



Trevena®

INNOVATING FOR PATIENTS

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



Mark A. Demitrack, M.D.

SVP, Chief Medical Officer



Patricia Drake

SVP, Chief Commercial Officer



Barry Shin

SVP, Chief Financial Officer



PiperJaffray

Robert T. Yoder

SVP, Chief Business Officer & Head of Commercial Operations



BOARD OF DIRECTORS

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Barbara Yanni



Michael R. Dougherty



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

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

Multiple Expected Catalysts

	PRE-CLIN	PHASE 1	PHASE 2	PHASE 3	NDA	POST-APPR	Highlights
OLINVYK® New chemical entity (mu-opioid receptor)	IV acute pain*					APPROVED >	<ul style="list-style-type: none"> Commercial launch ongoing
			Cleveland Clinic / Wake Forest Baptist Health collab.			VOLITION clinical outcomes >	<ul style="list-style-type: none"> Real world differentiation
			Cleveland Clinic / Wake Forest Baptist Health collab.			ARTEMIS clinical outcomes >	<ul style="list-style-type: none"> \$8.8k / 1.4 day savings
						Respiratory physiology >	<ul style="list-style-type: none"> Data reported
						Cognitive function >	<ul style="list-style-type: none"> Data reported
TRV045 Selective S1P receptor modulator							<ul style="list-style-type: none"> Data reported
							<ul style="list-style-type: none"> Data reported
TRV734 G-protein selective agonist (mu-opioid receptor)							<ul style="list-style-type: none"> POC study ongoing

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Ex-US Royalty-Based Financing Highlights

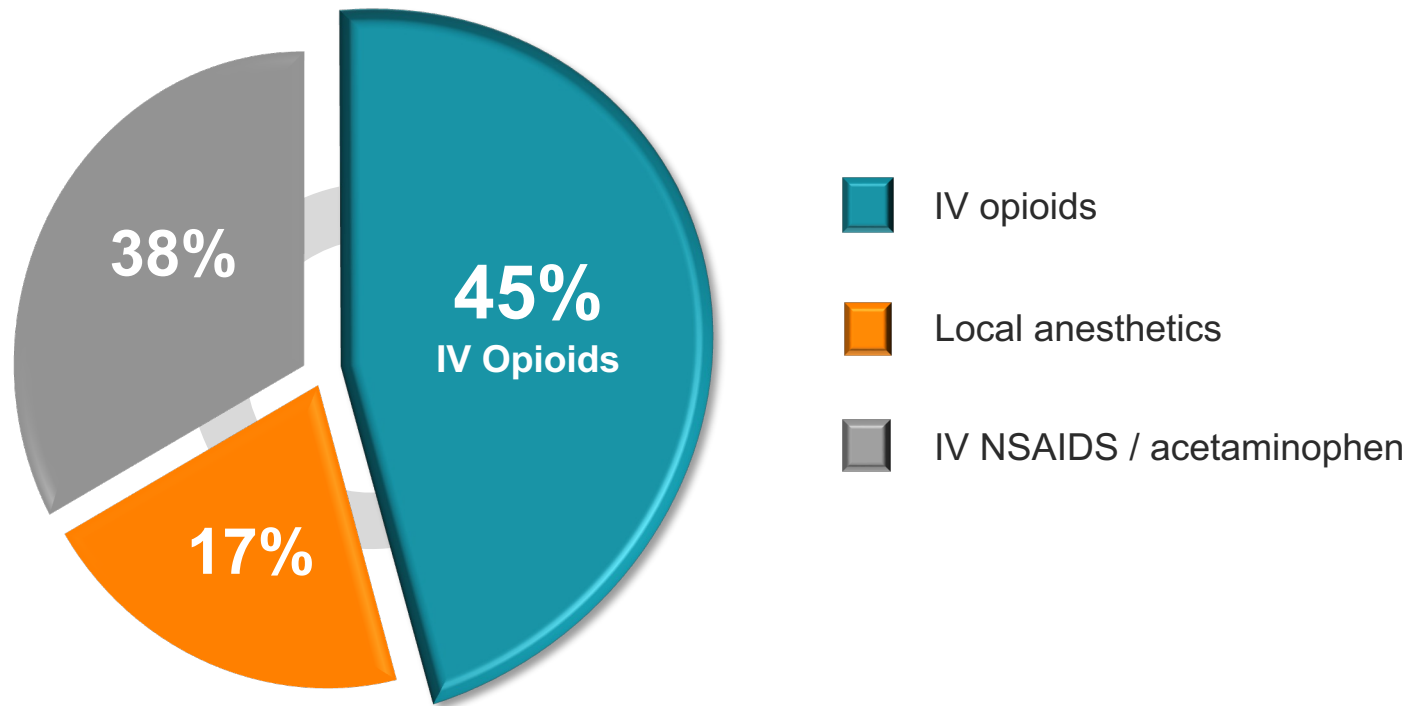
Blue Chip Investor	<p style="text-align: center;">R-Bridge Healthcare Fund affiliate of CBC Group (one of the largest and most active healthcare-dedicated investment firms in Asia)</p>
\$40M Total Financing	<p style="text-align: center;">Received 3Q 23 [</p> <ul style="list-style-type: none"> \$15M upfront \$15M on first commercial sale in China \$10M on commercial or financing milestone <p style="text-align: center;"><u> </u> \$40M total</p>
Flexible Payments*	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • No financial covenants



