UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **April 1, 2024**

TREVENA, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of incorporation)

001-36193	**26-1469215**
(Commission File No.)	(IRS Employer Identification No.)

955 Chesterbrook Boulevard, Suite 110
Chesterbrook, PA 19087
(Address of principal executive offices and zip code)

Registrant's telephone number, including area code: **(610) 354-8840**

Not applicable
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

¨ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
¨ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
¨ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
¨ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.001 par value	TRVN	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter). Emerging growth company ¨

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ¨

Item 2.02. Results of Operations and Financial Condition.

On April 1, 2024, Trevena, Inc. (the "Company") issued a press release announcing its financial results for the quarter and year ended December 31, 2023, and provided an overview of its 2024 year-to-date operational highlights. A copy of the press release is furnished hereto as Exhibit 99.1 and incorporated herein by reference.

The information under this caption and contained in the press release attached hereto as Exhibit 99.1 is furnished by the Company in accordance with Securities Exchange Commission Release No. 33-8216. This information shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act whether made before or after the date of this Current Report, except as shall be expressly set forth by specific reference in such a filing.

Item 7.01 Regulation FD Disclosure

On April 1, 2024, the Company updated its website to include an updated corporate presentation deck. A copy of the updated corporate presentation deck is attached hereto as Exhibit 99.2.

The information set forth on this Item 7.01 and furnished hereto as Exhibit 99.2 shall not be deemed "filed" for purposes of Section 18 of the Exchange Act or incorporated by reference into any of the Company's filings under the Securities Act or the Exchange Act, whether made before or after the date of this Current Report, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Number	Description
99.1	Press Release dated April 1, 2024
99.2	Updated Corporate Presentation Deck dated April 1, 2024
104	The cover page from this Current Report on Form 8-K, formatted in Inline XBRL

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

TREVENA, INC.

Date: April 1, 2024

By: /s/ Barry Shin
Barry Shin
Executive Vice President, Chief Operating Officer & Chief Financial Officer

Exhibit 99.1

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 1, 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:

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(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

Exhibit 99.2

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.

Trevena's Experienced Leadership Team

SENIOR MANAGEMENT

Carrie L. Bourdow	Chair, President & Chief Executive Officer	CUBIST PHARMACEUTICALS, MERCK
Mark A. Demitrack, M.D.	SVP, Chief Medical Officer	NEURONETICS, Lilly, ROIVANT SCIENCES
Patricia Drake	SVP, Chief Commercial Officer	MERCK, sesen bio
Barry Shin	EVP, Chief Operating Officer and CFO	MIZUHO, GUGGENHEIM, PiperJaffray
Robert T. Yoder	SVP, Chief Business Officer & Head of Commercial Operations	MERCK, OREXIGEN

BOARD OF DIRECTORS

Carrie L. Bourdow	Trevena	**Jake R. Nunn**	NEA., SR One
Scott Braunstein, M.D. Lead Independent Director	MARINUS PHARMACEUTICALS, AISLING CAPITAL, PACIRA BIOSCIENCES, INC.	**Anne M. Phillips, M.D.**	novo nordisk, gsk GlaxoSmithKline
Mark Corrigan, M.D.	TREMEAU PHARMACEUTICALS, SEPRACOR	**Barbara Yanni**	MERCK
Marvin H. Johnson, Jr.	MERCK		

