May 15, 2023

Trevena Reports First Quarter 2023 Results and Provides Business Update

OLINVYK receives regulatory approval in China, triggering $3 million milestone payment from Company's China partner Jiangsu Nhwa Pharmaceutical

Company expects to receive additional $15 million non-dilutive tranche from R-Bridge upon first commercial sale of OLINVYK in China

TRV045 topline data expected in 3Q 2023 for two proof-of-concept studies supporting continued development for potential use in epilepsy and chronic pain

Previously announced initial topline OLINVYK data demonstrated a statistically significant 1.6-day (~27%) reduction in average overall hospital length of stay compared to matched patients treated with other IV opioids, based on initial EMR analysis of patients at Wake Forest Baptist Health

Company continues to expect new OLINVYK respiratory data and additional health utilization and cost analyses from ~200 patient real-world clinical outcomes study in mid-2023

Company to host conference call today, May 15, 2023 at 8:00 a.m. ET

CHESTERBROOK, Pa., May 15, 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 first quarter ended March 31, 2023, and provided an overview of its recent operational highlights.

"This is an important year for Trevena as we expect topline data from two TRV045 proof-of-concept studies, one to support potential use in epilepsy and the other in chronic pain, and new OLINVYK respiratory data from the VOLITION study with Cleveland Clinic," said Carrie Bourdow, President and CEO of Trevena. "We were also pleased that Jiangsu Nhwa recently received approval of OLINVYK in China which will allow patients there to have access to this innovative therapeutic option".

First Quarter 2023 and Recent Corporate Highlights

- **OLINVYK receives Chinese regulatory approval; milestone and expected near-term commercialization provides up to $18 million of non-dilutive funding for Trevena.** Jiangsu Nhwa Pharmaceutical (Nhwa) recently announced regulatory approval of OLINVYK from the National Medical Products Administration (NMPA) of China. Based on this approval, the Company is eligible to receive a $3 million milestone payment from Nhwa (the Nhwa Milestone) and upon first commercial sale by Nhwa, which Nhwa expects in 3Q 2023, the Company may receive an additional $15

million non-dilutive funding tranche through its ex-US royalty-based financing with R-Bridge Healthcare Fund (the R-Bridge Financing).

- **TRV045 topline data expected in 3Q for two proof-of-concept studies, one supporting continued development for potential use in epilepsy and the other in chronic pain.** TRV045 is a novel S1P modulator selective for the S1P receptor subtype 1. The TRV045 Target Engagement Study and the Transcranial Magnetic Stimulation Study are each enrolling subjects, with enrollment completion expected by mid-2023. The studies will help inform the Company's future development path for TRV045, which has shown promising anti-inflammatory data in nonclinical models suggesting a potential disease-modifying role in CNS disorders. Subjects are being enrolled at study sites outside of the United States. The studies are not being conducted under the Investigational New Drug Application (IND) for TRV045.

- **Recent Electronic Medical Records (EMR) data from the ARTEMIS study provides additional clinical support for the use of OLINVYK.** The Company recently announced OLINVYK initial topline EMR data and has incorporated these data in its medical information resources. The data includes the statistically significant 1.6-day (~27%) reduction in average hospital length of stay vs matched patients treated with other IV opioids in ARTEMIS patients at Wake Forest Baptist Health. There was no statistically significant difference in the average duration of time in the PACU in this study. While an EMR analysis does not provide definitive data regarding group differences, as seen in a prospectively randomized study, the Company believes the EMR data bring a unique perspective to understanding how drugs may perform in the real world.

- **Respiratory data from real-world VOLITION study anticipated mid-2023.** In March 2023, the Company reported initial top-line data from the VOLITION study, a 203 patient, real-world, open-label, multi-site study led by clinical outcomes research experts from Cleveland Clinic and Wake Forest Baptist Medical Center. The data from the study demonstrated over 50% GI complete response rate (defined as a patient who did not vomit and did not require the use of antiemetics throughout the post-operative period) and less than 4% incidence of symptoms suggestive of delirium in patients treated with OLINVYK. The Company expects to report respiratory data from this study, assessed by continuous respiratory monitoring, in mid-2023. Additional health utilization data and cost analyses are also expected in mid-2023.

