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): **September 6, 2023**

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 7.01 Regulation FD Disclosure

On September 6, 2023, Trevena, Inc. (the "Company") updated its website to include an updated corporate presentation deck. A copy of the updated corporate deck is attached hereto as Exhibit 99.1.

Also on September 6, 2023, the Company updated its website to include a revised TRV045 overview deck. A copy of the TRV045 overview deck is attached hereto as Exhibit 99.2.

The information set forth on this Item 7.01 and furnished hereto as Exhibits 99.1 and 99.2 shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, and is not 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 hereof, except as shall be expressly set forth by specific reference in any such filing.

Item 8.01 Other Events.

On September 6, 2023, Trevena, Inc. (the "Company") issued two press releases. The first press release announced new preliminary data from the two Phase 1 proof-of-concept studies of TRV045. TRV045 is a novel sphingosine-1-phosphate receptor modulator selective for the S1P receptor subtype 1. The first study was the Target Engagement (PainCart®) proof-of-concept study, and the second study was the TMS proof-of-concept study. A copy of the first press release with more detail about both studies is furnished hereto as Exhibit 99.3 and incorporated herein by reference.

The Company's second press release announced, among other things, receipt of the $15 million tranche from its non-dilutive financing with R-Bridge Investment Four Pte. Ltd., an affiliate of CBC Group, as well as other general business updates. A copy of the second press release is furnished hereto as Exhibit 99.4 and incorporated herein by reference.

The information set forth in this Item 8.01 and furnished hereto as Exhibit 99.3 and 99.4 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 9.01. Financial Statements and Exhibits.

(d) Exhibits

Number	Description
99.1	Corporate Presentation Deck dated September 6, 2023
99.2	TRV045 Overview Deck dated September 6, 2023
99.3	Press Release dated September 6, 2023
99.4	Press Release dated September 6, 2023
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: September 6, 2023

By: /s/ Barry Shin
Barry Shin
Senior Vice President & Chief Financial Officer

Exhibit 99.1


Trevena®
INNOVATING FOR PATIENTS
Nasdaq: TRVN I September 2023

Forward-Looking Statements

To the extent that statements contained in this presentation are not descriptions of historical facts regarding Trevena, Inc. (the "Company" or "we"), they are forward-looking statements reflecting management's current beliefs and expectations. Forward-looking statements are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry's actual results, levels of activity, performance, or achievements to be materially different from those anticipated by such statements. You can identify forward-looking statements by terminology such as "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "objective," "predict," "project," "suggest," "target," "potential," "will," "would," "could," "should," "continue," "ongoing," or the negative of these terms or similar expressions. Forward-looking statements contained in this presentation include, but are not limited to, (i) statements regarding the timing of anticipated clinical trials for our product candidates; (ii) the timing of receipt of clinical data for our product candidates; (iii) our expectations regarding the potential safety, efficacy or clinical utility of our product candidates; (iv) the size of patient populations targeted by our product candidates and market adoption of our potential drugs by physicians and patients; (v) the timing or likelihood of regulatory filings and approvals; and (vi) our cash needs.

Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the commercialization of any approved drug product, the status, timing, costs, results and interpretation of our clinical trials or any future trials of any of our investigational drug candidates; the uncertainties inherent in conducting clinical trials; expectations for regulatory interactions, submissions and approvals, including our assessment of the discussions with the FDA or other regulatory agencies about any and all of our programs; uncertainties related to the commercialization of OLINVYK; available funding; uncertainties related to our intellectual property; other matters that could affect the availability or commercial potential of our therapeutic candidates; and other factors discussed in the Risk Factors set forth in our 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 we make with the SEC from time to time. In addition, the forward-looking statements included in this presentation represent our views only as of the date hereof. We anticipate that subsequent events and developments may cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so, except as may be required by law.

Trevena's Experienced Leadership Team

SENIOR MANAGEMENT

Carrie L. Bourdow	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	SVP, Chief Financial Officer	MIZUHO, GUGGENHEIM, PiperJaffray
Robert T. Yoder	SVP, Chief Business Officer & Head of Commercial Operations	MERCK, OREXIGEN

BOARD OF DIRECTORS

Leon O. Moulder, Jr. Chairman	TESARO, MGi PHARMA	**Marvin H. Johnson, Jr.**	MERCK
Carrie L. Bourdow	Trevena	**Jake R. Nunn**	NEA., SR One
Scott Braunstein, M.D.	MARINUS PHARMACEUTICALS, AISLING CAPITAL, PACIRA BIOSCIENCES, INC.	**Anne M. Phillips, M.D.**	novo nordisk, GlaxoSmithKline
Mark Corrigan, M.D.	TREMEAU PHARMACEUTICALS, SEPRACOR	**Barbara Yanni**	MERCK
Michael R. Dougherty	Adolor, centocor		

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 (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	$28.1M cash / equivalents / marketable securities @ 2Q 23 $15M non-dilutive tranche received 3Q 23 (ex-US royalty based financing)

*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 a the end of presentation. Full Prescribing Information at www.OLINVYK.com.

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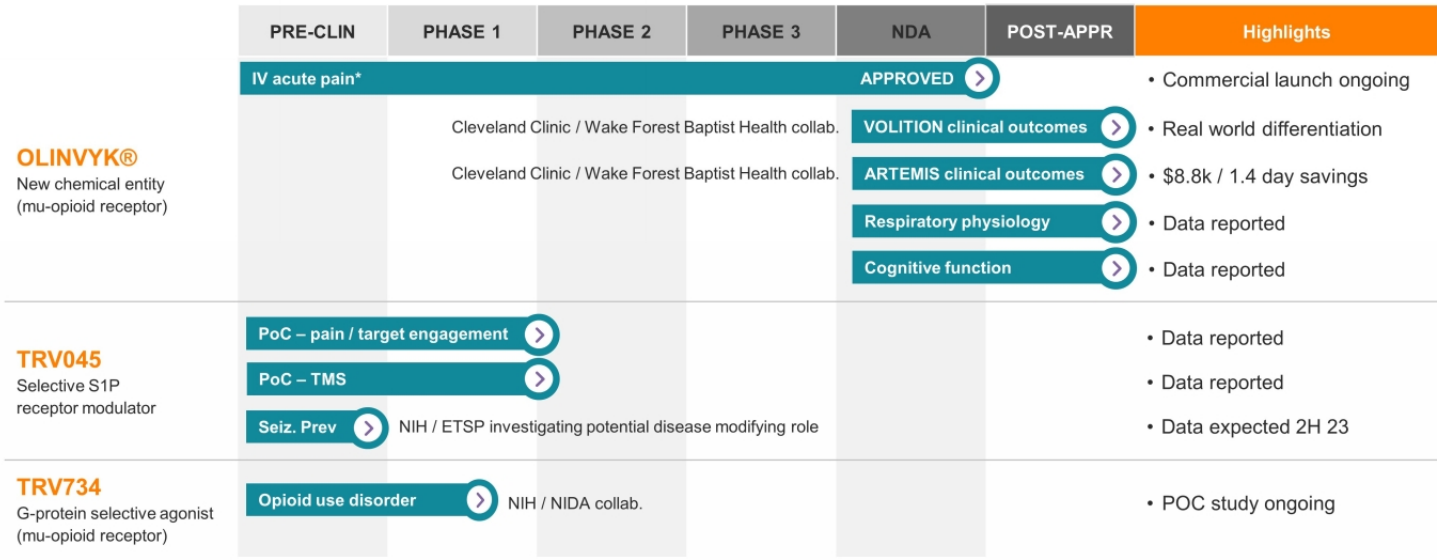
PoC = Proof of concept, NCE = New Chemical Entity; MOA = Mechanism of Action; NIH = National Institutes of Health

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.

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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, DNP = Diabetic Neuropathic Pain

Ex-US Royalty-Based Financing Highlights

Blue Chip Investor	**R-Bridge Healthcare Fund** affiliate of CBC Group (one of the largest and most active healthcare-dedicated investment firms in Asia)
$40M Total Financing	Received 3Q 23 [**$15M** upfront **$15M** on first commercial sale in China **$10M** on commercial or financing milestone **$40M total**
Flexible Payments*	• **Chinese Royalties.** All royalties from Nhwa partnership, TRVN retains milestones • **Capped US Royalty.** 4% royalty on US OLINVYK net sales, with $10M cap
Constructive Terms	• No financial covenants

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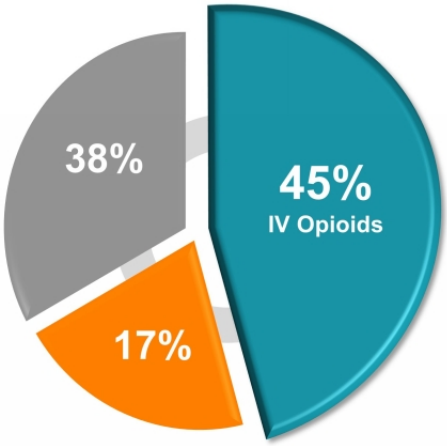
OLINVYK Overview

Large Market Opportunity – Acute Pain

US injectable analgesic hospital market unit volume[1]



- IV opioids
- Local anesthetics
- IV NSAIDS / acetaminophen

45M patients receive IV opioi annually to treat acute pain

IV opioids have unrivalled analgesic efficacy

Top surgeries:
Total knee arthroplasty, colectomy, hernia repair, spine fusion, C-section[2]

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. Opioids are associated with serious, potentially life-threatening adverse reactions.

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NSAIDs = nonsteroidal anti-inflammatory drugs. 1) IMS MIDAS sales audit 2017; IV NSAIDs and Ofirmev®. 2) Definitive database, and National Vital Statistics report, CDC 2018.

