

May 11, 2022



Trevena Reports First Quarter 2022 Results and Provides Business Update

OLINVYK refocused commercial strategy initiated mid-Q1

OLINVYK respiratory physiology study demonstrated statistically significant reduced impact on respiratory function compared to IV morphine, among elderly/overweight subjects

Cognitive function study for OLINVYK versus IV morphine on track for topline results mid-year

Continued progress of Phase I study for TRV045, novel S1P receptor modulator, for use in diabetic neuropathic pain (DNP); NIH preclinical studies in epilepsy ongoing

Closed \$40 million financing with R-Bridge Healthcare Fund; received first \$15 million tranche in April 2022

Company to host conference call today, May 11th, 2022 at 8:00 a.m. ET

CHESTERBROOK, Pa., May 11, 2022 (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, 2022 and provided an overview of its recent operational highlights.

“In the first quarter, we began to see hospitals opening up post the pandemic as evidenced by accelerated field execution of the OLINVYK strategy and an increase in educational programs and training,” said Carrie Bourdow, President and CEO of Trevena. “We also remained focused on advancing the clinical studies for OLINVYK and TRV045, our novel S1P receptor modulator and we strengthened our balance sheet following receipt of the initial \$15 million tranche of our ex-US royalty-based financing.”

First Quarter 2022 and Recent Corporate Highlights

OLINVYK (oliceridine) injection Milestones

- **Continued progress on launch execution.** Initiated launch acceleration and refocus of field sales organization in mid-February which led to 2,500 customer calls in the first quarter concentrated in critical care areas such as burn, colorectal and anesthesiology. 90% of customer interactions have been executed in an impactful face-to-face forum versus virtual engagements, and awareness is increasing via a presence at national congresses.
- **Announced results from respiratory physiology study in elderly/overweight subjects.** The Company announced topline results from its double blinded, crossover

study evaluating OLINVYK injection versus IV morphine for the management of acute pain in elderly/overweight subjects. The study was completed in collaboration with Dr. Albert Dahan and his research team at Leiden University Medical Center (LUMC). The data showed that OLINVYK had a significantly reduced impact on respiratory function compared to IV morphine among elderly/overweight subjects. The data replicated the results from a previously reported study in younger subjects. Dr. Dahan and his team are expected to report these results to the wider scientific community and submit for publication later this year. As with all opioids, serious, life-threatening, or fatal respiratory depression may occur in patients treated with OLINVYK as indicated in the boxed warning.

- **Top-line data from OLINVYK post-approval clinical outcomes studies expected later this year.** The Company expects to report topline data by mid-2022 from a study designed to assess the potential changes in cognitive function in subjects treated with OLINVYK compared to IV morphine. The study is being conducted in collaboration with the Netherlands-based Center for Human Drug Research. In addition, the Company expects to report topline data in the second half of 2022 from the VOLITION study, which is assessing the potential impact of OLINVYK on respiratory, gastrointestinal (GI), and cognitive function outcomes in the postoperative setting. The study is being led by clinical outcomes research experts from the Cleveland Clinic and the Wake Forest Baptist Health Medical Center.
- **Closed \$40M ex-US royalty-based financing agreement with R-Bridge Healthcare Fund in March 2022 and received first \$15 million tranche in April 2022.** The Company announced it received the \$15 million upfront tranche from its financing agreement with R-Bridge Healthcare Fund. The transaction is mainly focused on OLINVYK royalties expected from Trevena's partner in China, Jiangsu Nhwa Pharmaceutical. Trevena will receive an additional \$15 million upon first commercial sale of OLINVYK in China as well as a \$10 million tranche based on a financing or commercial milestone. If approved by year-end 2023, repayment will be limited to Chinese royalties from Nhwa, plus a 4% royalty (capped at \$10 million) on OLINVYK US net sales. Trevena retains all milestones from its partnership with Nhwa, including a potential \$3 million milestone on Chinese approval.

Pipeline Updates

- **Advanced Phase 1 study of TRV045, our novel S1P receptor modulator, for diabetic neuropathic pain.** 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 with potential application to other rare or orphan seizure disorders. 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. TRV045 reversed thermal hyperalgesia, a measure of neuropathic pain, in nonclinical models of diabetic peripheral neuropathy and chemotherapy-induced peripheral neuropathy and, in nonclinical studies, produced no changes in blood pressure, heart rate, or respiratory function at or above pharmacologically active doses.