OLINVYK Overview

Large Market Opportunity – Acute Pain

US injectable analgesic hospital market unit volume¹



45M patients receive IV opioids annually to treat acute pain¹

IV opioids have unrivalled analgesic efficacy

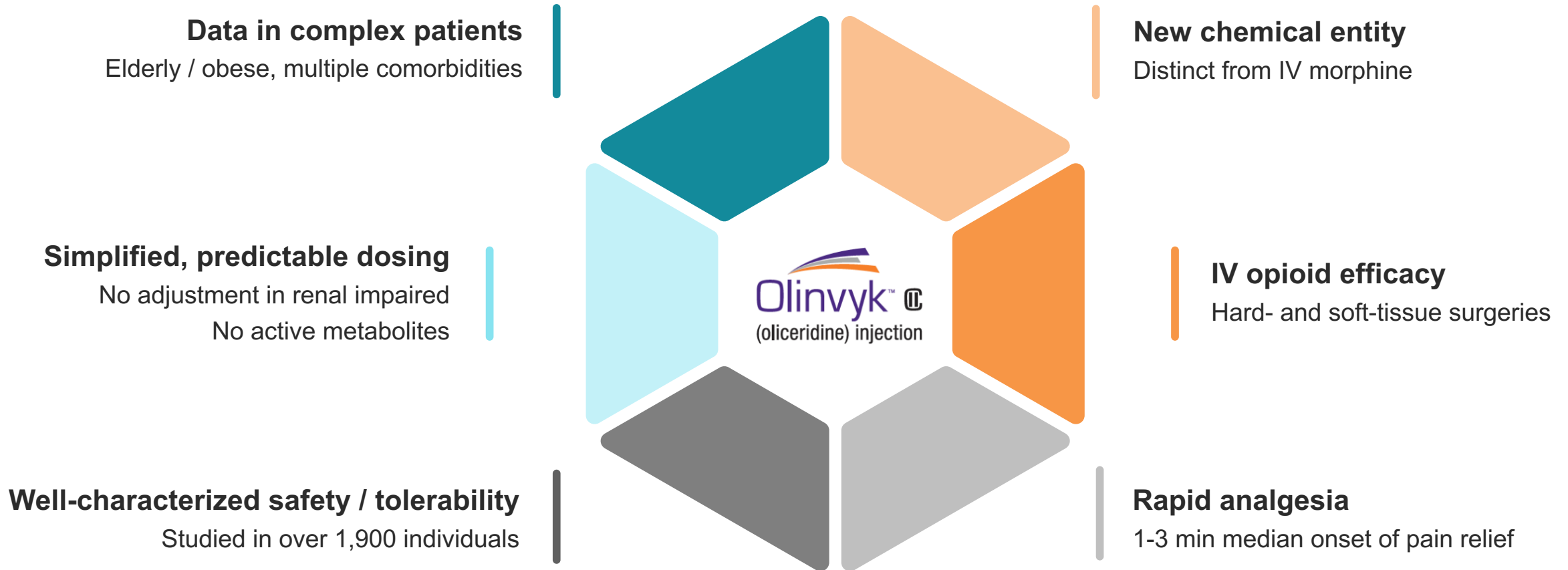
Top surgeries:
Total knee arthroplasty, colectomy, hernia repair, spine fusion, C-section²

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



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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



52.7% complete GI response¹

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 points²**

<4% symptoms of delirium³

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**

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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)

	Matched Patients Treated w/ other IV Opioids (N=982)		OLINVYK-Treated VOLITION Patients (N=201)	
Cost per Admission (avg)	\$45.9k	\$8.8k reduction →	\$37.1k	P<0.0001
Hospital Length of Stay (avg)	7.1 days	1.4 day reduction →	5.7 days	P<0.0001

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

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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 \approx morphine 5 mg¹**

27 mg cumulative daily dose limit

Do not administer single doses greater than 3 mg

No refrigeration / reconstitution



1 mg / 1mL

WAC:

\$17.50



2 mg / 2mL

\$25.75



30 mg / 30 mL

\$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

OLINVYK vs IV Morphine Health Economic Models

Published¹ and available to formulary committees

Representative Inputs:

AE rates*

Ph3 trials

Placebo (N = 152)	OLINVYK 5.27 mg (N = 316)	Morphine (N = 155)
73	86	96
35	52	70
10	26	52
30	26	30
11	18	25
9	14	14
3	12	17
6	9	19
5	7	13
4	6	10
4	6	8
4	4	8
1	2	10

Vomiting
Somnolence / sedation
O₂ saturation <90%

Cost of AEs

Gov't sources /
Publications

\$8k nausea / vomiting²
\$28k critical resp event³
+7 days hospital stay³

Drug cost



OLINVYK
IV morphine

Key Outputs:

