

September 6, 2023



Trevena Announces Receipt of \$15 Million Non-Dilutive Tranche and Provides General Business Update

\$15 million tranche from ex-US royalty-based financing, triggered by first commercial sale of OLINVYK by Jiangsu Nhwa, Trevena's partner in China

New OLINVYK respiratory data from VOLITION ~200 patient real-world outcomes study, using continuous respiratory monitoring, expected 3Q 2023

Three OLINVYK abstracts accepted for presentation at upcoming American Society of Anesthesiologists Meeting in 4Q 2023

Company to participate in upcoming HC Wainwright conference (September 11-13)

Company to Hold Conference Call on Wednesday, September 6 at 8 a.m. Eastern Time to discuss TRV045 Proof-of-Concept Data

CHESTERBROOK, Pa., Sept. 06, 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 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.

The \$15 million tranche is in addition to the \$28.1 million of cash and cash equivalents the Company previously reported as of June 30, 2023. As part of the R-Bridge Financing, Trevena may receive an additional \$10 million upon achievement of either a commercial or financing milestone.

The Company also announced additional expected near-term milestones:

- **New VOLITION Respiratory Data for OLINVYK.** The Company previously reported initial topline GI and delirium data from the ~200 patient OLINVYK VOLITION study, a real-world, open-label, multi-site study led by clinical outcomes research experts from Cleveland Clinic and Wake Forest Baptist Health Medical Center. Trevena expects to report new respiratory data from the study using continuous respiratory monitoring in 3Q 2023.
- **OLINVYK Abstracts Accepted at American Society of Anesthesiologists (ASA) 2023 Meeting.** The Company has three abstracts accepted for presentation at ASA,

which will be held in San Francisco from October 13th to the 17th. One abstract was selected for an oral presentation as a top research abstract. The abstracts are embargoed until the conclusion of the meeting and at which time they will be available at <https://www.trevena.com/publications>.

- **“ARTEMIS, A Real-World Evidence Trial Examining the Use of Oliceridine, a Biased Agonist at the μ (Mu) Receptor, in Patients Requiring Post-Surgical Pain Control.”** With lead author Todd L. Wandstrat, PharmD of Trevena, Inc.
- **“Postoperative Vomiting With IV Oliceridine in Postoperative Recovery: A Single-group Prospective Cohort Study”** with lead author Mark Demitrack, M.D of Trevena, Inc.
- **“Antinociception Versus Neurocognitive Effect of Biased Mu-opioid Receptor Oliceridine Versus Morphine- Utility Function Analysis”** with lead author Albert Dahan MD PhD of the Centre for Human Drug Research, Leiden, the Netherlands.
- **TRV045 Data.** The Company today reported results from its Target Engagement (PainCart®) and TMS Proof-of-Concept studies. In addition, a nonclinical study of TRV045 is ongoing, focused on the potential of TRV045 to treat infantile spasms, a rare pediatric disorder. TRV045 is also being studied by the NIH’s Epilepsy Therapy Screening Program as a potential disease-modifying therapeutic for the prevention of seizures. Nonclinical data from both of these studies are expected 2H 2023.
- **Trevena to Participate in Investor Conference.** The Company announces that members of management will participate in the HC Wainwright Global Investment Conference being held in-person and virtually in New York City on September 11-13. A link to the webcast will be available on the Events page of the Investors section of the Company’s website at: <https://www.trevena.com/investors/events-presentations/ir-calendar>

Conference Call and Webcast Information

The Company will host a conference call and webcast with the investment community on September 6, 2023 at 8:00 a.m. Eastern Time featuring remarks by Carrie Bourdow, President and Chief Executive Officer, Mark Demitrack, M.D., Senior Vice President and Chief Medical Officer, and Barry Shin, Chief Financial Officer.

Title:	Trevena Business Update Conference Call & Webcast
Date:	Wednesday, September 6, 2023
Time:	8:00 a.m. Eastern Time
Conference Details:	Call Toll-Free: 1- 877-704-4453 International: 1- 201-389-0920 Conference ID: 13740836

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

Webcast: https://viaid.webcasts.com/starthere.jsp?ei=1630911&tp_key=ea5c342481
<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 single 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 CO₂ retention, such as those with evidence of increased intracranial pressure or brain tumors, as a reduction in respiratory drive and the resultant CO₂ 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 $\geq 10\%$) 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 (S1P₁) 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 S1P₁ 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 Epilepsy

Epilepsy, one of the most common neurological diseases in the world, is a chronic disorder characterized by recurrent seizures. Epilepsy is defined as having two or more unprovoked

seizures separated by at least 24 hours or after one seizure with a high risk of more.

A seizure is a sudden surge of electrical activity in the brain caused by complex chemical changes that occur in nerve cells. Usually, there is a balance of cells that either encourage or stop other brain cells from sending messages. A seizure occurs when there may be too much or too little electrical activity in the brain causing an imbalance. Seizures are a symptom of many different disorders that can affect the brain. Nearly 50 million people suffer from epilepsy worldwide, including 3 million adults and 470,000 children in the U.S. 150,000 new cases of epilepsy are reported in the United States each year. According to the CDC, 56% of adults living with diagnosed epilepsy continue to have seizures.

About Diabetic Neuropathic Pain

Diabetic neuropathy is a common complication of both type 1 and type 2 diabetes, with pain in the extremities being one of the main symptoms. Other symptoms may include numbness, tingling, allodynia and hyperalgesia. Diabetic neuropathic pain is usually characterized as moderate to severe in nature and can substantially affect patients' quality of life as well as their social and psychological well-being.

Approximately 25% of people with diabetes are affected by DNP, equaling over 5 million people in the U.S. During their lifetime, approximately 50% to 70% of diabetic patients may experience symptoms of DNP.

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.

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.

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