Trevena: Innovative CNS Company

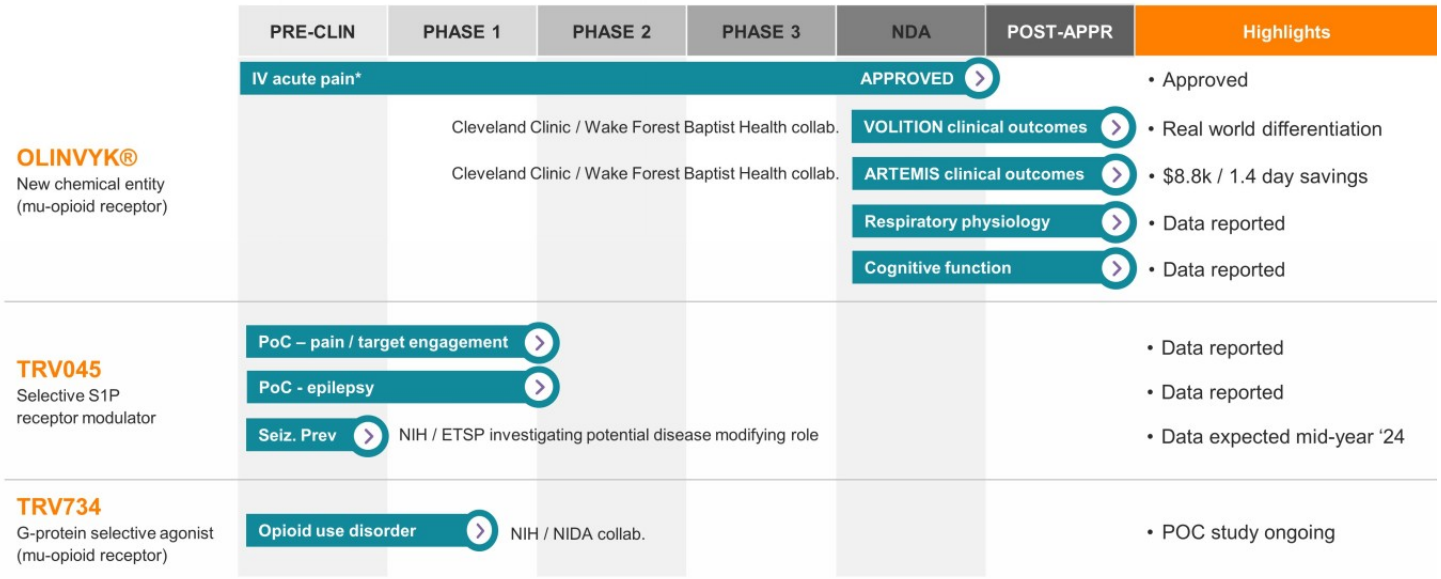
IV OLINVYK: Differentiated profile	NCE approved for the management of acute pain in adults* Significant cost savings / differentiation shown in 'real world' post-approval studies
TRV045: Selective S1PR modulator	**S1PR:** Validated target for blockbusters (fingolimod / siponimod / ozanimod / ponesimod) **TRV045:** Unique profile (with potential for no lymphopenia) for new indications
TRV045: Compelling PoC Data	Statistically significant, dose-dependent effect in validated model of neuropathic pain Statistically significant EEG changes and evidence of early reduction in cortical excitability
Novel CNS pipeline	New mechanisms for acute / neuropathic pain, epilepsy, acute migraine, opioid use disorder NCEs targeting significant unmet needs
Financial position	$33.0M cash and equivalents as of YE 2023

*OLINVYK 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. Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com

Trevena

NCE = New Chemical Entity; PoC = Proof of concept

Multiple Expected Catalysts



*OLINVYK 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. Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com

Trevena®

TRV045 and TRV734 are investigational products and are not approved by the FDA or any other regulatory agency
NDA = New Drug Application; PoC = Proof-of-Concept

Trevena

OLINVYK Overview

OLINVYK: Differentiated Profile for Acute Pain

OLINVYK 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

Data in complex patients
Elderly / obese, multiple comorbidities

New chemical entity
Distinct from IV morphine

Simplified, predictable dosing
No adjustment in renal impaired
No active metabolites

IV opioid efficacy
Hard- and soft-tissue surgeries

Well-characterized safety / tolerability
Studied in over 1,900 individuals

Rapid analgesia
1-3 min median onset of pain relief

Trevena

Please see Important Safety Information including BOXED WARNING at the end of presentation.
Full Prescribing Information at www.OLINVYK.com.

VOLITION Clinical Outcomes Study w/ Cleveland Clinic

Further characterizes respiratory, GI and cognitive outcomes

- Open-label, multi-site study led by experts at Cleveland Clinic and Wake Forest Baptist Health
- N = 203 adults undergoing major non-cardiac surgery treated with IV OLINVYK

GI Tolerability

52.7%
complete GI response[1]

defined as no vomiting / no antiemetic use through study period

[1] In pooled Phase 3 data for OLINVYK, GI complete response rate was 46.2% (0.35mg) and 39.7% (0.5mg)

Respiratory Outcomes

22.8% respiratory compromise

defined as any one of five respiratory events[2] over **48hrs** of continuous monitoring

[2] End-tidal PCO_2 ≤ 15 mmHg for ≥3 min; RR ≤ 5 breaths/min for ≥3 min; SpO_2 ≤ 85% for ≥3 min; apnea episode >30 sec; any serious respiratory event

Cognitive Function

90%+
alert / calm at all points[3]

<4% symptoms of delirium[4]

[3] Richmond Agitation-Sedation Scale
[4] 3D-CAM screening tool

As reflected in the OLINVYK label, nausea and vomiting were two of the most common AEs reported in the controlled clinical trials

As with all opioids, serious, life-threatening, or fatal respiratory depression may occur in patients treated with OLINVYK

Sedation is an established risk of opioids including OLINVYK

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Please see Important Safety Information including BOXED WARNING at the end of presentation
Full Prescribing Information at www.OLINVYK.com

ARTEMIS EMR-Based Clinical Outcomes Study

Statistically significant differentiation on a range of meaningful endpoints

- **201 OLINVYK-treated patients** at Cleveland Clinic and Wake Forest Baptist Health VOLITION sites
- **982 matched patients** undergoing similar surgical procedures, treated with other IV opioids, at same sites during VOLITION study