Financial Results for First Quarter 2023

For the first quarter of 2023, the Company reported a net loss attributable to common stockholders of $7.8 million, or $0.81 per share, compared to $16.4 million, or $2.48 per share in the first quarter of 2022.

Cash, cash equivalents and marketable securities were $27.4 million as of March 31, 2023, which the Company believes will be sufficient to fund the Company's operations through year-end 2023. Together with the expected $3 million Nhwa Milestone payment and $15 million available under the R-Bridge Financing upon Nhwa's first commercial sale of OLINVYK in China, the Company believes this will be sufficient to fund operations to mid-2024.

Conference Call and Webcast Information

The Company will host a conference call and webcast with the investment community on May 15, 2023, at 8:00 a.m. Eastern Time featuring remarks by Carrie Bourdow, President and Chief Executive Officer, Patricia Drake, Chief Commercial Officer, Mark Demitrack, M.D., Senior Vice President and Chief Medical Officer, and Barry Shin, Chief Financial Officer.

Title:	Trevena First Quarter 2023 Financial Results Conference Call & Webcast
Date:	Monday, May 15, 2023
Time:	8:00 a.m. ET
Conference Call Details:	Toll-Free: 1-844-825-9789 International: 1-412-317-5180 Conference ID: 10178141

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=1610714&tp_key=d4c27074df https://www.trevena.com/investors/events-presentations/ir-calendar

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).

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; uncertainties related to the ongoing COVID-19 pandemic, other matters that could affect the availability or commercial potential of the Company's therapeutic candidates and approved product; achieving the conditions to payment and borrowing under our license and financing agreements, respectively, 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.

For more information, please contact:

Investor Contact:

Dan Ferry
Managing Director
LifeSci Advisors, LLC
daniel@lifesciadvisors.com
(617) 430-7576

Company Contact:

Bob Yoder
SVP and Chief Business Officer
Trevena, Inc.
(610) 354-8840

TREVENA,INC.

Condensed Statements of Operations

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

	Three Months Ended Mar 31,	
	2023	2022
Product revenue	$ 6	$ -
License revenue	-	20
Total revenue	6	20
Operating expenses:		
Cost of goods sold	127	207
Selling, general and administrative	6,089	11,014
Research and development	3,909	5,259
Total operating expenses	10,125	16,480
Loss from operations	minus(10,119)	minus(16,460)
Other income	2,300	71
Net loss	$ minus(7,819)	$minus(16,389)
Per share information:		
Net loss per share of common stock, basic and diluted	minus($ 0.81)	minus($ 2.48)
Weighted average shares outstanding, basic and diluted	9,594,072	6,620,800

TREVENA,INC.

Condensed Balance Sheets

(Unaudited, in thousands)

	March 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 27,436	$ 38,320
Inventories	906	906
Prepaid expenses and other current assets	2,425	1,782
Total current assets	30,767	41,008
Restricted cash	1,968	1,960
Property and equipment, net	1,406	1,488
Right-of-use lease assets	4,092	4,224
Other assets	59	-
Total assets	$ 38,292	$ 48,680

Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable, net	$ 1,664	$ 2,372
Accrued expenses and other current liabilities	5,429	5,461
Current portion of lease liabilities	926	899
Total current liabilities	8,019	8,732
Loans payable, net	13,476	13,430
Leases, net of current portion	5,194	5,436
Warrant liability	1,449	5,483
Total liabilities	28,138	33,081
Common stock	9	8
Additional paid-in capital	565,736	563,362
Accumulated deficit	minus(555,591)	minus(547,772)
Accumulated other comprehensive income (loss)	-	1
Total stockholders' equity	10,154	15,599
Total liabilities and stockholders' equity	$ 38,292	$ 48,680

Source: Trevena, Inc.