HECON
model



>10x

Cost savings
for hospitals⁴

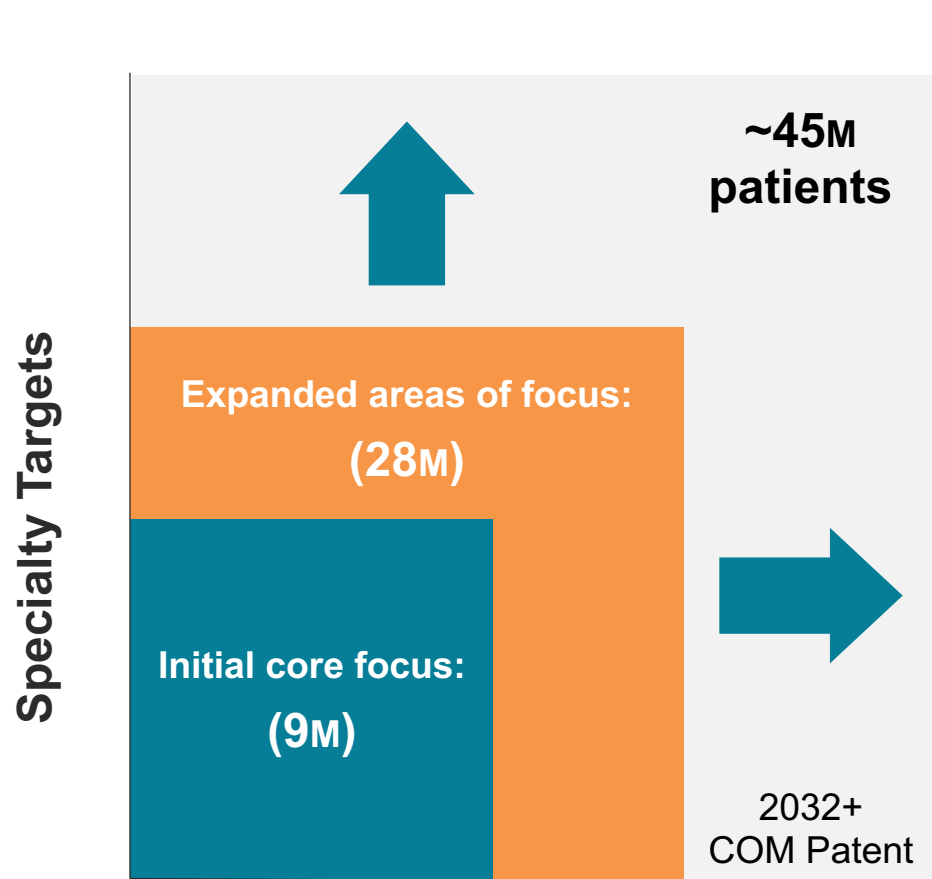
Due to improved
patient outcomes

* 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.

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

Patient & Procedure Risk

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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.



TRV045
S1P Receptor Modulator
Novel MOA for Diabetic Neuropathic Pain

S1P₁ Receptor – Novel Target for CNS Indications

S1P₁ receptors are highly expressed on key CNS cells involved in neuroinflammation

Potential therapeutic role in seizures, epileptogenesis and pain signaling

Epilepsy

- Neuroprotective effects³
- Modulates BBB permeability, anti-inflammatory effects^{4,5}