	Matched Patients Treated w/ other IV Opioids (N=982)		OLINVYK-Treated VOLITION Patients (N=201)	
Cost per Admission (avg)	$45.9k	**$8.8k** savings →	$37.1k	P<0.0001
Hospital Length of Stay (avg)	7.1 days	**1.4 days** shorter →	5.7 days	P<0.0001
Numerical Pain Score (1-10)				
24hr mean score	4.5	**15.0%** lower score →	3.9	P<0.0001
48hr mean score	4.3	**14.8%** lower score →	3.7	P<0.0001

As with all opioids, addiction, abuse and misuse, which can lead to overdose and death may occur in patients treated with OLINVYK as indicated in the boxed warning

EMR analysis does not provide definitive data of group differences as seen in a prospectively randomized study

Please see Important Safety Information including BOXED WARNING at the end of presentation
Full Prescribing Information at www.OLINVYK.com

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OLINVYK: Ease of Dosing and Administration

3 vials allow for flexible and tailored IV dosing

- **Bolus Dosing:** 1 mg and 2 mg vials (single dose)
- **PCA Dosing:** 30 mg vial (single patient use)
- **OLINVYK 1 mg ≈ morphine 5 mg**[1]

27 mg cumulative daily dose limit

Do not administer single doses greater than 3 mg

No refrigeration / reconstitution

	1 mg / 1mL	2 mg / 2mL	30 mg / 30 mL
WAC:	$17.50	$25.75	$110.00

~$100 / day
(estimated avg cost across procedures)

Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.

1) For an initial dose. PCA = Patient-Controlled Analgesia

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TRV045 Overview

$S1P_1$ Receptor – Novel Target for CNS Indications

$S1P_1$ receptors are highly expressed on key CNS cells involved in neuroinflammation

Potential therapeutic role in seizures, epileptogenesis and pain signaling

Epilepsy

- Neuroprotective effects[3]
- Modulates BBB permeability, anti-inflammatory effects[4,5]

Neuropathic pain

- Inhibits pain sensation[1]
- Inhibits excitatory neuronal signaling[2]

Existing S1PR-targeted drugs, however, are ill-suited for CNS indications due to known:

Lymphopenia
Cardiac AEs
Pulmonary AEs
Ophthalmologic AEs

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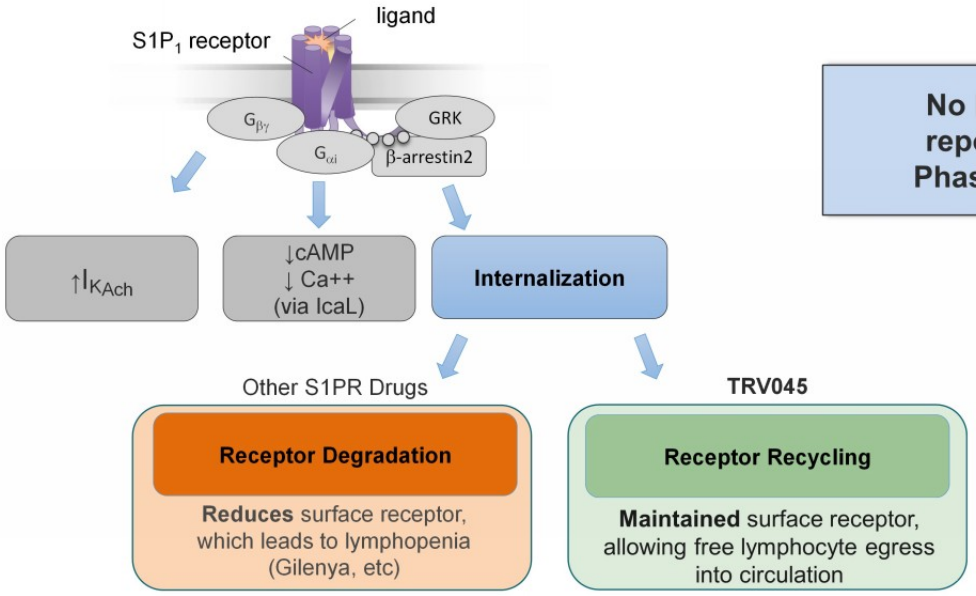
1) Sim-Selley et al., Journal of Pharmacology & Experimental Therapeutics, 2018. 2) Sim-Selley et al, Journal of Neurochemistry, 2008. 3) Gol et al., European Journal of Pharmaceutical Sciences, 2017. 4) Leo et al, CNS & Neurological Disorders - Drug Targets, 2017. 5) Choi, et al. PNAS 2011.