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

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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
- Initial topline data reported 1Q 23

Respiratory Outcomes

Assessment via continuous respiratory monitoring

(data expected 3Q 23)

GI Tolerability

52.2% 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)

Cognitive Function

90%+ alert / calm at all observation points[2]

<4% symptoms of delirium[3]

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

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

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

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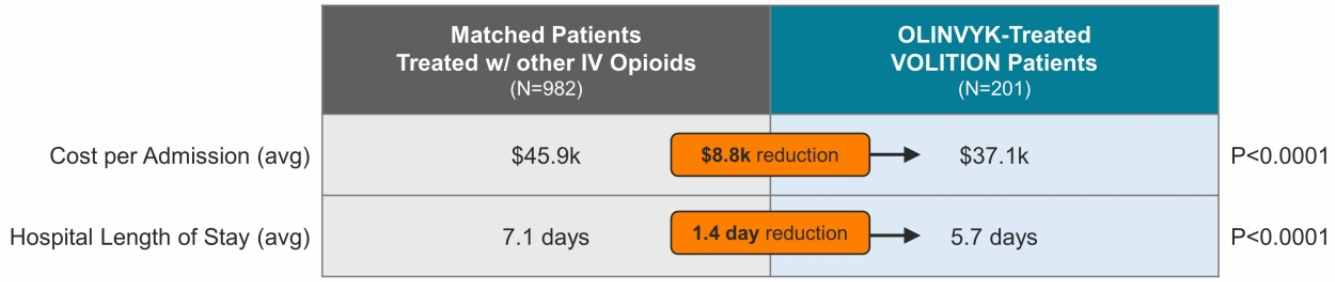
ARTEMIS – EMR Clinical Outcomes Study

OLINVYK electronic medical records (EMR) study at VOLITION sites

- **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
  - Based on 8 demographic/clinical characteristics (age, sex, type/duration of surgery, overall surgical/medical morbidity, insurance)



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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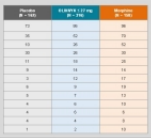
OLINVYK vs IV Morphine Health Economic Models

Published[1] and available to formulary committees

Representative Inputs:

AE rates*

Ph3 trials



Vomiting
Somnolence / sedation
O_2 saturation <90%

Cost of AEs

Gov't sources / Publications

$8k nausea / vomiting[2]
$28k critical resp event[3]
+7 days hospital stay[3]

Drug cost

OLINVYK
IV morphine

HECON model

Key Outputs:

>10x
Cost savings for hospitals[4]

Due to improved patient outcomes

*** As stated in the label these data are not an adequate basis for comparison of rates between OLINVYK treatment group and the morphine treatment group. The OLINVYK and morphine dosing regimens studied are not considered equipotent.**

1) Simpson KN, et al., J Comp Eff Res, 2021*; 10:1107-1119* and *Simpson KN, et al. Expert Rev Pharmacoecon Outcomes Res; 2022*
2) Oderda, GM, J Pain Palliative Care Pharm, 2019; data based on 5 surgical procedure categories including Cardiothoracic / vascular, General / Colorectal, Ob / Gyn, Orthopedic, and Urologic. 3) Overdyk FJ, PLoS One, 2016. More conservative inputs were used in the model. 4) Calculated based on total costs of Tx and average total costs of care. Image: flaticon.com.

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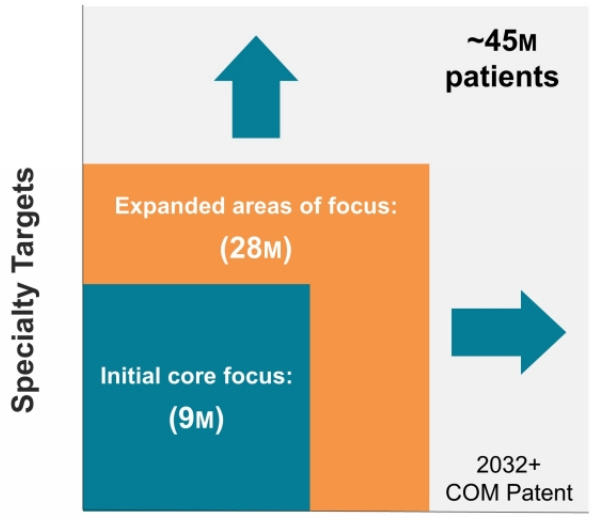
OLINVYK: Significant Opportunity in Acute Pain Market



~15M days of therapy (initial focus)
=
$1.5B+ market opportunity*

Core focus

- Ambulatory surgical centers
- Hospitals

Expanded areas of focus

- New cognitive function / respiratory / GI data versus IV morphine
- Additional HECON data focused on recovery time

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

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Source: Definitive Healthcare; American Hospital Association. *Assumes ~$100 / day price for OLINVYK

2032 composition of matter patent expiration does not include potential patent extensions.

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TRV045

S1P Receptor Modulator

Novel MOA for Diabetic Neuropathic Pain

$S1P_1$ 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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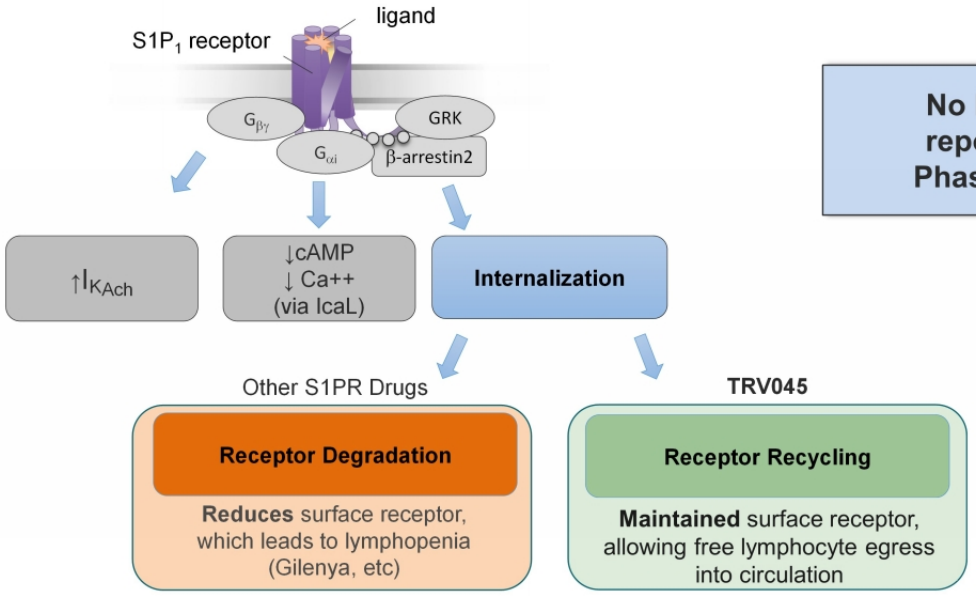
1) Sim-Selley et al., Journal of Pharmacology & Experimental Therapeutics, 2018. 2) Sim-Selley et al, Journal of Neurochemistry, 2008. 3) Gol et al., European Journal of Pharmaceutical Sciences, 2017. 4) Leo et al, CNS & Neurological Disorders - Drug Targets, 2017. 5) Choi, et al. PNAS 2011.

TRV045 MOA: Rapid Receptor Recycling

Maintained (rather than degraded) S1P receptors on cell surface



No lymphopenia reported in prior Phase 1 FIH study

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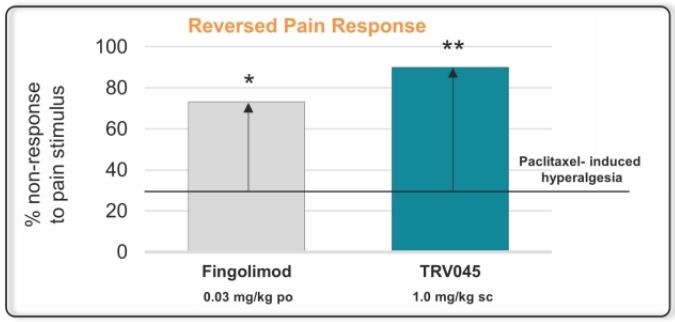
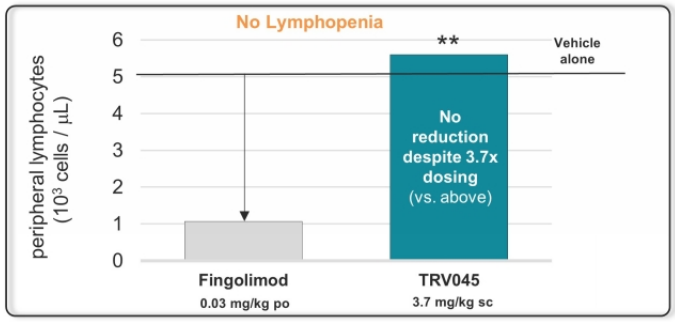
FIH = First in human

Source: Trevena data on file

TRV045 Efficacy in Nonclinical Chronic Pain Models (w/ no Lymphopenia)

