April 1, 2024

Trevena Reports Fourth Quarter 2023 Results and Provides Corporate Update

TRV045, novel S1P receptor modulator for chronic pain and epilepsy, advances toward important milestones in both non-clinical and clinical studies

Company announces reduction of OLINVYK commercial support and review of alternatives for OLINVYK

CHESTERBROOK, Pa., April 01, 2024 (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 fourth quarter ended December 31, 2023 and provided an overview of its recent operational highlights.

“Despite OLINVYK’s differentiated profile, the hospital environment continues to be challenging. Given performance to date, we are reducing commercial support and reviewing alternatives for OLINVYK to preserve capital,” said Carrie Bourdow, President and CEO of Trevena. “We will focus our resources on the continued development of TRV045 and we are pleased with the progress we have made toward potential Phase 2 readiness.”

Fourth Quarter 2023 and Recent Corporate Highlights

- **Company to focus resources on TRV045 development, reducing OLINVYK commercial support to preserve capital.** The Company announced today that it plans to focus its resources on the continued development of TRV045, with several near-term milestones expected. Despite OLINVYK’s differentiated profile for patients and demonstrated savings to hospitals, based on its sales performance to date and other factors, the Company has reduced commercial support of OLINVYK to help preserve capital. OLINVYK will remain available for purchase by customers, who can continue to order the product through their normal channels. The Company will continue to comply with all regulatory requirements, including post-marketing surveillance and reporting obligations. The Company is conducting a review of strategic alternatives for OLINVYK, which may include a sale, license or divestiture of OLINVYK. There can be no assurance regarding the schedule for completion of the strategic review process, that this strategic review process will result in the Company pursuing any transaction or that any transaction, if pursued, will be completed.
- **Previously, the Company reported data from two positive proof-of-concept studies demonstrating CNS target engagement for TRV045 and supporting further development in patients in neuropathic pain and epilepsy.** In a target engagement POC study, TRV045 demonstrated statistically significant analgesic effect in a capsaicin-induced model of neuropathic pain. In the second study, a TMS POC study provided statistically significant evidence of CNS activity of TRV045 through day 4 as measured by resting-state EEG power spectral analysis. In a review of safety and

tolerability across both studies, TRV045 was well tolerated with results generally consistent with prior first-in-human studies. There were no drug-related adverse events and no serious adverse events reported in the studies. Importantly, TRV045-treated subjects did not show any drug-related lymphopenia, bradycardia or change in blood pressure which have been reported with other S1P modulators.

- **TRV045 progresses towards Phase 2 readiness with advances in formulation development and toxicology studies.** The Company has successfully identified an optimized formulation of TRV045, which it believes is suitable for late-stage clinical studies and, if approved, commercialization. The modest food effect observed with the initial POC formulation has not been seen with the new formulation. TRV045 continues to demonstrate a favorable tolerability profile with the optimized formulation. In addition, the live phase of the reproductive toxicology and sub-chronic toxicology studies have been completed, with final reports expected in 2H 2024. The Company currently has an IND for TRV045 in diabetic neuropathic pain and may submit an IND application for TRV045 focused on epilepsy and seizure disorders.
- **NIH-Supported Epilepsy Therapy Screening Program (ETSP) continues to study TRV045 as a potential disease-modifying agent for the prevention of seizures.** Previous nonclinical studies indicate that TRV045's action on astrocytes may modify their inflammatory signaling with a net action to potentially reduce neuroinflammation and thereby may play a role in how seizures develop (epileptogenesis). The NIH continues to study TRV045 for the prevention of seizures and is currently conducting a nonclinical study in a kainic acid-induced spontaneously-recurring seizure model. Following an induction phase of status epilepticus, rats are randomized and prophylactically treated with either TRV045 15mg/kg or vehicle, dosed twice daily for seven days starting one hour after cessation of status epilepticus. The Company expects results from the studies to be available by mid-2024.

Financial Results for Fourth Quarter 2023

For the fourth quarter of 2023, the Company reported a net loss attributable to common stockholders of $16.5 million, or $1.06 per share, compared to $7.0 million, or $0.73 per share in the fourth quarter of 2022. For the full year ended December 31, 2023, net loss attributable to common stockholders was $40.3 million, or $3.16 per share, compared to $53.7 million, or $7.59 per share.

Cash and cash equivalents were $33.0 million as of December 31, 2023.

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 TRV045

TRV045 is a novel, highly 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. Subjects in both studies referenced in this press release were enrolled outside of the United States, and the studies were not conducted under the Investigational New Drug Application for TRV045.