- **Announced TRV027 enrollment in COVID-19 patients ceased as part of ACTIV-4 Host Tissue platform study.** The Company announced that it received notice that enrollment for TRV027 as part of the ACTIV-4 Host Tissue platform study has been halted. Based upon data at the interim analysis, the Data and Safety Monitoring Board (DSMB) unfortunately recommended that certain trials in the ACTIV-4 Platform, including the TRV027 vs placebo trial, should cease enrollment. The 90-day follow up of participants in the TRV207 trial will proceed as planned. Details about the trial results and conclusions will be disseminated once all data have been fully analyzed.

Financial Results for First Quarter 2022

For the first quarter of 2022, the Company reported a net loss attributable to common stockholders of \$16.4 million, or \$0.10 per share, compared to \$9.8 million, or \$0.06 per share, for the first quarter of 2021.

Cash and cash equivalents were \$48.7 million as of March 31, 2022, which the Company believes will be sufficient to fund the Company's operating expenses and capital expenditure requirements into 2023. This cash balance does not include proceeds from the receipt in April of the first \$15 million tranche from the royalty-based financing agreement with an affiliate of R Bridge Healthcare Fund.

In addition, the Company announced its Annual General Meeting will be held on June 9th, 2022. In the definitive proxy statements, the Company is requesting approval for additional authorized shares. The proposal would result in no immediate dilution for stockholders. The increase in authorized shares is intended to provide flexibility to execute on the Company's business development opportunities, achieve the \$10M tranche from our R-Bridge financing, and advance the Company's products and pipeline.

Conference Call and Webcast Information

The Company will host a conference call and webcast with the investment community on May 11th, 2022, 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, Senior Vice President and Chief Financial Officer.

Title: Trevena First Quarter 2022 Financial Results
Conference Call & Webcast

Date: Wednesday, May 11, 2022

Time: 8:00 a.m. ET

Conference Call Details: Toll-Free: 1-844-826-3033
International: 1-412-317-5185
Conference ID: 10166614

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=1545824&tp_key=fa08098dd7

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 four differentiated investigational drug candidates: TRV045 for diabetic neuropathic pain and epilepsy, TRV027 for acute respiratory distress syndrome and abnormal blood clotting in COVID-19 patients, TRV250 for the acute treatment of migraine and TRV734 for maintenance treatment of opioid use disorder.

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 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.](#)

For more information, please visit www.Trevena.com

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.

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.

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 and approved product, 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; 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 Mar 31,	
	2022	2021
Product revenue	\$ -	\$ 209
License revenue	20	-
Total revenue	<u>20</u>	<u>209</u>
Operating expenses:		
Cost of goods sold	207	163
Selling, general and administrative	11,014	7,368
Research and development	5,259	2,636
Total operating expenses	<u>16,480</u>	<u>10,167</u>
Loss from operations	(16,460)	(9,958)
Other income	71	116
Net loss	<u>\$ (16,389)</u>	<u>\$ (9,842)</u>
Per share information:		
Net loss per share of common stock, basic and diluted	<u>(\$0.10)</u>	<u>(\$0.06)</u>
Weighted average shares outstanding, basic and diluted	<u>165,520,007</u>	<u>160,508,373</u>

TREVENA, INC.
Condensed Balance Sheets
(Unaudited, in thousands)

	March 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	\$ 48,664	\$ 66,923
Accounts receivable, net	-	-
Inventories	2,745	2,352
Marketable securities		
Insurance recovery	-	-
Prepaid expenses and other current assets	2,840	1,448
Total current assets	<u>54,249</u>	<u>70,723</u>
Restricted cash	1,311	1,311
Property and equipment, net	1,736	1,841
Right-of-use lease assets	4,592	4,706
Other assets	<u>2,529</u>	<u>1,543</u>

Total assets	\$ 64,417	\$ 80,124
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable, net	\$ 2,408	\$ 4,547
Accrued expenses and other current liabilities	5,703	3,847
Estimated settlement liability	-	-
Current portion of loans payable, net		
Current portion of lease liabilities	815	792
Total current liabilities	<u>8,926</u>	<u>9,186</u>
Leases, net of current portion	6,096	6,309
Warrant liability	-	-
Total liabilities	<u>15,022</u>	<u>15,495</u>
Common stock	165	165
Additional paid-in capital	559,721	558,566
Accumulated deficit	<u>(510,491)</u>	<u>(494,102)</u>
Total stockholders' equity	<u>49,395</u>	<u>64,629</u>
Total liabilities and stockholders' equity	<u>\$ 64,417</u>	<u>\$ 80,124</u>



Source: Trevena, Inc.