Mouse chemotherapy-induced peripheral neuropathy (CIPN) model





Reversed neuropathic pain…

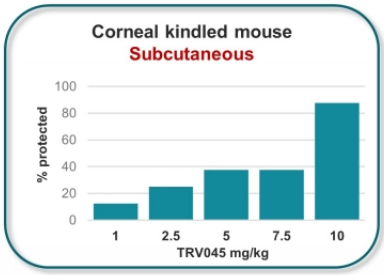
…with no lymphopenia

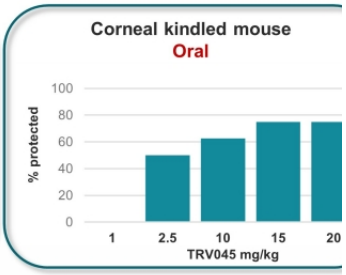
Source: Trevena data on file

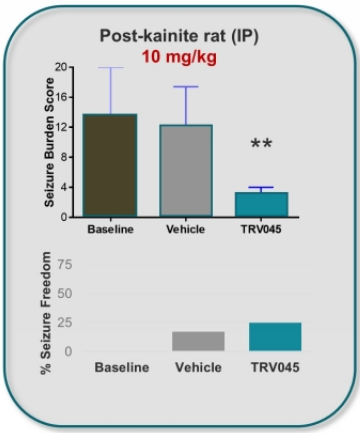
1) CIPN mouse model: Paclitaxel 6 mg/kg, i.p. on Days 1, 3, 5, 7. Hyperalgesia measured as % non-response to 0.4 g Von Frey filament vs. baseline, tested 30' after dosing on Day 13. Lymphocytes measured after 3 days of dosing. Data are mean ± s.e.m. n=5-7 mice/group. *p<0.05 or **p<0.01 vs. control

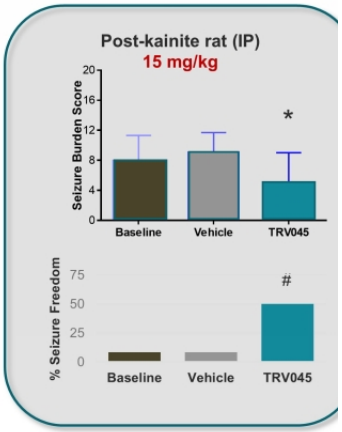
TRV045 Demonstrates Efficacy in Nonclinical Epilepsy Models

- NIH-supported Epilepsy Therapy Screening Program
- Acute seizure protection in max. electroshock model
  - Replicated in 3 independent experiments using either subcutaneous or oral administration
- Efficacy demonstrated in two different preclinical models of epilepsy (*data shown at right*)
  - Corneal-kindled seizure model (SC, PO)
    - Dose-dependent protection in seizure risk across two studies
  - Post-kainite spontaneous recurrent seizure model (IP*)
    - Dose-dependent reduction in seizure burden and increase in seizure freedom endpoints across two studies









Trevena® Data on file, Trevena, Inc., 2022; * IP = intraperitoneal

* p<0.05 v vehicle, ** p<0.05 v baseline; Wilcoxon rank sum
# p<0.05 v baseline and vehicle; Fisher's exact test

TRV045 Phase 1 Study – Safety / Tolerability / PK

Randomized, double-blinded, placebo-controlled study
3-parts: single dose (n=53), food effect (n=27), multiple dose (n=9)

Well Tolerated	• Favorable tolerability profile with no SAEs
Target Exposure	• Calculated free plasma concentrations exceeded targeted efficacy range[1]
Attractive PK Profile	• Half-life consistent with anticipated once-daily dosing
Highly Differentiated	• No lymphopenia and no reported cardiac / pulmonary / ophthalmologic AEs (AEs commonly associated with currently marketed S1P-targeted compounds)

[1] Based on nonclinical measures of in vitro and in vivo PD

POC Studies: Target Engagement / TMS

Target Engagement Study

Randomized, double-blind, placebo-controlled, 4x cross-over
(n=25 subjects)

Placebo or TRV045
(50 / 150 / 300mg)

PainCart® endpoints

TMS Study

Randomized, double-blind, placebo-controlled, multiple dose, 2x cross-over
(n=25 subjects)

Placebo or TRV045
(250mg / four days)

EEG / EMG endpoints

Results confirm activity of central action and
support advancement for neuropathic pain and other CNS indications

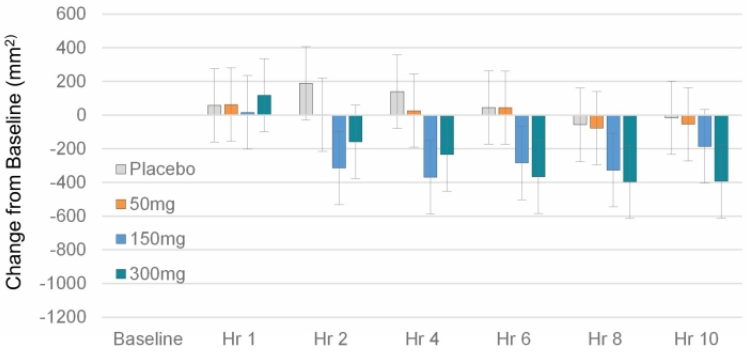
Studies were conducted outside the United States and not under the IND for TRV045

TE Study: Significantly Reduced Mechanical Allodynia

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

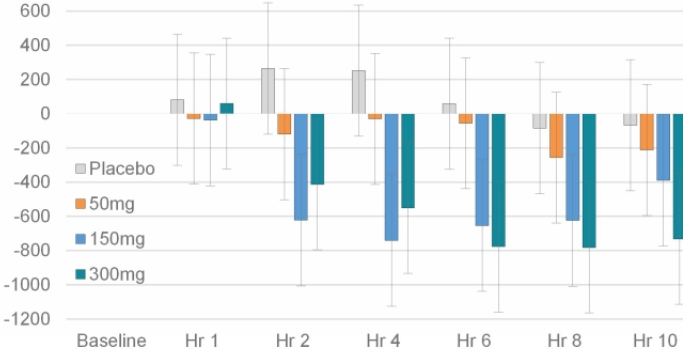
300mg TRV045 v Placebo; P=0.0023
150mg TRV045 v Placebo; P=0.0022

Secondary Allodynic Area



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

Total Allodynic Area



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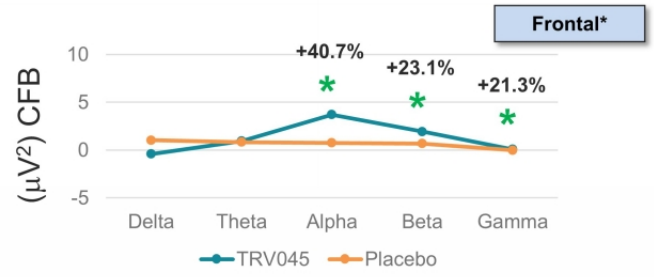
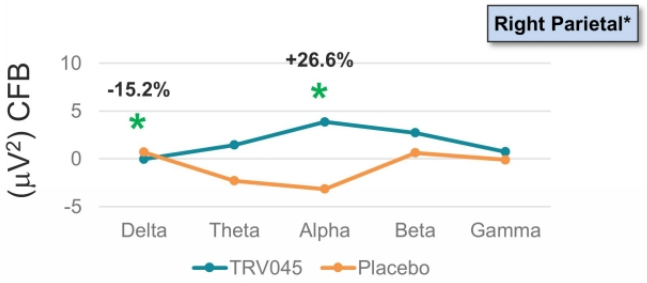
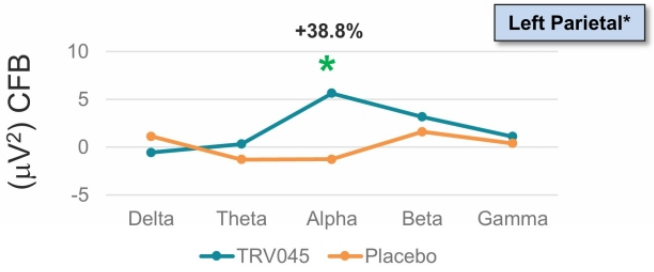
Source: Trevena data on file

TMS Study: Effect on Brain Wave Activity

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

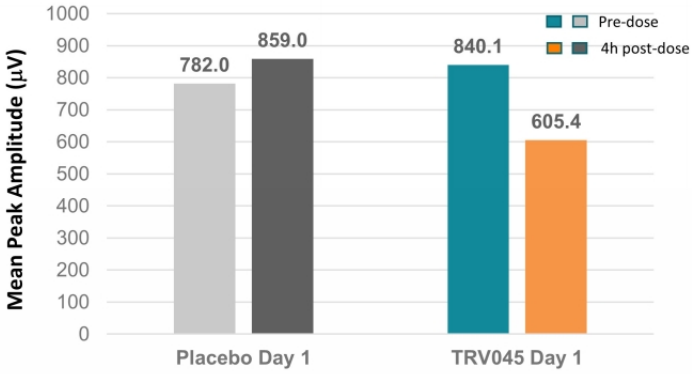
associated v
sedation / sl

* 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

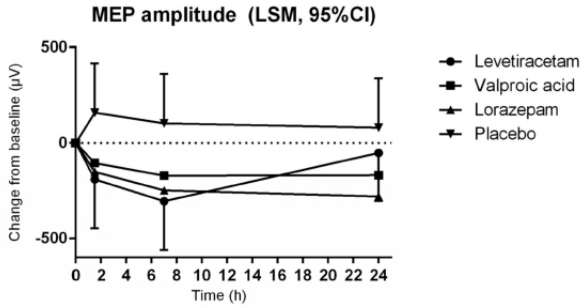
TMS Study: Effect on Cortical Excitability vs AEDs*

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

Overall TRV045 POC Study 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
- **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, which are both associated with sedation / sleep
- **Cortical Excitability.** Promising evidence of early reduction in cortical excitability

