November 9, 2022

Trevena Reports Third Quarter 2022 Results and Provides Business Update

OLINVYK commercialization progresses with Vizient contract and receipt of CMS outpatient pass-through reimbursement

Positive Phase 1 topline results for TRV045, a novel S1P receptor modulator; no serious adverse events and PK profile supports anticipated once daily dosing

Targeted TRV045 proof-of-concept study to assess CNS activity planned for early 2023

Cash balance of $40.4 million at Q3 funds operations into Q3 2023

Company to host conference call today, November 9, 2022 at 8:00 a.m. ET

CHESTERBROOK, Pa., Nov. 09, 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 third quarter ended September 30, 2022, and provided an overview of its recent operational highlights.

“We are pleased that OLINVYK received CMS pass-through reimbursement for ambulatory surgical centers and hospital outpatient settings. Our recently announced relationship with Vizient is advancing, which enables us to efficiently manage and allocate resources in this challenging hospital environment,” said Carrie Bourdow, President and CEO of Trevena. “We are also excited to report positive topline Phase 1 data for our novel S1P receptor modulator, TRV045. The results of the study support potential advancement of TRV045 in CNS areas such as non-opioid chronic pain and epilepsy. Based on this promising clinical data, we plan to move forward with a targeted proof-of-concept study with near term expected data.”

Third Quarter 2022 and Recent Corporate Highlights

- **Received CMS pass-through designation for OLINVYK® (oliceridine) injection:** Trevena received CMS pass-through designation for OLINVYK, effective October 1. CMS’s pass-through status will allow ambulatory surgery centers and outpatient hospital facilities to be reimbursed by Medicare and other insurance providers for OLINVYK using the unique C-code, which opens the opportunity for potential expanded utilization in the outpatient setting. These pass-through payments can be made for the next 3 years.

- **Progressed OLINVYK commercialization:** In July, Trevena entered into a multi-year agreement with Vizient, Inc., a leading hospital performance improvement company, which will allow for broad OLINVYK access to enhanced savings for member hospitals.

Trevena continues to work with Vizient to educate its members on the clinical and health economic benefits of OLINVYK as an alternative to IV morphine. OLINVYK is currently on formulary in 172 institutions, which includes a recent contract with a large ambulatory surgical center (ASC) provider.

- **Advanced differentiating clinical data for OLINVYK:** Presented respiratory physiology data in elderly/overweight subjects at annual American Society of Anesthesiologist (ASA) meeting. At ASA, Dr. Albert Dahan and his research team at Leiden University Medical Center (LUMC) presented a poster abstract titled, "A Randomized Double-blind Trial Comparing Oliceridine And Morphine On Ventilation In An Elderly Population." Separately, the Company expects enrollment in the collaborative real-world outcomes study, VOLITION, to be completed by the end of 2022. The VOLITION trial is being led by clinical outcomes research experts from the Cleveland Clinic and Wake Forest Baptist Health Medical Center. The study assesses the potential impact of OLINVYK on respiratory, gastrointestinal (GI) and cognitive function outcomes in the postoperative setting.

- **Announced positive topline Phase 1 and non-clinical data for TRV045, a novel S1P receptor modulator for diabetic neuropathic pain and epilepsy.** The Phase 1 study evaluated single-ascending and multiple dose phases, as well as a food effect study. There were no serious adverse events, and TRV045 was generally well tolerated. The observed PK profile was consistent with anticipated once-daily dosing. Consistent with prior nonclinical safety data, there was no evidence of reduction in lymphocytes, and no adverse event reports of cardiac, pulmonary or ophthalmologic events which are known to be associated with S1P modulators. The Company also announced the results of a nonclinical study of the effects of TRV045 on primary mouse astrocytes in cell culture. These data support the potential for TRV045 to play a role as a disease-modifying agent in the treatment of epilepsy.

Financial Results for Third Quarter 2022

For the third quarter of 2022, the Company reported a net loss attributable to common stockholders of $15.3 million, or $0.09 per share, compared to $13.8 million, or $0.08 per share in the third quarter of 2021.

Results for the third quarter of 2022 include a $2.2 million non-cash valuation adjustment for slow-moving or obsolete inventory due to the uncertainty of commercial activities underlying OLINVYK sales, which is recognized as a cost of goods expense. The results also include a $0.4 million non-cash adjustment in reserves for potential returns of OLINVYK held at wholesalers, which results in negative product revenue.

Cash, cash equivalents and marketable securities totaled $40.4 million as of September 30, 2022, which the Company believes will be sufficient to fund the Company's operating expenses and capital expenditure requirements into the third quarter of 2023.

Conference Call and Webcast Information

The Company will host a conference call and webcast with the investment community on November 9, 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, Chief

Financial Officer.

Title:	Trevena Third Quarter 2022 Financial Results Conference Call & Webcast
Date:	Wednesday, November 9, 2022
Time:	8:00 a.m. ET
Conference Call Details:	Toll-Free: 1-800-954-0687 International: 1-212-231-2935 Conference ID: 22021290

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=1572499&tp_key=b8766e3409

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

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; 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 Sep 30,		Nine Months Ended Sep 30,	
	2022	**2021**	**2022**	**2021**
Product revenue	$ minus(438)	$ 112	$ minus(438)	$ 499
License revenue	-	69	20	69
Total revenue	minus(438)	181	minus(418)	568
Operating expenses:				
Cost of goods sold	2,368	199	2,791	620
Selling, general and administrative	7,683	10,438	29,003	28,351
Research and development	5,266	3,404	14,816	9,489
Total operating expenses	15,317	14,041	46,610	38,460
Loss from operations	minus(15,755)	minus(13,860)	minus(47,028)	minus(37,892)
Other income	460	89	363	257
Net loss	minus(15,295)	minus(13,771)	minus(46,665)	minus(37,635)
Unrealized gain (loss) on marketable securities	$ 32	$ -	$ minus(28)	$ -
Comprehensive loss	$minus(15,263)	$minus(13,771)	$minus(46,693)	$minus(37,635)

Per share information:

Net loss per share of common stock, basic and diluted	$ minus(0.09)	$ minus(0.08)	$ minus(0.28)	$ minus(0.23)
Weighted average shares outstanding, basic and diluted	170,725,392	164,510,570	167,276,563	162,811,136

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

	Sep 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 22,431	$ 66,923
Marketable securities	17,961	-
Inventories	785	2,352
Prepaid expenses and other current assets	1,363	1,448
Total current assets	42,540	70,723
Restricted cash	2,557	1,311
Property and equipment, net	1,570	1,841
Right-of-use lease assets	4,352	4,706
Other assets	-	1,543
Total assets	$ 51,019	$ 80,124
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable, net	$ 1,416	$ 4,547
Accrued expenses and other current liabilities	6,794	3,847
Current portion of loans payable, net	174	-
Current portion of lease liabilities	873	792
Total current liabilities	9,257	9,186
Loans payable, net	13,359	-
Leases, net of current portion	5,672	6,309
Warrant liability	868	-
Total liabilities	29,156	15,495
Common stock	174	165
Additional paid-in capital	562,484	558,566
Subscription receivable	-	-
Accumulated deficit	minus(540,767)	minus(494,102)

Accumulated other comprehensive income (loss)	minus(28)	-
Total stockholders' equity	21,863	64,629
Total liabilities and stockholders' equity	$ 51,019	$ 80,124

Source: Trevena, Inc.