Neuropathic pain

- Inhibits pain sensation¹
- Inhibits excitatory neuronal signaling²



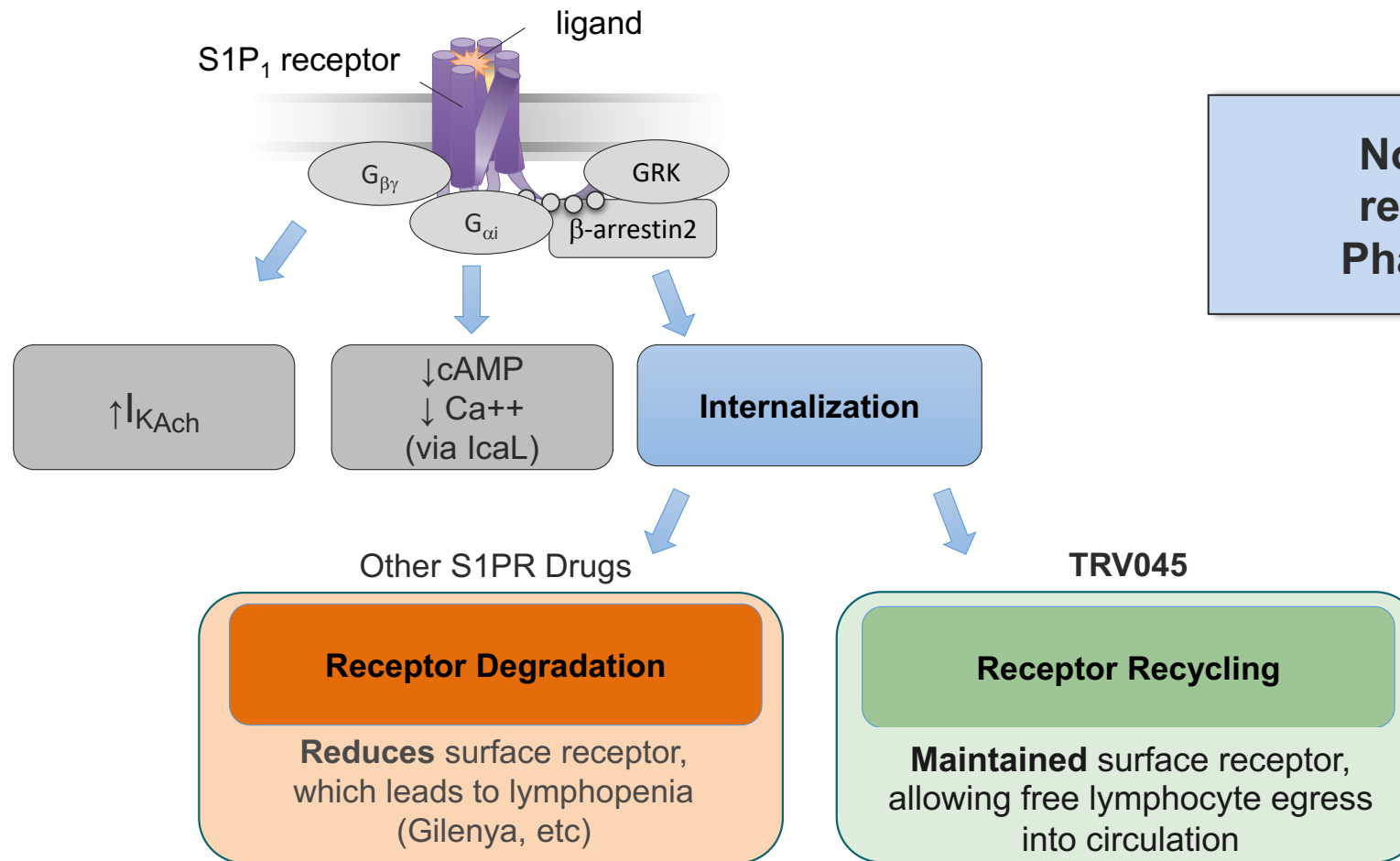
Existing S1PR-targeted drugs, however, are ill-suited for CNS indications due to known:

Lymphopenia
Cardiac AEs

Pulmonary AEs
Ophthalmologic AEs

TRV045 MOA: Rapid Receptor Recycling

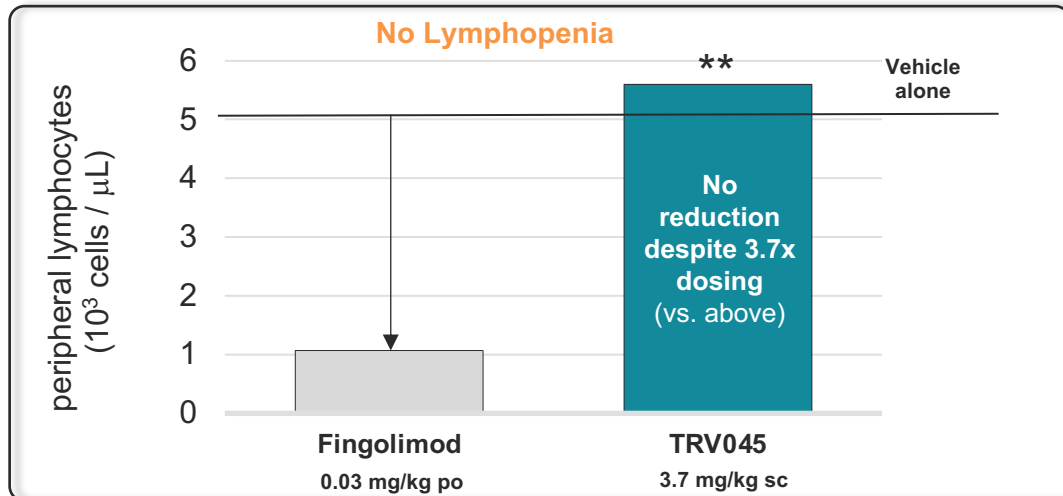
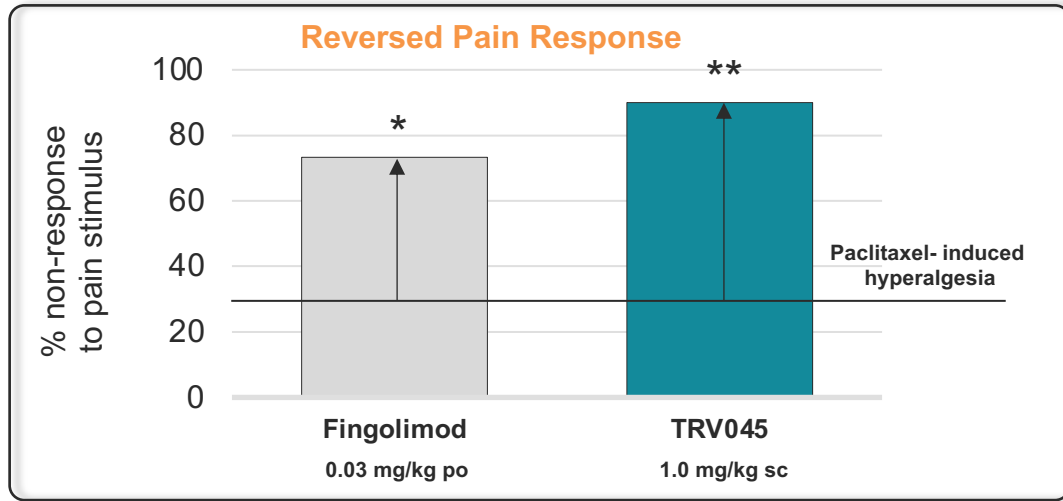
Maintained (rather than degraded) S1P receptors on cell surface