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

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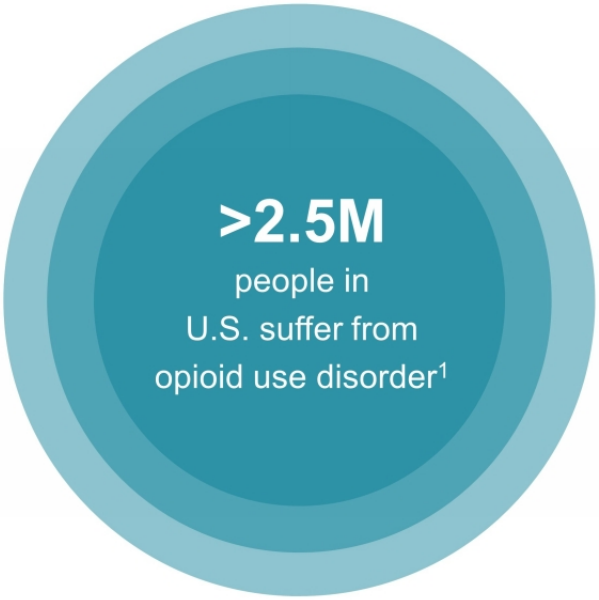
TRV734: Maintenance Therapy for Opioid Use Disorder

TRV734: Maintenance Therapy for Opioid Use Disorder

Selective agonism at μ receptor: nonclinical evidence of improved tolerability



Ongoing collaboration with National Institute on Drug Abuse (NIDA)

NIDA study demonstrated reduced drug-seeking behavior in animal model of relapse[2]

NIDA-funded proof-of-concept patient study initiated

- Randomized, double-blind, placebo- and positive-controlled study
- N = ~50 opioid-dependent patients undergoing stable methadone maintenance therapy
- **Primary endpoint:** suppression of withdrawal symptoms as measured by the Subjective Opioid Withdrawal Scale
- **Secondary outcomes:** assessments of safety, tolerability, and neurocognitive changes

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1) Center for Behavioral Health Statistics and Quality. 2) NIDA data on file.

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 (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	$28.1M cash / equivalents / marketable securities @ 2Q 23 $15M non-dilutive tranche received 3Q 23 (ex-US royalty based financing)

*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 a the end of presentation. Full Prescribing Information at www.OLINVYK.com.

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PoC = Proof of concept, NCE = New Chemical Entity; MOA = Mechanism of Action; NIH = National Institutes of Health

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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 a new chemical entity 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 OLI for use in patients for whom alternative treatment options [e.g., non-opioid analgesics or opioid combinatio 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 incre 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 equipmer
- 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 a 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 u recommended, especially in patients with chronic pulmonary disease, or in elderly, cachectic and debil patients. The risk is greatest during initiation of OLINVYK therapy, following a dose increase, or whe with other drugs that depress respiration. Proper dosing of OLINVYK is essential, especially when con patients from another opioid product to avoid overdose. Management of respiratory depression may inc close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinic status.
- Opioids can cause sleep-related breathing disorders including central sleep apnea (CSA) and sleep-rela hypoxemia with risk increasing in a dose-dependent fashion. In patients who present with CSA, consic decreasing the dose of opioid using best practices for opioid taper.

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WARNINGS AND PRECAUTIONS

- 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.
- There is increased risk in patients whose ability to maintain blood pressure has already been compromis 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 cardia output and blood pressure.
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- 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 t risk of seizures in vulnerable patients. Monitor patients with a history of seizure disorders for worsene seizure control.
- Do not abruptly discontinue OLINVYK in a patient physically dependent on opioids. Gradually taper t dosage to avoid a withdrawal syndrome and return of pain. Avoid the use of mixed agonist/antagonist (pentazocine, nalbuphine, and butorphanol) or partial agonist (e.g., buprenorphine) analgesics in patient 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 activiti such as driving a car or operating machinery.
- Although self-administration of opioids by patient-controlled analgesia (PCA) may allow each patient t 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 monitorin patients receiving PCA analgesia should be instructed in the need for appropriate monitoring for excess 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.

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

Exhibit 99.2


Trevena®
INNOVATING FOR PATIENTS
Nasdaq TRVN I September 2023

Forward-Looking Statements

To the extent that statements contained in this presentation are not descriptions of historical facts regarding Trevena, Inc. (the "Company" or "we"), they are forward-looking statements reflecting management's current beliefs and expectations. Forward-looking statements are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry's actual results, levels of activity, performance, or achievements to be materially different from those anticipated by such statements. You can identify forward-looking statements by terminology such as "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "objective," "predict," "project," "suggest," "target," "potential," "will," "would," "could," "should," "continue," "ongoing," or the negative of these terms or similar expressions. Forward-looking statements contained in this presentation include, but are not limited to, (i) statements regarding the timing of anticipated clinical trials for our product candidates; (ii) the timing of receipt of clinical data for our product candidates; (iii) our expectations regarding the potential safety, efficacy, or clinical utility of our product candidates; (iv) the size of patient populations targeted by our product candidates and market adoption of our potential drugs by physicians and patients; (v) the timing or likelihood of regulatory filings and approvals; and (vi) our cash needs.

Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the commercialization of any approved drug product, the status, timing, costs, results and interpretation of our clinical trials or any future trials of any of our investigational drug candidates; the uncertainties inherent in conducting clinical trials; expectations for regulatory interactions, submissions and approvals, including our assessment of the discussions with the FDA or other regulatory agencies about any and all of our programs; uncertainties related to the commercialization of OLINVYK; available funding; uncertainties related to our intellectual property; other matters that could affect the availability or commercial potential of our therapeutic candidates; and other factors discussed in the Risk Factors set forth in our 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 we make with the SEC from time to time. In addition, the forward-looking statements included in this presentation represent our views only as of the date hereof. We anticipate that subsequent events and developments may cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so, except as may be required by law.

Trevena Overview

Focused on Innovative Medicines For CNS Disorders

Detailed in Following Slides

Olinvyk IV*	S1P Modulator Program	Innovative CNS Pipeline
Approved NCE for the management of acute pain in adults*	**Novel $S1P_1R$ modulator with differentiated MOA** (lead asset: TRV045)	**Based on Nobel-prize winning biased ligand technology**
Proven track record of Trevena internal discovery and development through approval	Preliminary data from proof-of-concept studies for CNS disorders	NCEs addressing acute / neuropathic pain, epilepsy, acute migraine, OUD[1]

* 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.

[1] OUD = opioid use disorder

TRV045: Innovative Clinical-Stage $S1P_1R$ Modulator

TRV045: Selective S1PR Modulator	**S1PR:** Validated target for multiple blockbusters (fingolimod / siponimod / ozanimod / ponesimod) **TRV045:** Unique profile ($S1P_1R$ specific, receptor recycling, no lymphopenia) for new indications
Compelling Clinical 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
Large Addressable Target Indications	Initial investigation for orphan / non-orphan **non-opioid chronic pain** and **epilepsy** Broad potential application in CNS disorders, autoimmune disease and inflammatory disease
Strong MOA Support	Nonclinical models demonstrated positive efficacy outcomes, avoiding known S1PR safety issues **NIH collaboration**: Epilepsy Therapy Screening Program & Preclinical Screening Pain Platform
Novel Family of S1PR Modulators	New chemical entity; potent and selective for subtype 1; developed in-house with strong IP Platform of S1PR backup opportunities for longer term value creation

$S1P_1$ 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]

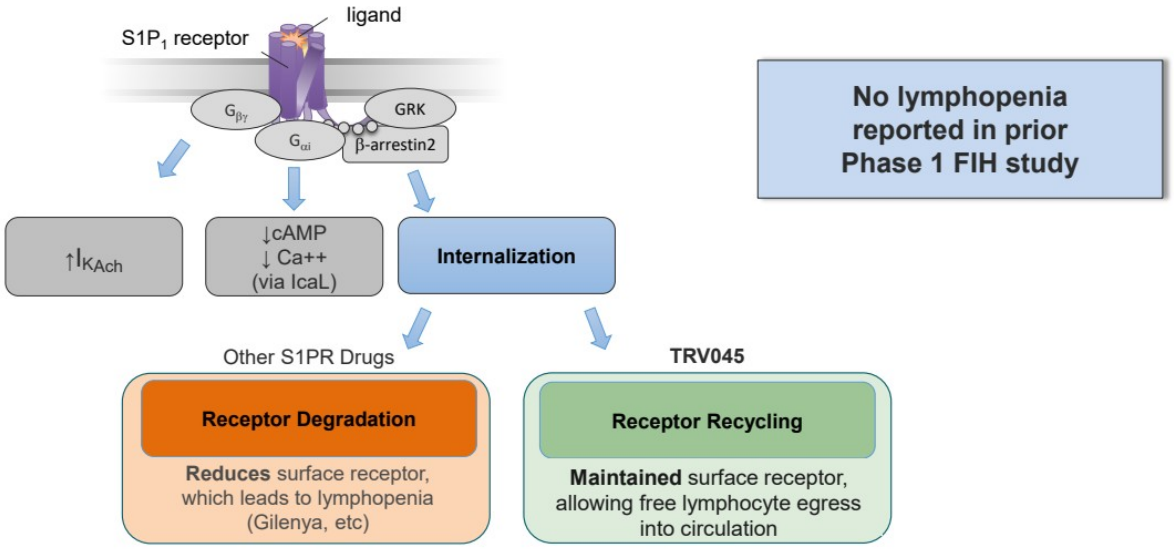
Existing S1PR-targeted drugs, however, are ill-suited for CNS indications due to known:

Lymphopenia
Cardiac AEs
Pulmonary AEs
Ophthalmologic AEs

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



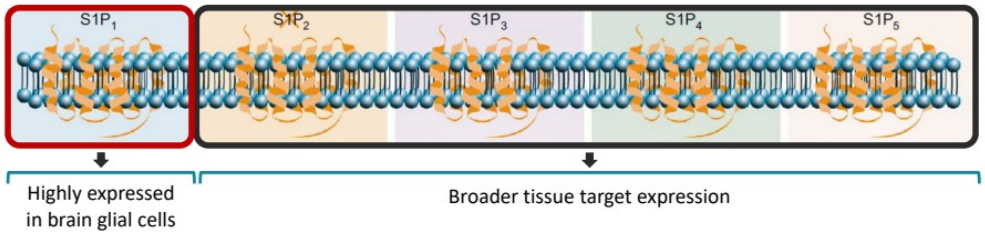
FIH = First in human
Source: Trevena data on file