TRV045 MOA (1): Rapid Receptor Recycling

Maintained (rather than degraded) S1P receptors on cell surface



No lymphopenia reported in prior Phase 1 FIH study

FIH = First in human

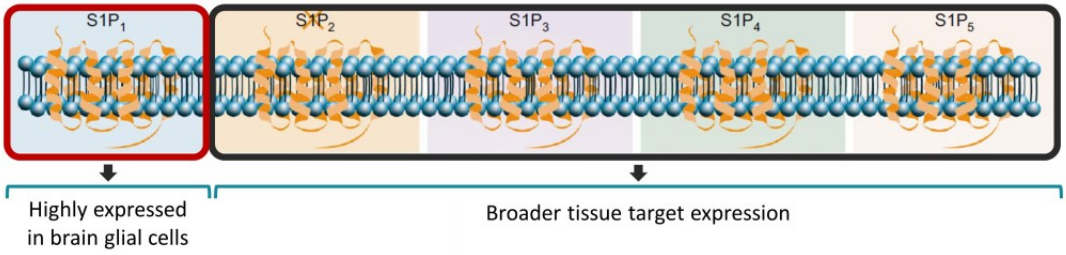
Source: Trevena data on file

TRV045 MOA (2): S1PR Subtype-1 Selectivity

Subtype-1 is broadly expressed in the CNS and may avoid effects associated with other subtypes

- S1P acts on 5 distinct subtypes of receptors ($S1P_{1-5}$)
- TRV045 is **potent and selective for S1P subtype-1 receptor**
  - $S1P_1R$ is highly expressed on astrocytes / other glial cells
  - May play role in central pain signaling, as well as development and persistence of seizures

Highly expressed in key CNS / brain cells



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Adapted from: Chun, J, et al., Drugs (2021) 81:207–231

TRV045 MOA (3): Anti-Inflammatory Effect (nonclinical)

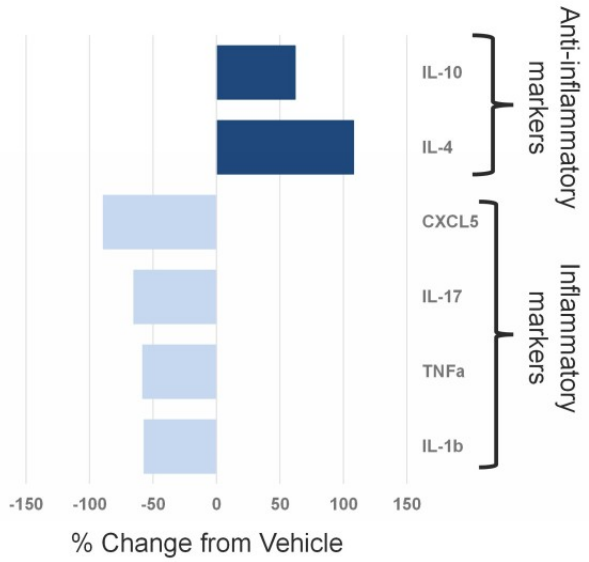
Anti-inflammatory actions (cytokines / chemokines) on astrocytes in cell culture

- **Main Findings:** Net anti-inflammatory action (statistically significant) on astrocyte cytokine / chemokine release
  - Increased all **anti-inflammatory** markers measured[1]
  - Reduced all **inflammatory** markers measured[1]

- **Method:** Primary mouse astrocytes in monolayer cell culture, incubated for 24hrs w/ 5 μM TRV045
  - 17 cytokines / chemokines[2] assessed by ELISA

TRV045-affected cytokines / chemokines play a role in many CNS disorders

(epilepsy, pain, neuropsych / neurodegen diseases)



1) P<0.05 v vehicle
2) Full cytokine / chemokine panel studied: (Inflammatory markers) – TNFa, IL-6, IL-1b, IL-17, IL-23, IL-33, CCL1, CCL2, CCL20, CXCL5, CXCL12, CX3CL1, IFNg, Csf2, Substance P; (Anti-inflammatory markers) – IL-10, IL-4. (Trevena, Inc., data on file)

TRV045 Proof-of-Concept Study Program – Highlights

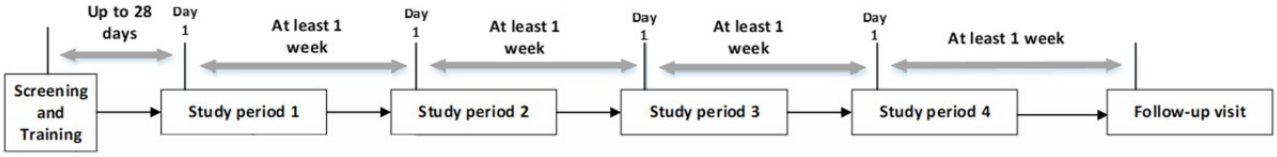
- **Target Engagement.** Demonstrated CNS penetration and target engagement
- **Neuropathic Pain.** Statistically significant, dose-dependent effect in validated model of neuropathic pain
- **EEG Spectral Power.** Statistically significant ***increases*** in brain waves (alpha, beta, gamma) associated with arousal, alertness, cognitive processing, learning and memory

  Statistically significant ***decrease*** in delta brain waves, and ***no significant change*** in theta brain waves, both of which are associated with sedation / sleep
- **Cortical Excitability.** Directional evidence of early reduction in cortical excitability

