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): **March 30, 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 2.02. Results of Operations and Financial Condition.

On March 30, 2023, Trevena, Inc. (the "Company") issued a press release announcing its financial results for the quarter and year ended December 31, 2022, and provided an overview of its 2023 year-to-date operational highlights. A copy of the press release is furnished hereto as Exhibit 99.1 and incorporated herein by reference.

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

Item 7.01 Regulation FD Disclosure

On March 30, 2023, the Company updated its website to include an updated corporate presentation deck. A copy of the updated corporate presentation deck is attached hereto as Exhibit 99.2.

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

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Number	Description
99.1	Press Release dated March 30, 2023
99.2	Updated Corporate Presentation Deck dated March 30, 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: March 30, 2023

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

Exhibit 99.1

Trevena Reports Fourth Quarter 2022 Results and Provides Business Update

Company announces initial topline OLINVYK data including GI and cognitive outcomes, and length of stay data from ~200 patient real-world clinical outcomes study

TRV045, a novel S1P receptor modulator, continues to advance as a potential treatment for epilepsy, diabetic neuropathic pain and other CNS disorders, with two proof-of-concept studies expected to complete enrollment by mid-2023

Cash balance of $38.3 million at year end 2022

Company to host conference call today, March 30, 2023 at 8:00 a.m. ET

CHESTERBROOK, Pa., March 30, 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 reported its financial results for the fourth quarter ended December 31, 2022 and provided an overview of its recent operational highlights.

“We are excited to report initial topline data from the OLINVYK real-world outcomes studies, VOLITION and ARTEMIS. The GI and cognitive results build upon the extensive data set for OLINVYK, and we look forward to reporting respiratory outcome data as soon as it is available.” said Carrie Bourdow, President and CEO of Trevena. “We are also pleased to now have two proof-of-concept studies underway for TRV045, and we expect to report top-line data later this year.”

Fourth Quarter 2022 and Recent Corporate Highlights

- **Initial topline data from new real-world VOLITION study demonstrated over 50% GI complete response and less than 4% incidence of symptoms suggestive of delirium in patients treated with OLINVYK.** The VOLITION study, a 203-patient, real world, open-label, multi-site study led by clinical outcomes research experts from Cleveland Clinic and Wake Forest Baptist Health Medical Center, demonstrated a 52.2% GI complete response rate. A complete GI response was defined as a patient who did not vomit and did not require the use of antiemetics throughout the post-operative period. As reference, in pooled data for the Company’s pivotal Phase 3 studies of OLINVYK, the GI complete response rate was 46.2% (0.35mg) and 39.7% (0.50mg). As reflected in the OLINVYK label, nausea and vomiting were two of the most common adverse events reported in the controlled clinical trials.

  Over 90% of OLINVYK-treated patients in VOLITION reported feeling “alert and calm” from the morning of the first post-operative day and at every observation point thereafter, based on the Richmond Agitation-Sedation Scale, and only 3.9% of OLINVYK-treated patients exhibited symptoms suggesting delirium at any point in the 48-hour post-operative period, based on the validated 3D-Confusion Assessment Method (3D-CAM) screening tool. Sedation is an established risk of opioids including OLINVYK. Analysis of respiratory data from VOLITION is not yet available, and the Company expects to report these data mid-2023.

- **Initial topline data from electronic medical records (EMR) based study, ARTEMIS, demonstrated a statistically significant 1.6-day reduction in average hospital length of stay vs matched patients treated with other IV opioids at Wake Forest Baptist Health.** OLINVYK-treated patients in VOLITION were matched with comparable patients treated with other IV opioids, undergoing similar surgical procedures at VOLITION study sites during the same period of time that the VOLITION study was enrolled. EMR data analysis is currently available from the single largest contributing site, Wake Forest Baptist Health, representing 96 OLINVYK treated patients and 457 matched patients. Based on this initial data, OLINVYK-treated patients had a statistically significant 1.6-day (~27%) reduction in average overall hospital length of stay compared to matched patients treated with other IV opioids(P=0.0001). There was no statistically significant difference in the average duration of time in the post-anesthesia care unit (PACU), with 2.4 hours observed for both OLINVYK-treated and matched patients (P=0.8174). While an EMR analysis does not provide definitive data of group differences as seen in a prospectively randomized study, the Company believes the EMR data bring a unique perspective to understanding how drugs may perform in the real world.

- **OLINVYK commercial team advances targeted customer outreach.** In the fourth quarter of 2022, the commercial team signed contracts with three new specialty distributors that focus primarily on ambulatory surgery centers (ASCs). Hospital outpatient and ASCs are becoming an increasingly important setting of care. The Company remains flexible and adaptive as it sees a shift in customer inquiries and requests for OLINVYK in the hospital outpatient setting.