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

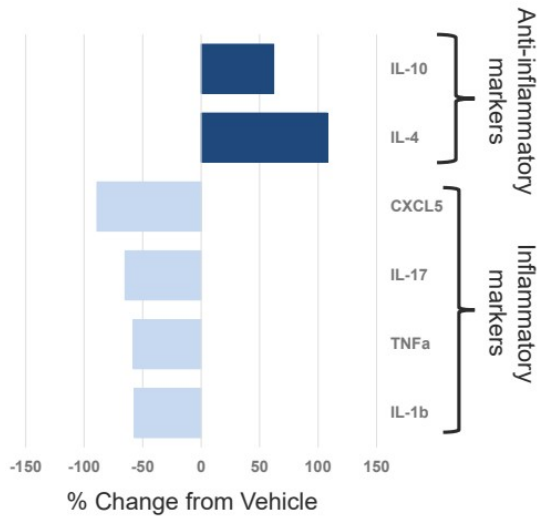
TRV045 MOA (3): Anti-Inflammatory Effect (nonclinical)

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

Preliminary data*

- **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

TRV045 POC Study Program – Overall Objectives

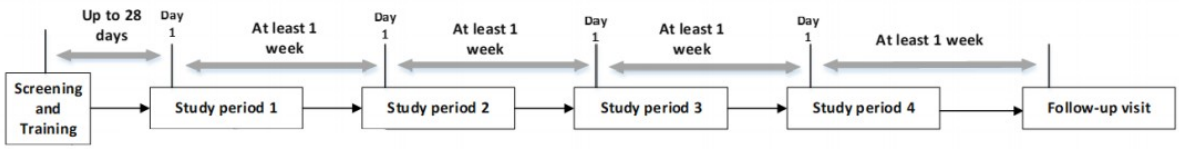
Preliminary data*

- Provide evidence of CNS penetration and target engagement via pharmacodynamic effects on validated experimental study endpoints in humans, using:
  - Battery of acute and chronic pain models (characterize 'analgesic phenotype' for TRV045)
  - EEG and EMG measures of changes in resting state brain electrical activity on and off drug and TMS-stimulated brain cortical excitability
- Provide PK-PD exposure data to guide future formulation development efforts and dose range selection for future Phase 2 studies
  - Prior phase 1 data demonstrated PK profile consistent with anticipated once-daily dosing
- Provide additional safety and tolerability data to support results of initial Phase 1 FIH study
  - No lymphopenia
  - No cardiovascular signals of concern
  - No evidence of ophthalmologic, pulmonary adverse effects

* Complete safety and tolerability data expected early 4Q 2023
Studies were conducted outside the United States and not under the IND for TRV045
Source: Trevena data on file

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

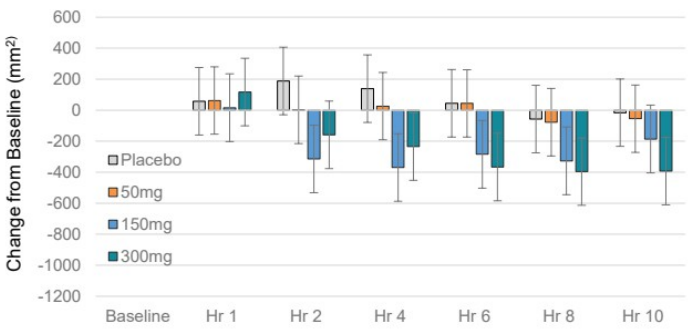
Studies were conducted outside the United States and not under the IND for TRV045
Source: Trevena data on file

TRV045 Significantly Reduced Mechanical Allodynia

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

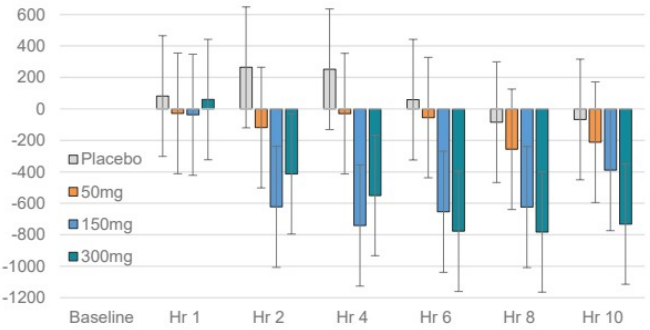
300mg TRV045 v Placebo; P=0.0023
150mg TRV045 v Placebo; P=0.0022

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

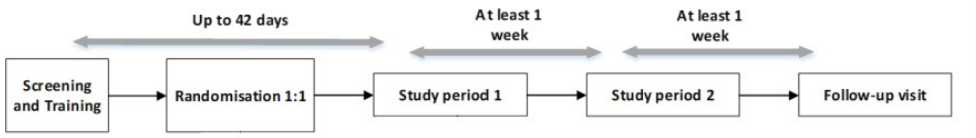
Target Engagement (PainCart®) Study

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 for 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 study
- No SAEs, no drug-related study discontinuations; full safety and tolerability data expected early 4Q 23

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



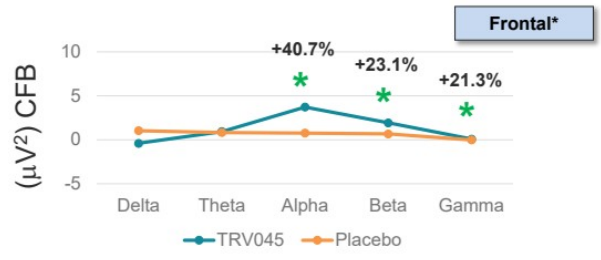
- TMS-EEG Pharmacodynamic endpoints:
  - Resting qEEG power spectral analysis (eyes open/eyes closed): Alpha, Beta, Delta, Gamma, Theta bands
  - TMS-evoked EEG response (single and paired-pulse TMS)

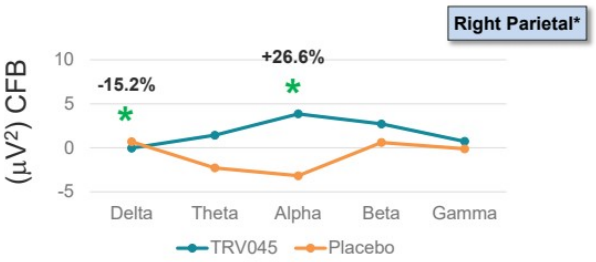
- TMS-EMG Pharmacodynamic endpoints:
  - Motor-evoked potential (MEP), resting motor threshold (single pulse TMS), paired-pulse TMS

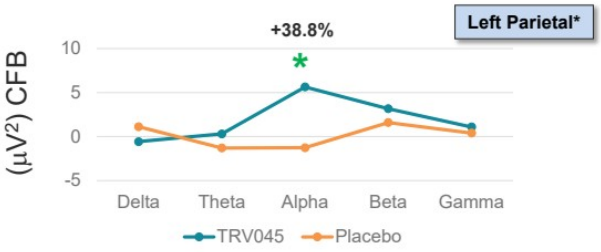
Studies were conducted outside the United States and not under the IND for TRV045
TMS = Transcranial magnetic stimulation
Source: Trevena data on file

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

associated with alertness / arousal memory / learning

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

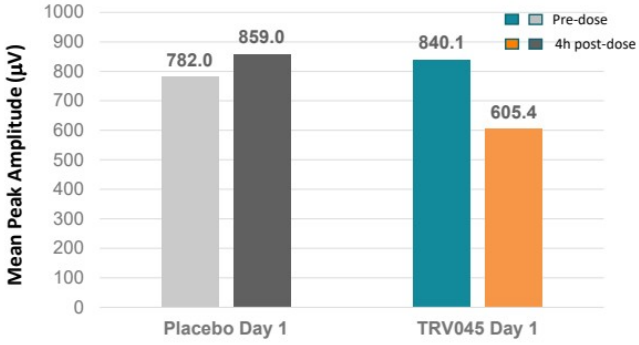
associated with sedation / sleep

* 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 (2018)[15]

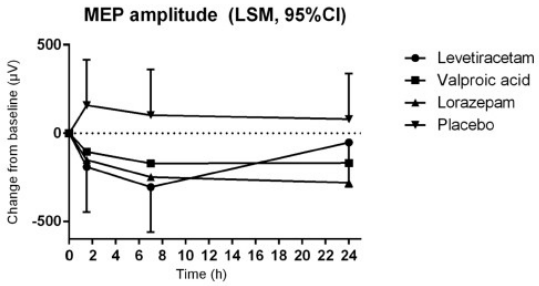
TRV045 Effect on Cortical Excitability vs AEDs*

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<0.01
- 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

Overall TRV045 POC Study Conclusions

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
- **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, which are both associated with sedation / sleep
- **Cortical Excitability.** Promising evidence of early reduction in cortical excitability

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)

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

TRV045: Innovative Clinical-Stage $S1P_1R$ Modulator

TRV045: Selective S1PR Modulator	**S1PR:** Validated target for multiple blockbusters (fingolimod / siponimod / ozanimod / ponesimod) **TRV045:** Unique profile ($S1P_1R$ specific, receptor recycling, no lymphopenia) for new indications
Compelling Clinical 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
Large Addressable Target Indications	Initial investigation for orphan / non-orphan **non-opioid chronic pain** and **epilepsy** Broad potential application in CNS disorders, autoimmune disease and inflammatory disease
Strong MOA Support	Nonclinical models demonstrated positive efficacy outcomes, avoiding known S1PR safety issues **NIH collaboration**: Epilepsy Therapy Screening Program & Preclinical Screening Pain Platform
Novel Family of S1PR Modulators	New chemical entity; potent and selective for subtype 1; developed in-house with strong IP Platform of S1PR backup opportunities for longer term value creation

