27 mg. Total cumulative daily doses exceeding 27 mg per day were not studied and may increase the risk for QTc interval prolongation. Therefore, the cumulative total daily dose of OLINVYK should not exceed 27 mg.
- Increased plasma concentrations of OLINVYK may occur in patients with decreased Cytochrome P450 (CYP) 2D6 function or normal metabolizers taking moderate or strong CYP2D6 inhibitors; also in patients taking a moderate or strong CYP3A4 inhibitor, in patients with decreased CYP2D6 function who are also receiving a moderate or strong CYP3A4 inhibitor, or with discontinuation of a CYP3A4 inducer. These patients may require less frequent dosing and should be closely monitored for respiratory depression and sedation at frequent intervals. Concomitant use of OLINVYK with CYP3A4 inducers or discontinuation of a moderate or strong CYP3A4 inhibitor can lower the expected concentration, which may decrease efficacy, and may require supplemental doses.
- Cases of adrenal insufficiency have been reported with opioid use (usually greater than one month). Presentation and symptoms may be nonspecific and include nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If confirmed, treat with physiologic replacement doses of corticosteroids and wean patient from the opioid.
- OLINVYK may cause severe hypotension, including orthostatic hypotension and syncope in ambulatory patients. There is increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (e.g., phenothiazines or general anesthetics). Monitor these patients for signs of hypotension. In patients with circulatory shock, avoid the use of OLINVYK as it may cause vasodilation that can further reduce cardiac output and blood pressure.
- Avoid the use of OLINVYK in patients with impaired consciousness or coma. OLINVYK should be used with caution in patients who may be susceptible to the intracranial effects of CO_2 retention, such as those with evidence of increased intracranial pressure or brain tumors, as a reduction in respiratory drive and the resultant

CO_2 retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy.
- As with all opioids, OLINVYK may cause spasm of the sphincter of Oddi, and may cause increases in serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis, for worsening symptoms.
- OLINVYK may increase the frequency of seizures in patients with seizure disorders and may increase the risk of seizures in vulnerable patients. Monitor patients with a history of seizure disorders for worsened seizure control.
- Do not abruptly discontinue OLINVYK in a patient physically dependent on opioids. Gradually taper the dosage to avoid a withdrawal syndrome and return of pain. Avoid the use of mixed agonist/antagonist (e.g., pentazocine, nalbuphine, and butorphanol) or partial agonist (e.g., buprenorphine) analgesics in patients who are receiving OLINVYK, as they may reduce the analgesic effect and/or precipitate withdrawal symptoms.
- OLINVYK may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery.
- Although self-administration of opioids by patient-controlled analgesia (PCA) may allow each patient to individually titrate to an acceptable level of analgesia, PCA administration has resulted in adverse outcomes and episodes of respiratory depression. Health care providers and family members monitoring patients receiving PCA analgesia should be instructed in the need for appropriate monitoring for excessive sedation, respiratory depression, or other adverse effects of opioid medications.

ADVERSE REACTIONS

Adverse reactions are described in greater detail in the Prescribing Information.

The most common (incidence ≥10%) adverse reactions in Phase 3 controlled clinical trials were nausea, vomiting, dizziness, headache, constipation, pruritus, and hypoxia.

MEDICAL INFORMATION

For medical inquiries or to report an adverse event, other safety-related information or product complaints for a company product, please contact the Trevena Medical Information Contact Center at **1-844-465-4686** or email **MedInfo@Trevena.com**.

You are encouraged to report suspected adverse events of prescription drugs to the FDA. Visit **www.fda.gov/medwatch** or call **1-800-FDA-1088**.

Please see Full Prescribing Information, including Boxed Warning.

About TRV045

TRV045 is a novel, selective sphingosine-1-phosphate subtype 1 ($S1P_1$) receptor modulator being developed as a potential treatment for acute and chronic neuropathic pain secondary to diabetic peripheral neuropathy. Through a collaboration with the National Institutes of Health, Trevena is also exploring TRV045 as a potential treatment for epilepsy.

S1P receptors are located throughout the body, including the central nervous system, where

they are believed to play a role in modulating neurotransmission and membrane excitability.

Trevena's discovery efforts have identified a family of compounds that are highly selective for the $S1P_1$ receptor. TRV045 reversed thermal hyperalgesia, a measure of neuropathic pain, in nonclinical models of diabetic peripheral neuropathy and chemotherapy-induced peripheral neuropathy. TRV045 was not associated with lymphopenia and produced no changes in blood pressure, heart rate, or respiratory function at or above pharmacologically active doses in nonclinical studies. TRV045 is an investigational product and is not yet approved by the FDA.

About Trevena

Trevena, Inc. is a biopharmaceutical company focused on the development and commercialization of innovative medicines for patients with CNS disorders. The Company has one approved product in the United States, OLINVYK® (oliceridine) injection, indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate. The Company's novel pipeline is based on Nobel Prize winning research and includes three differentiated investigational drug candidates: TRV045 for diabetic neuropathic pain and epilepsy, TRV250 for the acute treatment of migraine and TRV734 for maintenance treatment of opioid use disorder.