No lymphopenia reported in prior Phase 1 FIH study

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

Mouse chemotherapy-induced peripheral neuropathy (CIPN) model



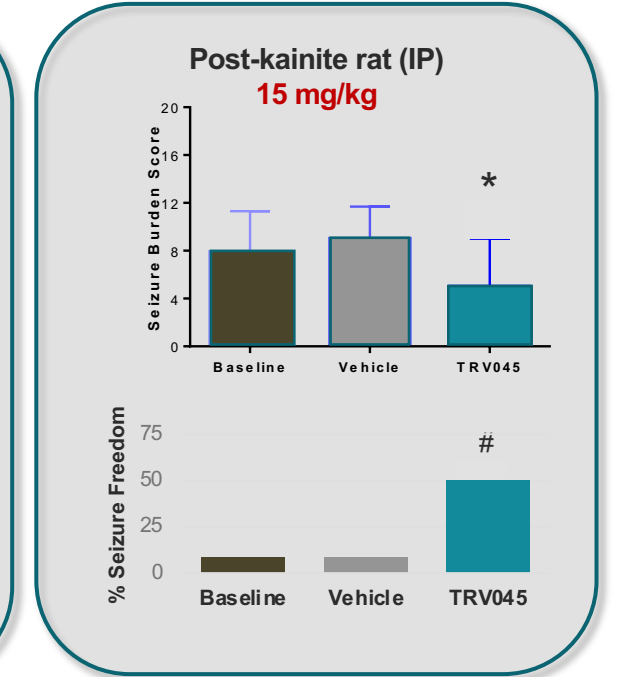
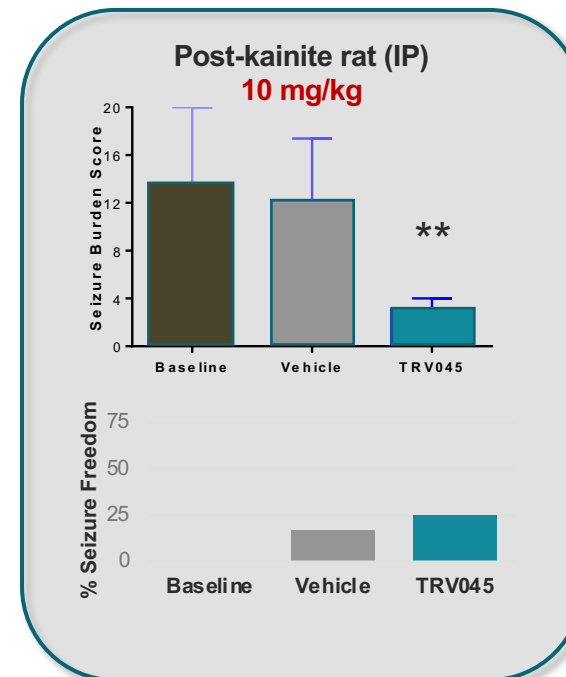
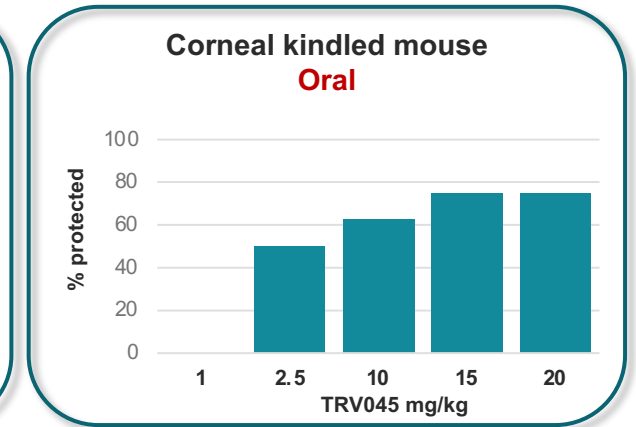
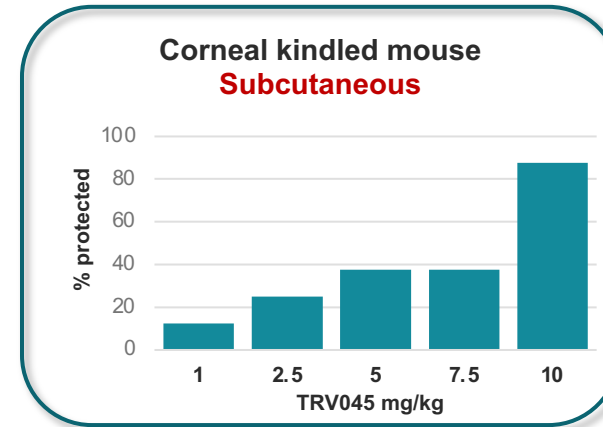
Reversed neuropathic pain...