TRV045

Prior FIH Phase 1 Study

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TRV045 Phase 1 Study – Safety / Tolerability / PK

Randomized, double-blinded, placebo-controlled study
3-parts: single dose (n=53), food effect (n=27), multiple dose (n=9)

Well Tolerated	• Favorable tolerability profile with no SAEs
Target Exposure	• Calculated free plasma concentrations exceeded targeted efficacy range[1]
Attractive PK Profile	• Half-life consistent with anticipated once-daily dosing
Highly Differentiated	• No lymphopenia and no reported cardiac / pulmonary / ophthalmologic AEs (AEs commonly associated with currently marketed S1P-targeted compounds)

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[1] Based on nonclinical measures of in vitro and in vivo PD

TRV045

Nonclinical Data - Epilepsy

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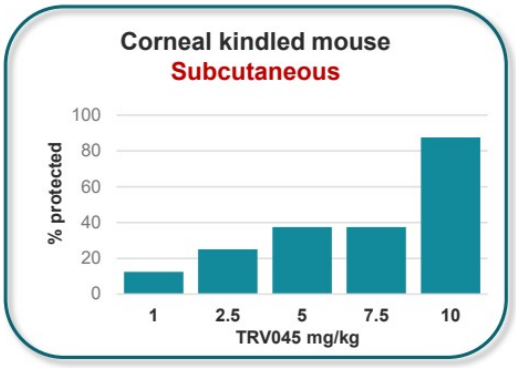
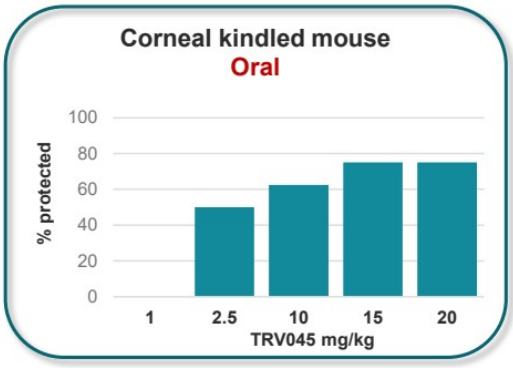
TRV045: Dose Dependent Seizure Protection (nonclinical)

Corneal-kindled Seizure Model

TRV045 demonstrated
dose-dependent protection in seizure risk
in corneal-kindled seizure models

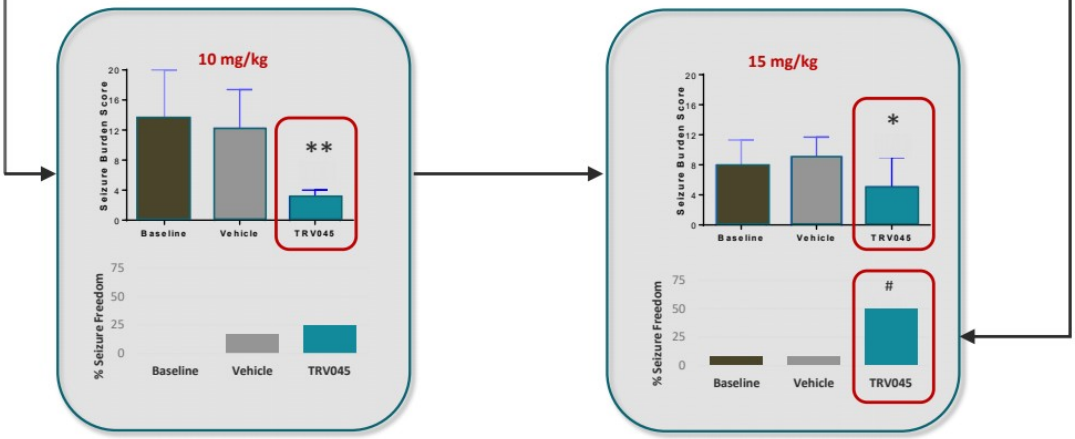




TRV045: Improved Seizure Burden / Freedom in Nonclinical Model

Post-kainate Spontaneous Recurrent Seizure Model

TRV045 demonstrated a dose-dependent reduction in **seizure burden** and increase in **seizure freedom** in post-kainate spontaneous recurrent seizure models



* p<0.05 v vehicle, ** p<0.05 v baseline; Wilcoxon rank sum

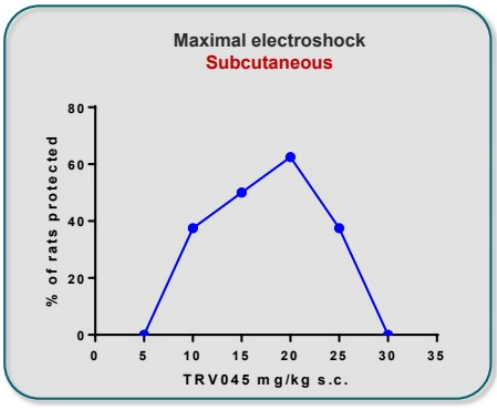
\# p<0.05 v baseline and vehicle; Fisher's exact test

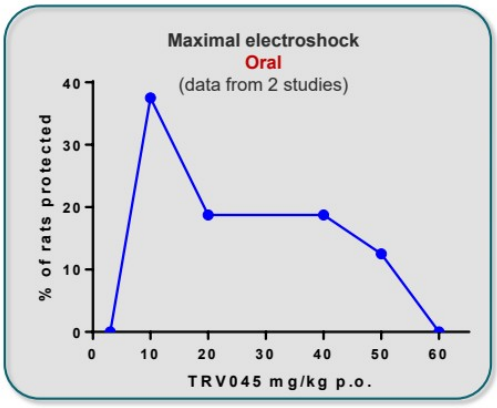
Data from NIH-supported Epilepsy Therapy Screening Program

TRV045: Protection from Acute Seizures in Nonclinical Model

Maximal Electroshock Model

TRV045 demonstrated
protection from acute seizures
in three replicated experiments





TRV045

Nonclinical Data – Non-opioid Pain Indications

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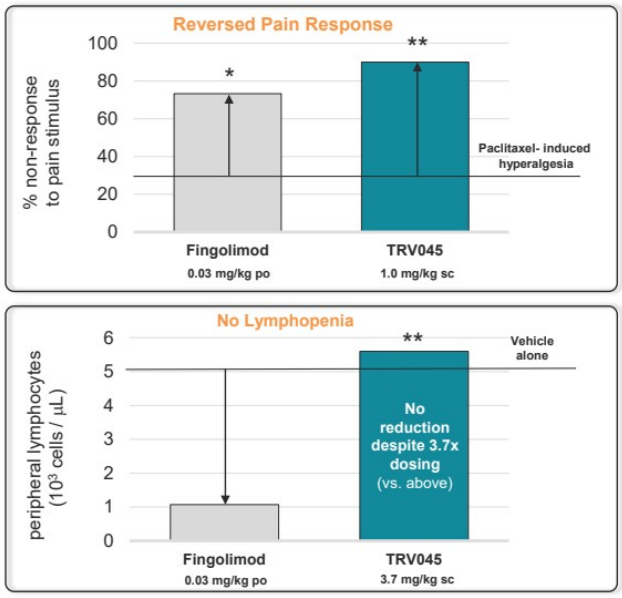
TRV045 Efficacy in Nonclinical Chronic Pain Models (w/ no Lymphopenia)

Mouse chemotherapy-induced peripheral neuropathy (CIPN) model



Reversed neuropathic pain…

…with no lymphopenia

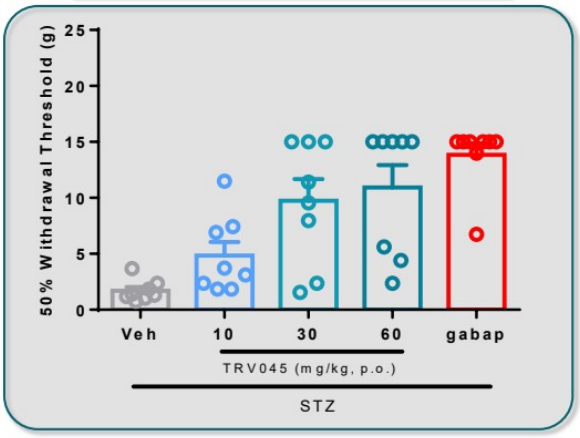
Source: Trevena data on file

1) CIPN mouse model: Paclitaxel 6 mg/kg, i.p. on Days 1, 3, 5, 7. Hyperalgesia measured as % non-response to 0.4 g Von Frey filament vs. baseline, tested 30' after dosing on Day 13. Lymphocytes measured after 3 days of dosing. Data are mean ± s.e.m. n=5-7 mice/group. *p<0.05 or **p<0.01 vs. control

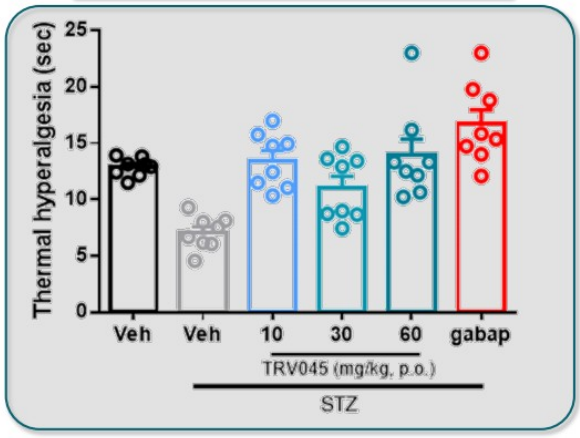
TRV045: Reversed Hyperalgesia in Nonclinical Model

Rat diabetic peripheral neuropathic pain (STZ) model

Effective on **mechanical pain** endpoint



Effective on **thermal pain** endpoint



Source: Trevena data on file

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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 a new chemical entity 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.