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: SERIOUS AND LIFE-THREATENING RISKS FROM USE

OF OLINVYK

Addiction, Abuse, and Misuse

Because the use of 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 prior to prescribing and reassess all patients regularly for the development of these behaviors and conditions.

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of OLINVYK, especially during initiation or following a dosage increase. To reduce the

risk of respiratory depression, proper dosing and titration of OLINVYK are essential.

Risks From Concomitant Use With Benzodiazepines Or Other CNS Depressants

Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing of OLINVYK and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.

Neonatal Opioid Withdrawal Syndrome

If opioid use is required for an extended period of time in a pregnant woman, advise the patient of the risk of NOWS, which may be life-threatening if not recognized and treated. Ensure that management by neonatology experts will be available at delivery.

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, which can occur at any dosage or duration, 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.

CONTRAINDICATIONS

OLINVYK is contraindicated in patients with:

- Significant respiratory depression
- Acute or severe bronchial asthma in an unmonitored setting or in 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.
- Profound sedation, respiratory depression, coma, and death may result from the concomitant use of OLINVYK with benzodiazepines and/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.
- Use of OLINVYK for an extended period of time 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 opioids for a prolonged period of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.
- 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.
- Opioid-Induced Hyperalgesia (OIH) occurs when an opioid analgesic paradoxically causes an increase in pain, or an increase in sensitivity to pain. This differs from tolerance where increasing doses are required to maintain the desired effect. Symptoms of OIH include, but may not be limited to, increased levels of pain upon dose increase, decreased levels of pain upon dose decrease, or pain from ordinarily non-painful stimuli (allodynia). These symptoms may suggest OIH only if there is no evidence of disease progression, opioid tolerance, withdrawal, or addictive behavior. If OIH is suspected, carefully consider appropriately decreasing the dose of the current opioid analgesic or opioid rotation.
- 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 www.OLINVYK.com for full prescribing information including BOXED warning and important safety information

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 expectations surrounding the continued advancement of the Company's product pipeline; the potential safety and efficacy of the Company's product candidates and their regulatory and clinical development; the Company's intention to pursue strategic alternatives for OLINVYK and the ability of any such strategic alternative to provide shareholder value; the expected financial and operational impacts of the Company's decision to reduce commercial support for OLINVYK; 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 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.

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 Dec 31,		Year Ended Dec 31,	
	2023	**2022**	**2023**	**2022**
Product revenue	$ (81)	$ -	$ (54)	$ (438)
License revenue	-	-	3,179	20
Total revenue	(81)	-	3,125	(418)
Operating expenses:				
Cost of goods sold	1,281	228	1,670	3,018
Selling, general and administrative	4,610	5,723	20,410	34,728
Research and development	4,174	3,396	16,333	18,211
Total operating expenses	10,065	9,347	38,413	55,957
Loss from operations	(10,146)	(9,347)	(35,288)	(56,375)
Other income	(6,381)	2,342	(5,001)	2,705
Loss before income tax expense	(16,527)	(7,005)	(40,289)	(53,670)
Unrealized gain on marketable securities	-	-	-	1
Net loss	$ (16,527)	$ (7,005)	$ (40,289)	$ (53,669)
Per share information:				
Net loss per share of common stock, basic and diluted	($1.06)	($0.73)	($3.16)	($7.59)
Weighted average shares outstanding, basic and diluted	15,649,160	9,594,072	12,735,010	7,072,362

TREVENA, INC.

Condensed Balance Sheets

(Unaudited, in thousands)

	December 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 32,975	$ 38,320
Inventories	-	906
Prepaid expenses and other current assets	2,230	1,782
Total current assets	35,205	41,008
Restricted cash	540	1,960
Property and equipment, net	1,195	1,488
Right-of-use lease assets	3,665	4,224
Total assets	$ 40,605	$ 48,680
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable, net	$ 2,303	$ 2,372
Accrued expenses and other current liabilities	4,239	5,461
Current portion of lease liabilities	1,012	899
Total current liabilities	7,554	8,732
Loans payable, net	30,809	13,430
Leases, net of current portion	4,424	5,436
Warrant liability	5,475	5,483
Total liabilities	48,262	33,081
Common stock	17	8
Additional paid-in capital	580,387	563,362
Accumulated deficit	(588,061)	(547,772)
Accumulated other comprehensive income (loss)	-	1
Total stockholders' equity	(7,657)	15,599
Total liabilities and stockholders' equity	$ 40,605	$ 48,680

Trevena

Source: Trevena, Inc.