...with no lymphopenia

Source: Trevena data on file

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



* 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 range¹

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)

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

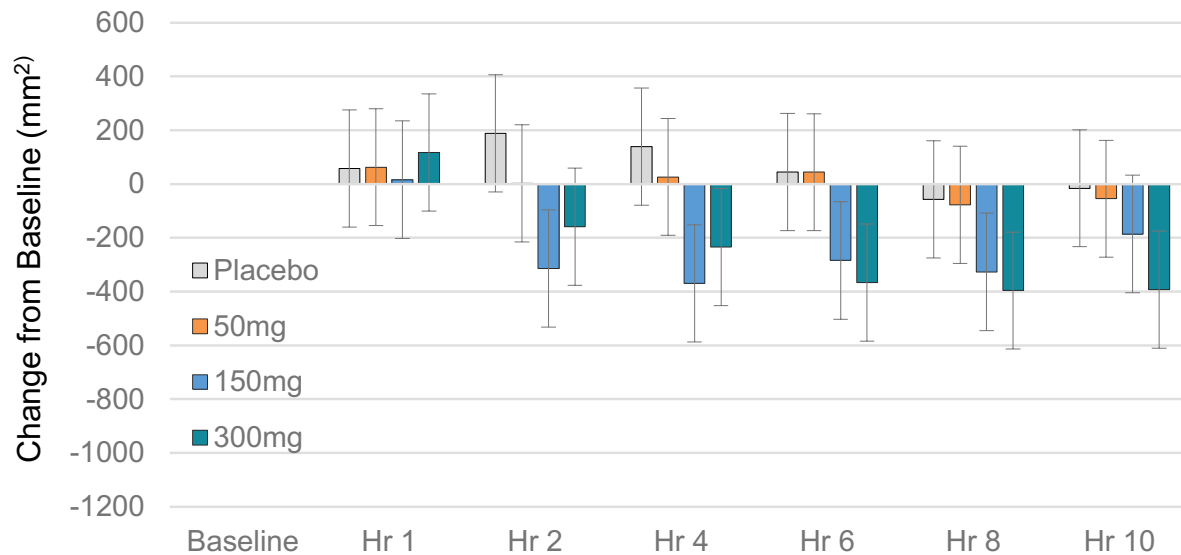
TE Study: Significantly Reduced Mechanical Allodynia

1% capsaicin-treated dominant volar forearm – Von Frey filament allodynic area (CFB, mm²)

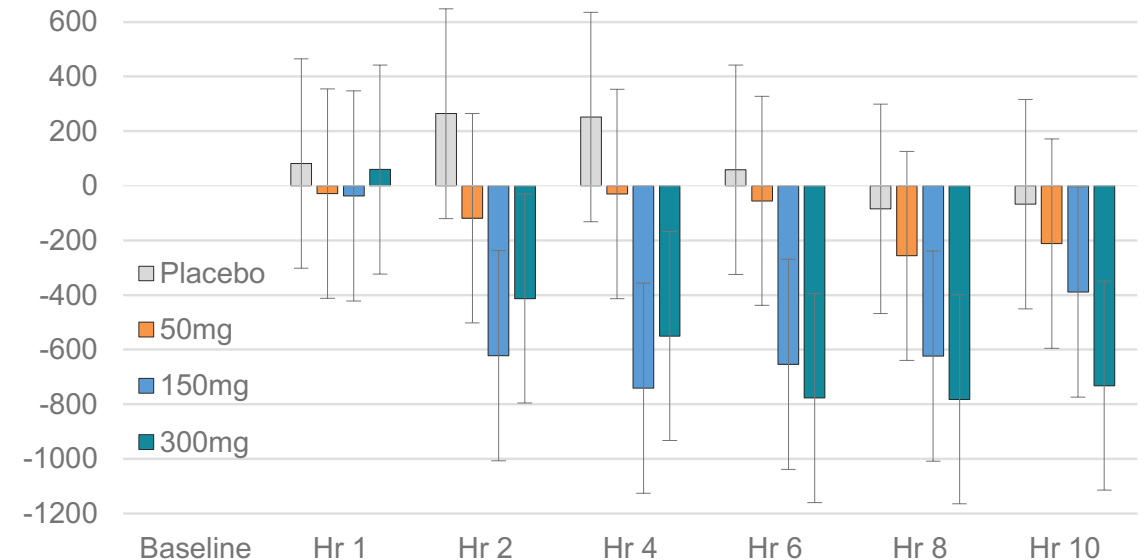
300mg TRV045 v Placebo; P=0.0023
150mg TRV045 v Placebo; P=0.0022