WARNINGS AND PRECAUTIONS

- 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.
- 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.

Exhibit 99.3

Trevena Announces Preliminary TRV045 Data from Two Proof-of-Concept Studies Evaluating S1PR Mechanism of Action and CNS Target Engagement

TRV045 Demonstrated Statistically Significant Analgesic Effect in Capsaicin-induced Model of Neuropathic Pain in Target Engagement POC Study

TMS POC Study Provided Statistically Significant Evidence of CNS Activity of TRV045 on Day 4 as Measured by EEG Power Spectral Analysis

No SAEs and No Study Drug-Related Discontinuations were reported; Full Safety and Tolerability Data Expected in early 4Q 2023

Company to Hold Conference Call on Wednesday, September 6 at 8 a.m. Eastern

CHESTERBROOK, Pa., September 6, 2023 (GLOBE NEWSWIRE) –Trevena, Inc. (Nasdaq: TRVN), a biopharmaceutical company focused on the development and commercialization of novel medicines for patients with central nervous system (CNS) disorders, today announced preliminary topline data from two Phase 1 proof-of-concept studies of TRV045, a novel sphingosine-1-phosphate receptor modulator selective for the S1P receptor subtype 1.

“We’re very excited about the progress we’ve made with TRV045 and I’m pleased that both proof-of-concept studies demonstrated CNS target engagement. This dataset marks another significant milestone for Trevena and our ongoing commitment to focus on innovative new therapies,” said Carrie Bourdow, President and CEO of Trevena. “As a novel, non-opioid therapy, we believe TRV045 has the potential to make a meaningful difference in the lives of patients and we look forward to advancing TRV045, on our own or with a strategic partner, for potential treatment of neuropathic pain and other CNS disorders.”

Data from both studies demonstrated CNS penetration and target engagement, as well as plasma exposures in the anticipated active dose range, supporting the therapeutic potential of TRV045. In a capsaicin-induced neuropathic pain model, a validated model of neuropathic pain, TRV045 showed a statistically significant, dose-dependent treatment effect. In the transcranial magnetic stimulation (TMS) proof-of-concept study, TRV045 demonstrated statistically significant changes in the power spectral density in several bands.

“These preliminary studies strongly suggest to me that this compound has an impact on the central processing of pain, and is potentially working by reducing neural hyperexcitability,” said Daniel Clauw, MD, Professor of Anesthesiology, Medicine and Psychiatry at the University of Michigan.” There is a clear need for innovative new medications for the treatment of chronic pain. TRV045’s novel mechanism of action, accompanied by the early data suggesting it is well tolerated, make this an exciting new potential therapeutic approach.”

Target Engagement (PainCart®) POC Study

The Target Engagement POC study was a randomized, double-blind, placebo-controlled, single dose four-way cross-over study (n=25 subjects) designed to evaluate evidence of target engagement for TRV045, using a select battery of pharmacodynamic outcomes. The study used the validated PainCart® set of analgesic tests to evaluate potential central and peripheral nervous system effects and to provide insight into the potential anti-inflammatory actions of TRV045. Each subject received three different single doses of TRV045 (50mg, 150mg and 300mg) and placebo on four separate visits across the study duration. Plasma exposures of TRV045 in this study were comparable to levels seen in the previously reported Phase 1, FIH study and reached the anticipated targeted active dose range.

TRV045 demonstrated a statistically significant, dose-dependent reduction in mechanical allodynia following topical capsaicin application at 150mg and 300mg v. placebo. Allodynia was assessed by cutaneous pain sensation upon mechanical stimulation with Von Frey hair filaments, a validated model of neuropathic pain. The difference was measured for each dose of TRV045 compared to placebo as the change from baseline in both the secondary area of allodynic sensation and the total area of allodynia across 10 hours following the dose of study medication. The change from baseline in painful surface area at the final 10 hour timepoint is shown below, along with the associated P-values for each treatment difference across the entire 10 hour period of observation. Differences were evident for both the 150mg and 300mg doses beginning at hour 2 and continuing through the entire period of study observation at hour 10.

Outcome	**Treatment**	**Change from Baseline in Painful Surface Area at Final 10 Hour Timepoint (mm^2)***	**P-Value for Overall Treatment Difference v Placebo**
Total Allodynic Area (mm^2)	Placebo	-67.19	
	TRV045 50mg	-211.61	0.1844
	TRV045 150mg	-389.45	0.0002
	TRV045 300mg	-731.78	0.0001
Secondary Allodynic Area (mm^2)	Placebo	-15.79	
	TRV045 50mg	-54.98	0.5313
	TRV045 150mg	-186.14	0.0022
	TRV045 300mg	-393.05	0.0023

* Least squares (LS) mean change from baseline

TRV045 further demonstrated a dose-dependent trend in change from baseline in the cold pressor test, and also demonstrated trends in reduction to heat pain detection threshold on both unexposed and capsaicin-treated forearm skin, on heat pain detection threshold on unexposed skin on the upper back, and pain tolerance in the electrical burst stimulation test, though these endpoints did not achieve statistical significance. TRV045 did not show a statistically significant difference or trend compared to placebo in other pain modalities.

TMS POC Study

The TMS POC study was a randomized, double-blind, placebo-controlled, multiple dose, two-way cross-over study (n=25 subjects) designed to evaluate the pharmacodynamic effects of TRV045 (250mg) on cortical excitability in healthy male adults, using both EEG and EMG to measure the impact of TRV045 on the electrical excitation of the brain. The goal of the study was to provide further insight into TRV045 CNS target engagement and mechanism of action for the potential treatment of epilepsy and other CNS disorders. Each subject received one of two treatment sequences in random order: TRV045 at a dose of 250mg, followed by placebo; or placebo followed by 250mg of TRV045, each treatment sequence given once daily for four consecutive days. Plasma exposures of TRV045 in this study were comparable to levels seen in the previously reported Phase 1, FIH study and reached the anticipated targeted active dose range.

Among the EEG-related endpoints measured in the study, resting state EEG obtained before and after administration of TRV045, demonstrated statistically significant increases in the power spectral density on day 4 in several of the middle to higher frequency bands including alpha, beta and gamma waves. The changes in alpha waves are generally considered to be associated with conscious arousal and alertness, while beta waves are thought to be associated with GABA-mediated inhibitory cortical neurotransmission, and gamma waves are generally associated with cognitive processing, learning and memory. Alpha waves demonstrated this statistically significant increase in power in the frontal region (P=0.0164), as well as both left parietal (P=0.0047), and right parietal (P=0.0418) regions. This statistically significant increase in power was observed in the frontal region for beta waves (P=0.0235) and gamma waves (P=0.0343).

With respect to slow brain waves, which are generally associated with sedation or sleep, TRV045 showed a statistically significant decrease in the delta brain waves on day 4 in the right parietal region (P=0.0432), and no significant difference in theta brain waves at any of the three observed regions.

Among the EMG-related endpoints measured in the study, TRV045 demonstrated evidence of reduction in cortical excitability, as measured by change in peak motor-evoked potential (MEP) amplitude, on Day 1 comparable in magnitude to the reduction in cortical excitability reported in similar test conditions in the same laboratory for approved anti-epileptic drugs, though this result did not achieve statistical significance. There was no difference in mean peak MEP amplitude on Day 4, and no difference in resting motor threshold (RMT) on Day 1 or Day 4 or other EMG-related endpoints.

There were no serious adverse events reported, and no drug-related discontinuations from either study. Full safety and tolerability data for these studies are not yet available. This data is expected in early 4Q 2023. In the previously reported Phase 1 study of TRV045, the only adverse event assessed by study investigators as probably or definitely related to drug was headache in four subjects across all three parts of the study (n=53, n=27, n=9).

Subjects in both studies were enrolled outside of the United States, and the studies were not conducted under the Investigational New Drug Application for TRV045.

Conference Call and Webcast Information

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

Title:	Trevena Business Update Conference Call & Webcast
Date:	Wednesday, September 6, 2023
Time:	8:00 a.m. ET
Conference Call Details:	Toll-Free:1-844-825-9789 International:1-412-317-5180 Conference ID: 10178141

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=1610714&tp_key=d4c27074df https://www.trevena.com/investors/events-presentations/ir-calendar

The webcast should be accessed 15 minutes prior to the conference call start time. A replay of the webcast will be available following the conclusion of the live broadcast and will be accessible on the Company's website.

About 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 Epilepsy

Epilepsy, one of the most common neurological diseases in the world, is a chronic disorder characterized by recurrent seizures. Epilepsy is defined as having two or more unprovoked seizures separated by at least 24 hours or after one seizure with a high risk of more.

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

About Diabetic Neuropathic Pain

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

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

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; 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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Exhibit 99.4

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

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

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

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

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

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

CHESTERBROOK, Pa., September 6, 2023 (GLOBE NEWSWIRE) – **Trevena, Inc. (Nasdaq: TRVN)**, a biopharmaceutical company focused on the development and commercialization of novel medicines for patients with central nervous system (CNS) disorders, today announced receipt of a $15 million tranche under its non-dilutive ex-US royalty-based financing (the R-Bridge Financing). This tranche of funding was triggered by the first commercial sale of OLINVYK in China by Jiangsu Nhwa, the Company's licensee in China. As previously announced, OLINVYK has been approved in China for use in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate.