Not all of the results were statistically significant;
details of the findings are presented on the following slides

Target Engagement (PainCart®) POC Study Design

- **Design:** Randomized, double-blind, placebo-controlled, single dose, four-way cross-over (N=25 subjects; 8F/17M, mean age 37.6 years, range 18-53)
  - Placebo or TRV045 (50/150/300mg)



- Pharmacodynamic Endpoints:
  - Mechanical allodynia (Von Frey hair testing on capsaicin-treated skin), pressure pain, heat pain (capsaicin-treated, UVB-exposed, and unexposed skin), cold pain (CPT), electrical pain (stair, burst conditions), conditioned pain modulation (electrical pain pre- and post-CPT)
- PK exposure parameters (C_{max}, t½)
- Safety and tolerability

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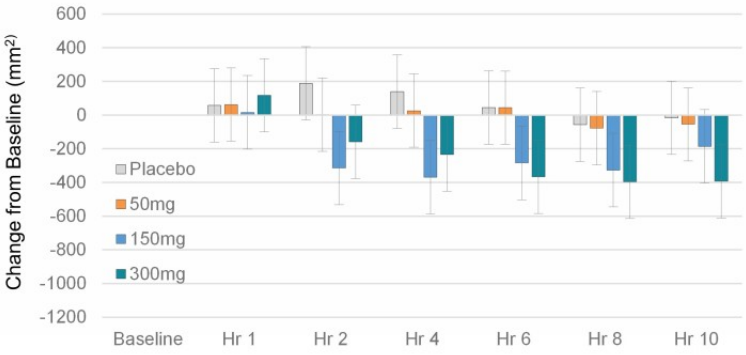
Studies were conducted outside the United States and not under the IND for TRV045
Source: Trevena data on file

TRV045 Significantly Reduced Mechanical Allodynia

1% capsaicin-treated dominant volar forearm – Von Frey filament allodynic area (CFB, mm^2)

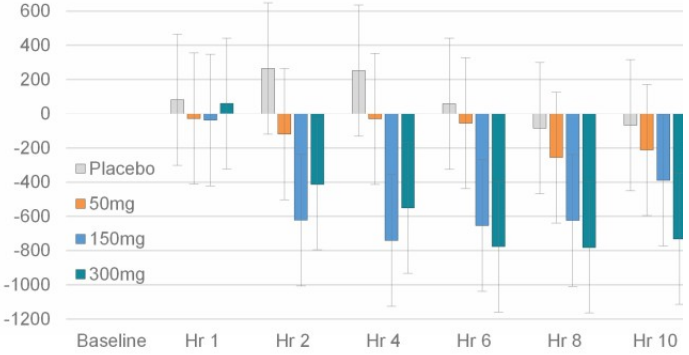
300mg TRV045 v Placebo; P=0.0023
150mg TRV045 v Placebo; P=0.0022

Secondary Allodynic Area



300mg TRV045 v Placebo; P=0.0001
150mg TRV045 v Placebo; P=0.0002

Total Allodynic Area



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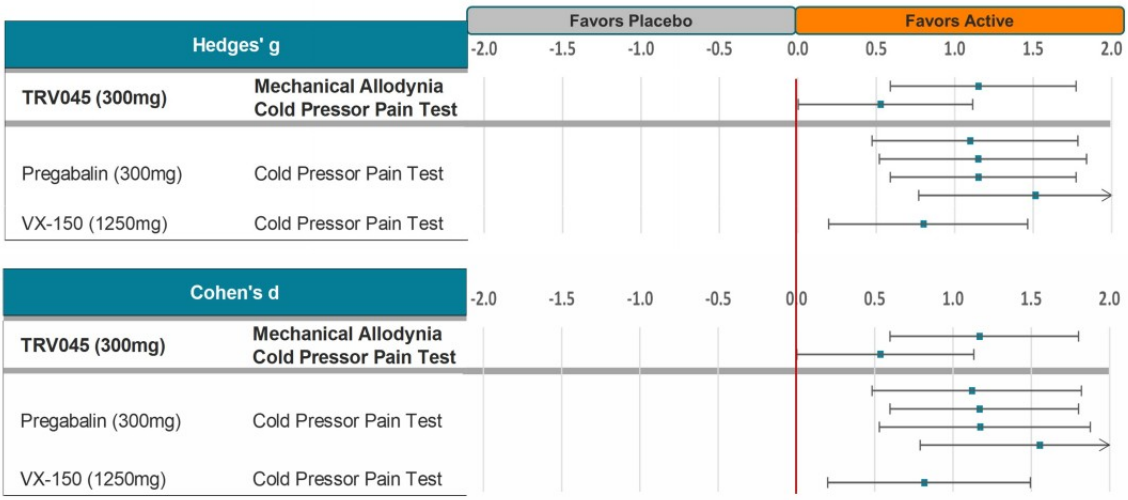
Source: Trevena data on file

Effect Size Comparison: TRV045 v Other Analgesics



Effect Size:

+0.2 – small effect

+0.5 – medium effect

+0.8 – large effect

- Studies for comparators conducted at **same** lab (CHDR) conducting TRV045 studies
- Single highest result for each comparator provided (cold pressor) from a battery of CHDR tests conducted
  - Mechanical allodynia test was not conducted on comparators

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Target Engagement (PainCart®) Study

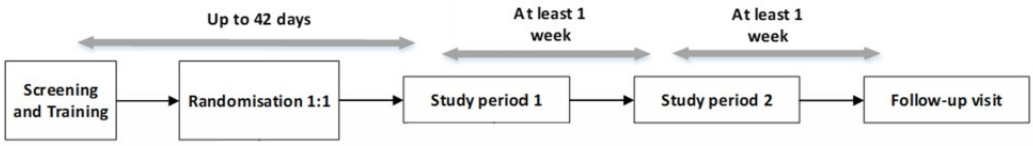
PainCart observations

- Statistically significant, dose-dependent, treatment effect in model of capsaicin-induced mechanical allodynia provides evidence of the therapeutic potential of TRV045 in neuropathic pain
  - Recognized and validated study index of central pain processing ('central sensitization')
  - Note that effect appeared similar with both 150mg and 300mg dose, potentially guiding future decisions on dose range use in Phase 2
- Supportive evidence of analgesic action in select other nociceptive models
  - Other endpoints did not show trend / statistically significant results (pressure pain / conditioned pain modulation)
- Overall, strong support for CNS penetrance and engagement of pain signaling pathways in the brain
  - PK exposure consistent with parameters observed at comparable doses studied under fed conditions in Phase 1 FIH st
- No SAEs, no drug-related study discontinuations

Source: Trevena data on file

TMS POC Study Design

- **Design:** Randomized, double-blind, placebo-controlled, multiple dose, two-way cross-over (n=25 male subjects; mean age 31.5 years, range 21-55)
  - Placebo or TRV045 (250mg) for 4 days; post-dose assessments performed at 4 hours



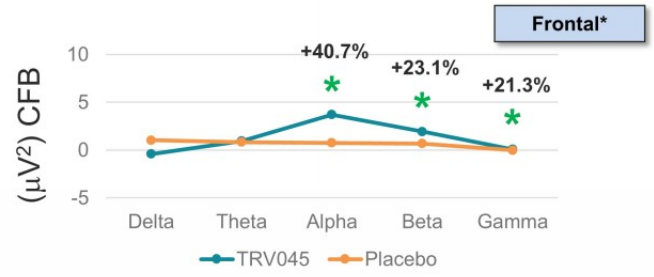
- TMS-EEG Pharmacodynamic endpoints:
  - Resting qEEG power spectral analysis (eyes open/eyes closed): Alpha, Beta, Delta, Gamma, Theta bands
  - TMS-evoked EEG response (single and paired-pulse TMS)

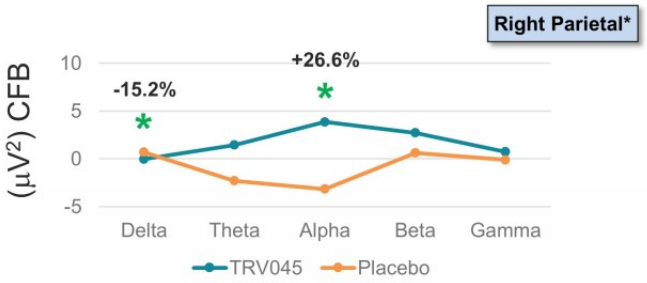
- TMS-EMG Pharmacodynamic endpoints:
  - Motor-evoked potential (MEP), resting motor threshold (single pulse TMS), paired-pulse TMS

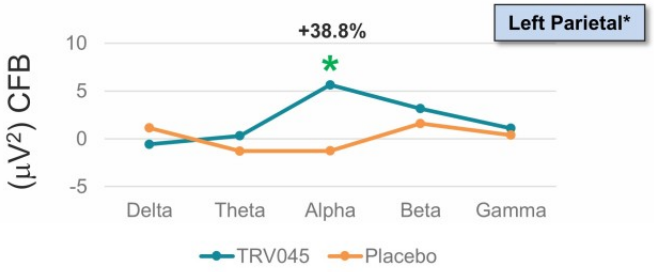
Studies were conducted outside the United States and not under the IND for TRV045
TMS = Transcranial magnetic stimulation
Source: Trevena data on file

EEG Shifts in Alpha, Beta, Gamma, Delta Power Spectra

Resting qEEG Power Spectral Analysis – Eyes Open, Day 4 TRV045 v Placebo All Bands







Alpha: Significant increase across all regions
Beta/**Gamma**: Significant increase in frontal region