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

Secondary Allodynic Area

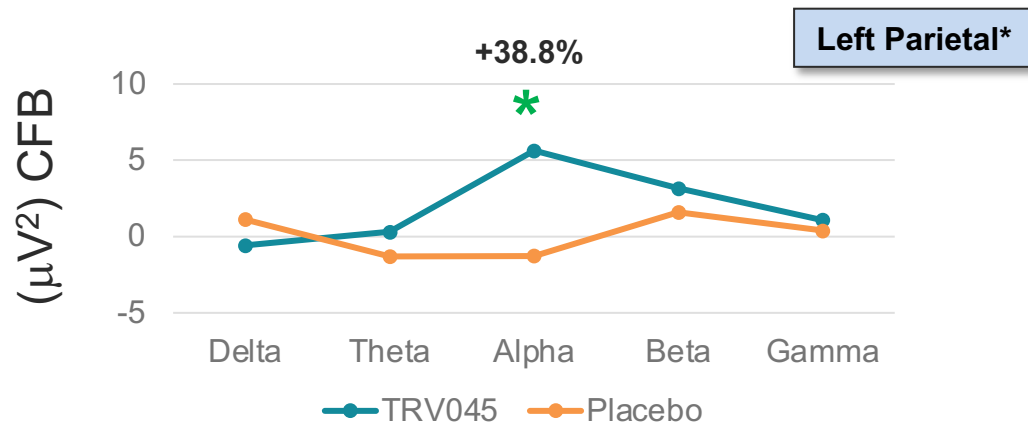
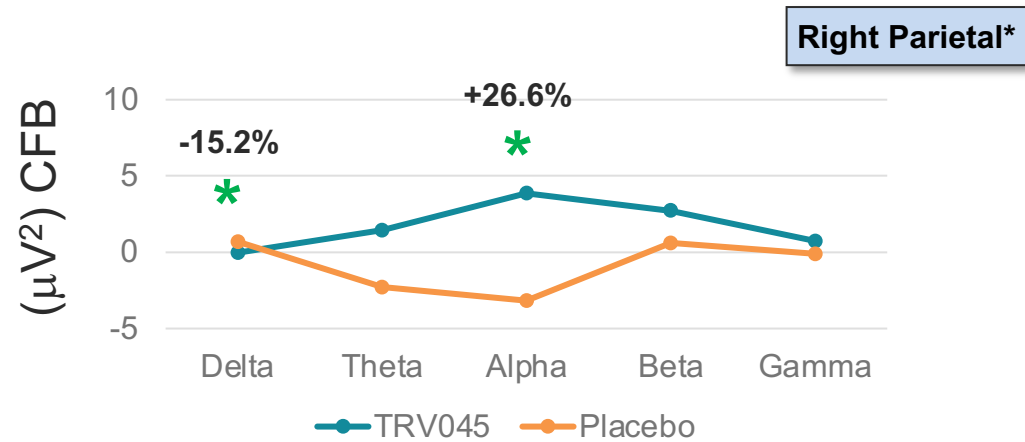
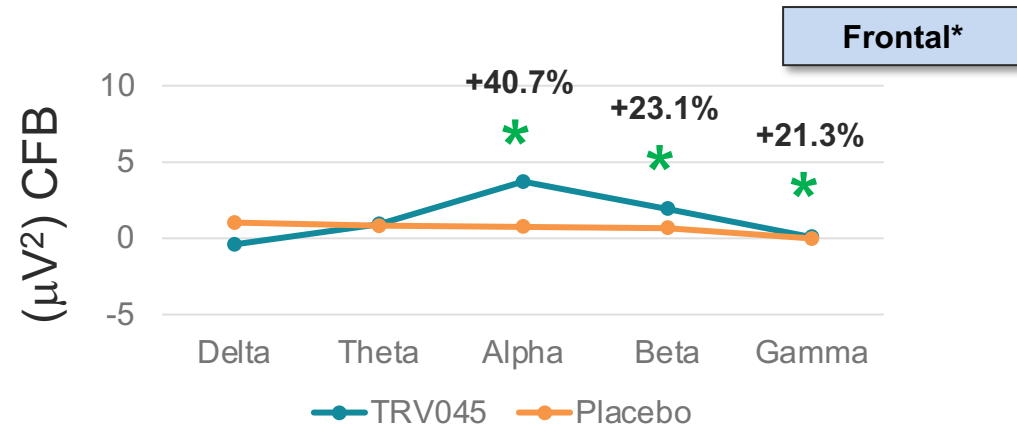