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

The Company also announced additional expected near-term milestones:

- **New VOLITION Respiratory Data for OLINVYK.** The Company previously reported initial topline GI and delirium data from the ~200 patient OLINVYK VOLITION study, a real-world, open-label, multi-site study led by clinical outcomes research experts from Cleveland Clinic and Wake Forest Baptist Health Medical Center. Trevena expects to report new respiratory data from the study using continuous respiratory monitoring in 3Q 2023.

- **OLINVYK Abstracts Accepted at American Society of Anesthesiologists (ASA) 2023 Meeting.** The Company has three abstracts accepted for presentation at ASA, which will be held in San Francisco from October 13th to the 17th. One abstract was selected for an oral presentation as a top research abstract. The abstracts are embargoed until the conclusion of the meeting and at which time they will be available at https://www.trevena.com/publications.

- "**ARTEMIS, A Real-World Evidence Trial Examining the Use of Oliceridine, a Biased Agonist at the μ(Mu) Receptor, in Patients Requiring Post-Surgical Pain Control.**" With lead author Todd L. Wandstrat, PharmD of Trevena, Inc.

- **"Postoperative Vomiting With IV Oliceridine in Postoperative Recovery: A Single-group Prospective Cohort Study"** with lead author Mark Demitrack, M.D of Trevena, Inc.

- "**Antinociception Versus Neurocognitive Effect of Biased Mu-opioid Receptor Oliceridine Versus Morphine- Utility Function Analysis"** with lead author Albert Dahan MD PhD of the Centre for Human Drug Research, Leiden, the Netherlands

· **TRV045 Data.** The Company today reported results from its Target Engagement (PainCart®) and TMS Proof-of-Concept studies. In addition, a nonclinical study of TRV045 is ongoing, focused on the potential of TRV045 to treat infantile spasms, a rare pediatric disorder. TRV045 is also being studied by the NIH's Epilepsy Therapy Screening Program as a potential disease-modifying therapeutic for the prevention of seizures. Nonclinical data from both of these studies are expected 2H 2023.

· **Trevena to Participate in Investor Conference.** The Company announces that members of management will participate in the HC Wainwright Global Investment Conference being held in-person and virtually in New York City on September 11-13. A link to the webcast will be available on the Events page of the Investors section of the Company's website at: https://www.trevena.com/investors/events-presentations/ir-calendar

Conference Call and Webcast Information

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

Title:	Trevena Business Update Conference Call & Webcast
Date:	Wednesday, September 6, 2023
Time:	8:00 a.m. Eastern Time
Conference Call Details:	Toll-Free:1-844-825-9789 International:1-412-317-5180 Conference ID: 10178141

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=1610714&tp_key=d4c27074df

https://www.trevena.com/investors/events-presentations/ir-calendar

The webcast should be accessed 15 minutes prior to the conference call start time. A replay of the webcast will be available following the conclusion of the live broadcast and will be accessible on the Company's website.

About OLINVYK® (oliceridine) injection

OLINVYK is a new chemical entity approved by the FDA in August 2020. OLINVYK contains oliceridine, an opioid, which is a Schedule II controlled substance with a high potential for abuse similar to other opioids. It is indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate. OLINVYK is available in 1 mg/1 mL and 2 mg/2 mL single-dose vials, and a 30 mg/30 mL single-patient-use vial for patient-controlled analgesia (PCA). Approved PCA doses are 0.35 mg and 0.5 mg and single doses greater than 3 mg should not be administered. The cumulative daily dose should not exceed 27 mg. Please see Important Safety Information, including the BOXED WARNING, and full prescribing information at www.OLINVYK.com.

IMPORTANT SAFETY INFORMATION

WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; NEONATAL OPIOID WITHDRAWAL SYNDROME; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CENTRAL NERVOUS SYSTEM (CNS) DEPRESSANTS

ADDICTION, ABUSE, AND MISUSE – OLINVYK exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk before prescribing OLINVYK, and monitor all patients regularly for the development of behaviors or conditions.

LIFE-THREATENING RESPIRATORY DEPRESSION – Serious, life-threatening, or fatal respiratory depression may occur with use of OLINVYK. Monitor for respiratory depression, especially during initiation of OLINVYK or following a dose increase.

NEONATAL OPIOID WITHDRAWAL SYNDROME – Prolonged use of OLINVYK during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

RISK FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS – Concomitant use of opioids with benzodiazepines or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation.

INDICATIONS AND USAGE

OLINVYK is an opioid agonist indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate.

LIMITATIONS OF USE

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve OLINVYK for use in patients for whom alternative treatment options [e.g., non-opioid analgesics or opioid combination products]:

- Have not been tolerated, or are not expected to be tolerated
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

The cumulative total daily dose should not exceed 27 mg, as total daily doses greater than 27 mg may increase the risk for QTc interval prolongation.

CONTRAINDICATIONS

OLINVYK is contraindicated in patients with:

- Significant respiratory depression
- Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment
- Known or suspected gastrointestinal obstruction, including paralytic ileus
- Known hypersensitivity to oliceridine (e.g., anaphylaxis)

WARNINGS AND PRECAUTIONS

- OLINVYK contains oliceridine, a Schedule II controlled substance, that exposes users to the risks of addiction, abuse, and misuse. Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed OLINVYK. Assess risk, counsel, and monitor all patients receiving opioids.
- Serious, life-threatening respiratory depression has been reported with the use of opioids, even when used as recommended, especially in patients with chronic pulmonary disease, or in elderly, cachectic and debilitated patients. The risk is greatest during initiation of OLINVYK therapy, following a dose increase, or when used with other drugs that depress respiration. Proper dosing of OLINVYK is essential, especially when converting patients from another opioid product to avoid overdose. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status.
- Opioids can cause sleep-related breathing disorders including central sleep apnea (CSA) and sleep-related hypoxemia with risk increasing in a dose-dependent fashion. In patients who present with CSA, consider decreasing the dose of opioid using best practices for opioid taper.

- Prolonged use of opioids during pregnancy can result in withdrawal in the neonate that may be life-threatening. Observe newborns for signs of neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using OLINVYK for a prolonged period of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

- Profound sedation, respiratory depression, coma, and death may result from the concomitant use of OLINVYK with benzodiazepines or other CNS depressants (e.g., non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, or alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate, prescribe the lowest effective dose, and minimize the duration.

- OLINVYK was shown to have mild QTc interval prolongation in thorough QT studies where patients were dosed up to 27 mg. Total cumulative daily doses exceeding 27 mg per day were not studied and may increase the risk for QTc interval prolongation. Therefore, the cumulative total daily dose of OLINVYK should not exceed 27 mg.

- Increased plasma concentrations of OLINVYK may occur in patients with decreased Cytochrome P450 (CYP) 2D6 function or normal metabolizers taking moderate or strong CYP2D6 inhibitors; also in patients taking a moderate or strong CYP3A4 inhibitor, in patients with decreased CYP2D6 function who are also receiving a moderate or strong CYP3A4 inhibitor, or with discontinuation of a CYP3A4 inducer. These patients may require less frequent dosing and should be closely monitored for respiratory depression and sedation at frequent intervals. Concomitant use of OLINVYK with CYP3A4 inducers or discontinuation of a moderate or strong CYP3A4 inhibitor can lower the expected concentration, which may decrease efficacy, and may require supplemental doses.

- Cases of adrenal insufficiency have been reported with opioid use (usually greater than one month). Presentation and symptoms may be nonspecific and include nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If confirmed, treat with physiologic replacement doses of corticosteroids and wean patient from the opioid.

- OLINVYK may cause severe hypotension, including orthostatic hypotension and syncope in ambulatory patients. There is increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (e.g., phenothiazines or general anesthetics). Monitor these patients for signs of hypotension. In patients with circulatory shock, avoid the use of OLINVYK as it may cause vasodilation that can further reduce cardiac output and blood pressure.

- Avoid the use of OLINVYK in patients with impaired consciousness or coma. OLINVYK should be used with caution in patients who may be susceptible to the intracranial effects of 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.

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About Jiangsu Nhwa:

Jiangsu Nhwa Pharmaceutical Co., Ltd. (SZ002262), founded in 1978, is a leading CNS company in China. Over the past 40 years, Nhwa is exclusively dedicated to developing innovative and differentiated pipeline in the areas of anesthesia, analgesia, psychiatry and neurology via in-house R&D and global partnership.

As a fully integrated pharmaceutical company with more than 4000 employees, Nhwa has comprehensive capabilities in research, clinical development, manufacturing and commercialization of CNS drugs. In recent years, Nhwa has further strengthened its leadership in CNS field in China by providing the services of precision diagnosis of CNS disorders (Shanghai N-yuen Biotechnology Company), and investing the largest Chinese CNS internet health platform (Happy Mood).

About R-Bridge (CBC Group)

CBC Group is Asia's largest and most active healthcare-dedicated investment firm with over US$5 billion AUM, focused on platform-building, buyout opportunities, and alternative financing across three core areas: pharmaceutical & biotech, medtech, and healthcare services. CBC has a leading team of investment, industry and portfolio management professionals, headquartered in Singapore with offices in New York, Shanghai, Beijing, and Hong Kong and presence in Boston, San Diego, San Francisco and Tokyo.

Founded in February 2020, R-Bridge Healthcare Fund is an affiliate of CBC Group and it is dedicated in providing alternative, non-dilutive financing backed by royalties, revenue interest and other cash flows generated by the sale of healthcare products and services in China, the first of its kind for the asset class and the region. R-Bridge provides additional sources of capital to leading healthcare companies to continue their extraordinary growth trajectories, commercializing their products and services in China and on a global scale.

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