Delta: Significant reduction in right parietal region
Theta: No significant difference

associated w
alertness / ar
memory / lea

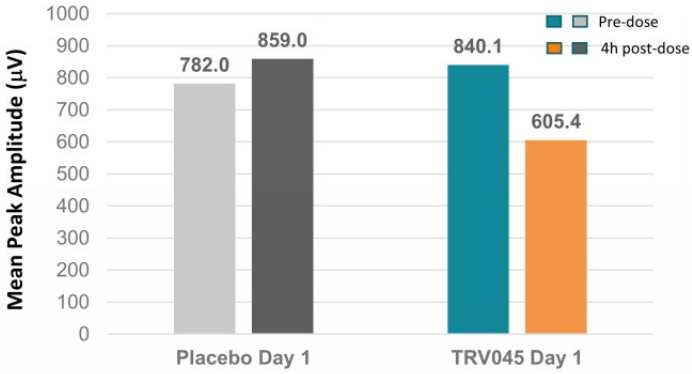
associated v
sedation / sl

* Denotes pairwise comparison P < 0.05
Frontal = Fz-Cz; left parietal = Pz-O1; right parietal = PzO2
CFB = change from baseline; Source: Trevena data on file

Mantini, D, et al. PNAS (2007); Beste, C, et al. Nature Comm Biol (2023);
Edwards, DJ and Trujillo, LT, Brain Sci (2021); Holler, Y, et al., CNS Drugs (20

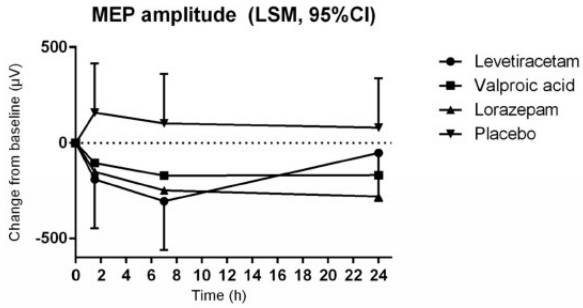
TRV045 Effect on Cortical Excitability vs AEDs*

Mean change from baseline in motor-evoked potential (MEP) measured by peak-to-peak amplitude



Est. difference TRV045 v placebo (not stat. sig.)

- -304.14 μV, 95% CI -688.19 to 79.919 (P=0.1182)



Estimated difference vs placebo:

- Levetiracetam: -378.4 μV, 95% CI -644.3 to -112.5; P<0.
- Valproic acid: -268.8 μV, 95% CI -532.9 to -4.6; P=0.047
- Lorazepam: -330.7.4 μV, 95% CI -595.6 to -65.8; P=0.02

Mean change from baseline in MEP on Day 1 with TRV045 comparable in magnitude to MEP reductions seen with known AEDs, including levetiracetam, valproic acid, and lorazepam, performed in the same laboratory

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* AEDs = Antiepileptic drugs
Source: Trevena data on file

Ruijs, TQ, et al. BJCP (2022) 88:2926-2937

Safety and Tolerability Summary

POC data generally consistent with FIH study

- No AEs assessed as probably / definitely related to study drug; no AEs reported as severe; no SAEs
  - 98% of AEs (102 of 104) in PainCart® study reported as mild
  - 99% of AEs (79 of 80) in TMS study reported as mild
- Screening / follow-up physical exams (including ophthalmologic exams) with no clinically significant findings
- Lab results showed **no drug-related**:
  - Reduction in total lymphocyte count
  - Changes in heart rate or blood pressure
  - Changes in ECG interval measures (no prolongation of PR or QTcF intervals)

Safety and Tolerability Summary

Generally well tolerated and consistent with FIH study

- AEs with incidence of ≥10% for any TRV045 dose shown below (none deemed drug related)

PainCart Study		Placebo		TRV045 50mg		TRV045 150mg		TRV045 300mg	
		N (%)	Events	N (%)	Events	N (%)	Events	N (%)	Events
General Disorders	Fatigue	3 (12%)	3	1 (4%)	1	3 (12%)	3	2 (8%)	2
Nervous System Disorders	Dizziness	2 (8%)	2	0	0	3 (12%)	3	3 (12%)	3
	Headache	2 (8%)	2	3 (12%)	3	8 (32%)	9	8 (32%)	9
	Somnolence	2 (8%)	3	2 (8%)	2	5 (20%)	5	8 (32%)	8

TMS Study		Placebo		TRV045 250mg	
		N (%)	Events	N (%)	Events
General Disorders	Fatigue	1 (4%)	3	3 (12%)	5
Nervous System Disorders	Headache	6 (22%)	8	9 (36%)	12
	Somnolence	4 (15%)	3	3 (12%)	4

- No clinically signficant difference (vs placebo) in any AEs including:
  - Sedation
  - Nausea
  - Balance Disorders
  - Dry Mouth
  - Attention Disturbances
  - Blurred Vision

FIH = First in human

Overall Conclusions

TRV045 Proof-of-Concept Study Program

Taken together, these two POC studies provide
strong support and direction for future development of TRV045