For more information, please visit www.Trevena.com

About Jiangsu Nhwa:

Jiangsu Nhwa Pharmaceutical Co., Ltd. (SZ002262), founded in 1978, is a leading CNS company in China. Over the past 40 years, Nhwa is exclusively dedicated to developing innovative and differentiated pipeline in the areas of anesthesia, analgesia, psychiatry and neurology via in-house R&D and global partnership.

As a fully integrated pharmaceutical company with more than 4000 employees, Nhwa has comprehensive capabilities in research, clinical development, manufacturing and commercialization of CNS drugs. In recent years, Nhwa has further strengthened its leadership in CNS field in China by providing the services of precision diagnosis of CNS disorders (Shanghai N-yuen Biotechnology Company), and investing the largest Chinese CNS internet health platform (Happy Mood).

About R-Bridge (CBC Group)

CBC Group is Asia's largest and most active healthcare-dedicated investment firm with over US$5 billion AUM, focused on platform-building, buyout opportunities, and alternative financing across three core areas: pharmaceutical & biotech, medtech, and healthcare services. CBC has a leading team of investment, industry and portfolio management professionals, headquartered in Singapore with offices in New York, Shanghai, Beijing, and Hong Kong and presence in Boston, San Diego, San Francisco and Tokyo.

Founded in February 2020, R-Bridge Healthcare Fund is an affiliate of CBC Group and it is dedicated in providing alternative, non-dilutive financing backed by royalties, revenue interest and other cash flows generated by the sale of healthcare products and services in China,

the first of its kind for the asset class and the region. R-Bridge provides additional sources of capital to leading healthcare companies to continue their extraordinary growth trajectories, commercializing their products and services in China and on a global scale.

Forward-Looking Statements

Any statements in this press release about future expectations, plans and prospects for the Company, including statements about the Company's strategy, future operations, clinical development and trials of its therapeutic candidates, plans for potential future product candidates and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "suggest," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the status, timing, costs, results and interpretation of the Company's clinical trials or any future trials of any of the Company's investigational drug candidates; the uncertainties inherent in conducting clinical trials; expectations for regulatory interactions, submissions and approvals, including the Company's assessment of discussions with FDA; available funding; uncertainties related to the Company's intellectual property; other matters that could affect the availability or commercial potential of the Company's therapeutic candidates and approved product; and other factors discussed in the Risk Factors set forth in the Company's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q filed with the Securities and Exchange Commission (SEC) and in other filings the Company makes with the SEC from time to time. In addition, the forward-looking statements included in this press release represent the Company's views only as of the date hereof. The Company anticipates that subsequent events and developments may cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so, except as may be required by law.

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TREVENA, INC.

Condensed Statements of Operations

(Unaudited, in thousands except share and per share data)

	Three Months Ended Sept 30,		Nine Months Ended Sept 30,	
	2023	**2022**	**2023**	**2022**
Product revenue	$ 1	$ (438)	$ 28	$ (438)
License and royalty revenue	179	-	3,179	20
Total revenue	180	(438)	3,207	(418)
Operating expenses:				
Cost of goods sold	175	2,368	389	2,791
Selling, general and administrative	4,572	7,683	15,799	29,003
Research and development	4,260	5,266	12,160	14,816
Total operating expenses	9,007	15,317	28,348	46,610
Loss from operations	(8,827)	(15,755)	(25,141)	(47,028)
Other income	897	460	1,380	363
Net loss	$ (7,930)	$ (15,295)	$ (23,761)	$ (46,665)
Per share information:				
Net loss per share of common stock, basic and diluted	($ 0.57)	($ 2.24)	($ 2.03)	($ 6.97)
Weighted average shares outstanding, basic and diluted	13,964,301	6,829,013	11,728,842	6,691,061

TREVENA, INC.

Condensed Balance Sheets

(Unaudited, in thousands)

	September 30, 2023	**December 31, 2022**
Assets		
Current assets:		
Cash and cash equivalents	$ 34,952	$ 38,320
Accounts receivable, net	179	-
Inventories	900	906
Prepaid expenses and other current assets	3,447	1,782

Total current assets	39,478	41,008
Restricted cash	540	1,960
Property and equipment, net	1,259	1,488
Right-of-use lease assets	3,813	4,224
Other assets	43	-
Total assets	$ 45,133	$ 48,680
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable, net	$ 1,545	$ 2,372
Accrued expenses and other current liabilities	3,629	5,461
Current portion of lease liabilities	982	899
Total current liabilities	6,156	8,732
Loans payable, net	29,642	13,430
Leases, net of current portion	4,689	5,436
Warrant liability	1,097	5,483
Total liabilities	41,584	33,081
Common stock	15	8
Additional paid-in capital	575,067	563,362
Accumulated deficit	(571,533)	(547,772)
Accumulated other comprehensive income (loss)	-	1
Total stockholders' equity	3,549	15,599
Total liabilities and stockholders' equity	$ 45,133	$ 48,680

Source: Trevena, Inc.