Total Allodynic Area



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 with alertness / arousal
memory / learning

associated with sedation / sleep

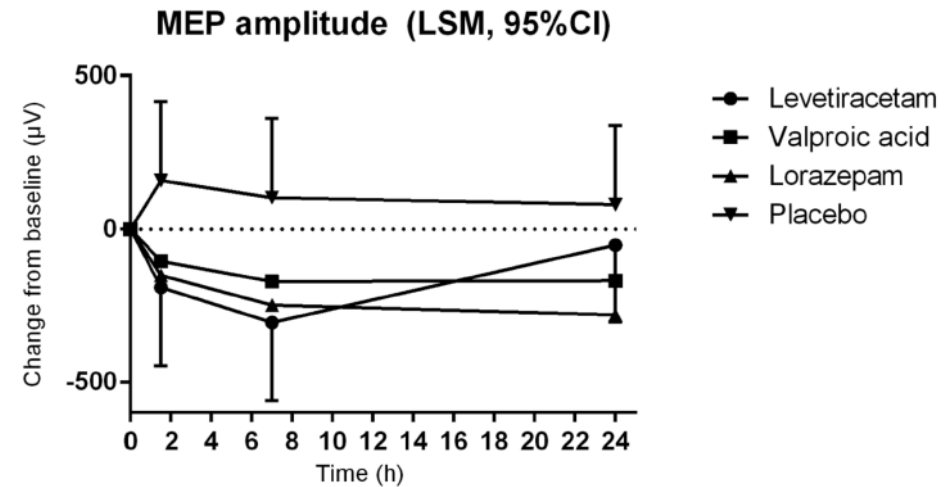
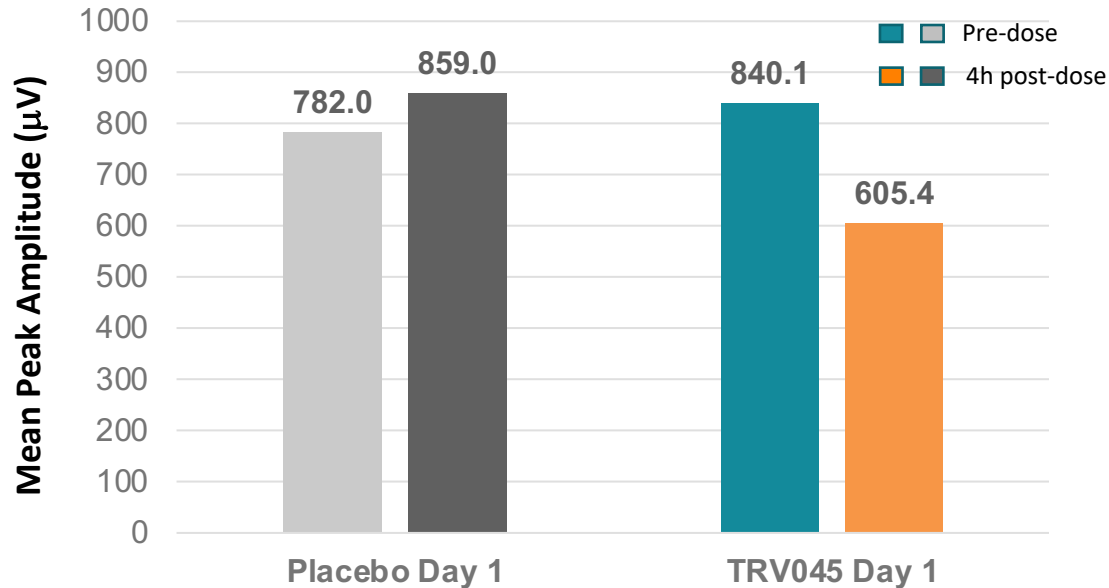
* Denotes pairwise comparison $P < 0.05$

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)²³

TMS Study: Effect on Cortical Excitability vs AEDs*

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



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

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



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 relapse²

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



>2.5M
people in
U.S. suffer from
opioid use disorder¹

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



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 CO₂ retention, such as those with evidence of increased intracranial pressure or brain tumors, as a reduction in respiratory drive and the resultant CO₂ retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy.
- As with all opioids, OLINVYK may cause spasm of the sphincter of Oddi, and may cause increases in

serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis, for worsening symptoms.

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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 the risk of seizures in vulnerable patients. Monitor patients with a history of seizure disorders for worsened seizure control.
- Do not abruptly discontinue OLINVYK in a patient physically dependent on opioids. Gradually taper the dosage to avoid a withdrawal syndrome and return of pain. Avoid the use of mixed agonist/antagonist (e.g., pentazocine, nalbuphine, and butorphanol) or partial agonist (e.g., buprenorphine) analgesics in patients who are receiving OLINVYK, as they may reduce the analgesic effect and/or precipitate withdrawal symptoms.
- OLINVYK may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery.
- Although self-administration of opioids by patient-controlled analgesia (PCA) may allow each patient to individually titrate to an acceptable level of analgesia, PCA administration has resulted in adverse outcomes and episodes of respiratory depression. Health care providers and family members monitoring patients receiving PCA analgesia should be instructed in the need for appropriate monitoring for excessive sedation, respiratory depression, or other adverse effects of opioid medications.

ADVERSE REACTIONS

Adverse reactions are described in greater detail in the Prescribing Information.

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

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