- **Target Engagement.** Demonstrated CNS penetration and target engagement
- **Neuropathic Pain.** Statistically significant, dose-dependent effect in validated model of neuropathic pain
- **Epilepsy.** Promising evidence of early reduction in cortical excitability

  Statistically significant ***increases*** in brain waves (alpha, beta, gamma) associated with arousal, alertness, cognitive processing, learning and memory

  Statistically significant ***decrease*** in delta brain waves, and ***no significant change*** in theta brain waves, which are both associated with sedation / sleep
- **Differentiated Profile.** Novel MOA; expected once-daily oral dosing; potentially effective with favorable safety / tolerability

Studies were conducted outside the United States and not under the IND for TRV045

TRV045: Broad Potential Applicability

Unique MOA Produces Compelling Profile

Potent and selective $S1P_1R$ target engagement
anti-inflammatory and nociceptive effects

No lymphopenia (in FIH study)
potentially limits other S1PR modulators

May avoid AEs associated with approved S1PR drugs
cardiac / pulmonary / ophthalmologic

Potential fields for development may include:

- **Seizure treatment** (anticonvulsant)
- **Prevention of seizure** (epileptogenesis) ← potential disease-modifying MOA
- **Pain** (DPN, CIPN)
- **Autoimmune** (MS, RA, UC, Crohn's Disease)
- **Neuropsychiatric / neurodegenerative** (MDD, schizophrenia, AD, PD)

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DPN: diabetic neuropathic pain; CIPN: chemotherapy-induced peripheral neuropathy; MS: multiple sclerosis; RA: rheumatoid arthritis; MDD: major depressive disorder; AD: Alzheimer's disease; PD: Parkinson's disease

Trevena: Innovative CNS Company

IV OLINVYK: Differentiated profile	NCE approved for the management of acute pain in adults* Significant cost savings / differentiation shown in 'real world' post-approval studies
TRV045: Selective S1PR modulator	**S1PR:** Validated target for blockbusters (fingolimod / siponimod / ozanimod / ponesimod) **TRV045:** Unique profile (with potential for no lymphopenia) for new indications
TRV045: Compelling PoC Data	Statistically significant, dose-dependent effect in validated model of neuropathic pain Statistically significant EEG changes and evidence of early reduction in cortical excitability
Novel CNS pipeline	New mechanisms for acute / neuropathic pain, epilepsy, acute migraine, opioid use disorder NCEs targeting significant unmet needs
Financial position	$33.0M cash and equivalents as of YE 2023

*OLINVYK 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. Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com

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NCE = New Chemical Entity; PoC = Proof of concept

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IMPORTANT SAFETY INFORMATION

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.

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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 treatm are inadequate.

Limitations of Use

Because of the risks of addiction, abuse, and misuse with opi which can occur at any dosage or duration, reserve OLINVYK use in patients for whom alternative treatment options [e.g., n opioid analgesics or opioid combination products]:

- Have not been tolerated or are not expected to be tolerat
- Have not provided adequate analgesia or are not expecte 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 sett in absence of resuscitative equipment
- Known or suspected gastrointestinal obstruction, includir 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 pulmo 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 d 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 fashi 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 non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, or alcohol). Because of risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate, prescribe the lowest effective dose 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 sig neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using opioids for a prolonged period of the risk of neonatal opioid withd 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 exceedi 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 modera strong CYP2D6 inhibitors; also in patients taking a moderate or strong CYP3A4 inhibitor, in patients with decreased CYP2D6 function who are also receiving a moc or strong CYP3A4 inhibitor, or with discontinuation of a CYP3A4 inducer. These patients may require less frequent dosing and should be closely monitored for respi depression and sedation at frequent intervals. Concomitant use of OLINVYK with CYP3A4 inducers or discontinuation of a moderate or strong CYP3A4 inhibitor can 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 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 increase, decreased levels of pain upon dose decrease, or pain from ordinarily non-painful stimuli (allodynia). These symptoms may suggest OIH only if there evidence of disease progression, opioid tolerance, withdrawal, or addictive behavior. If OIH is suspected, carefully consider appropriately decreasing the dose current opioid analgesic or opioid rotation.

WARNINGS AND PRECAUTIONS

- 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.

Trevena®

ADVERSE REACTIONS

Adverse reactions are described in greater d
the Prescribing Information.

The most common (incidence ≥10%) adverse
reactions in Phase 3 controlled clinical trials
nausea, vomiting, dizziness, headache,
constipation, pruritus, and hypoxia.

MEDICAL INFORMATION

For medical inquiries or to report an adverse
other safety-related information or product
complaints for a company product, please co
the Trevena Medical Information Contact Cer
1-844-465-4686 or email MedInfo@Trevena.

You are encouraged to report suspected adv
events of prescription drugs to the FDA. Visit
www.fda.gov/medwatch or call 1-800-FDA-1(

PLEASE see www.OLINVYK.com for full prescribing information including BOXED warning and important safety information