- **Jiangsu Nhwa, Trevena's partner in China, expects a regulatory decision for OLINVYK in the first half of this year**. We continue to work closely with NHWA in support of potential approval of OLINVYK in China. If approved, Trevena would be eligible to receive a $3 million milestone payment from NHWA and would expect an additional $15 million of non-dilutive funding from R-Bridge Healthcare payable upon first commercial sale in China.

- **Initiated two proof-of-concept studies for TRV045, a novel S1P receptor modulator selective for the S1P receptor subtype 1.** The Company advanced the clinical development program for TRV045, its novel S1P receptor modulator, initiating two proof-of-concept studies. These studies will help inform the Company's future development path for TRV045 which has shown promising anti-inflammatory data in nonclinical models suggesting a potential disease-modifying role in CNS disorders.

    - ***TRV045 Target Engagement Study***. The first study is a randomized, double-blind, placebo-controlled, four-way cross-over study designed to test the mechanism of action and measure evidence of target engagement for TRV045. The study will use a validated 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.

- ***TRV045 Transcranial Magnetic Stimulation Study***. The second study is a randomized, double-blind, placebo-controlled, two-way cross-over, multiple dose study designed to evaluate the pharmacodynamic effects of TRV045 on the cortical excitability in healthy male adults. The study will use Transcranial Magnetic Stimulation Electromyography (TMS-EMG) and Electroencephalography (TMS-EEG) to measure the potential effect of TRV045 on brain function, relevant to epilepsy and other CNS disorders.

Both studies are expected to complete enrollment by mid-2023, and the Company expects to report top-line data in 3Q 2023

Financial Results for Fourth Quarter 2022

For the fourth quarter of 2022, the Company reported a net loss attributable to common stockholders of $7.0 million, or $0.73 per share, compared to $14.0 million, or $2.12 per share in the fourth quarter of 2021. For the full year ended December 31, 2022, net loss attributable to common stockholders was $53.7 million, or $7.59 per share, compared to $51.6 million, or $7.90 per share.

Cash and cash equivalents were $38.3 million as of December 31, 2022, which the Company believes will be sufficient to fund the Company's operating expenses and capital expenditure requirements into the fourth quarter of 2023.

Conference Call and Webcast Information

The Company will host a conference call and webcast with the investment community on March 30, 2023, at 8:00 a.m. Eastern Time featuring remarks by Carrie Bourdow, President and Chief Executive Officer, Patricia Drake, Chief Commercial Officer, Mark Demitrack, M.D., Senior Vice President and Chief Medical Officer, and Barry Shin, Chief Financial Officer.

Title:	Trevena Third Quarter 2022 Financial Results Conference Call & Webcast
Date:	Thursday, March 30, 2023
Time:	8:00 a.m. ET
Conference Call Details:	Toll-Free: 1-877-704-4453 International: 1-201-389-0920 Conference ID: 13736610

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=1600316&tp_key=4a1d148855

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 doses greater than 3 mg should not be administered. The cumulative daily dose should not exceed 27 mg. Please see Important Safety Information, including the BOXED WARNING, and full prescribing information at www.OLINVYK.com.

IMPORTANT SAFETY INFORMATION

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

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

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

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

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

INDICATIONS AND USAGE

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

Limitations of Use

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

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

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

CONTRAINDICATIONS

OLINVYK is contraindicated in patients with:

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

WARNINGS AND PRECAUTIONS

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

- Profound sedation, respiratory depression, coma, and death may result from the concomitant use of OLINVYK with benzodiazepines or other CNS depressants (e.g., non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, or alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate, prescribe the lowest effective dose, and minimize the duration.
- OLINVYK was shown to have mild QTc interval prolongation in thorough QT studies where patients were dosed up to 27 mg. Total cumulative daily doses exceeding 27 mg per day were not studied and may increase the risk for QTc interval prolongation. Therefore, the cumulative total daily dose of OLINVYK should not exceed 27 mg.
- Increased plasma concentrations of OLINVYK may occur in patients with decreased Cytochrome P450 (CYP) 2D6 function or normal metabolizers taking moderate or strong CYP2D6 inhibitors; also in patients taking a moderate or strong CYP3A4 inhibitor, in patients with decreased CYP2D6 function who are also receiving a moderate or strong CYP3A4 inhibitor, or with discontinuation of a CYP3A4 inducer. These patients may require less frequent dosing and should be closely monitored for respiratory depression and sedation at frequent intervals. Concomitant use of OLINVYK with CYP3A4 inducers or discontinuation of a moderate or strong CYP3A4 inhibitor can lower the expected concentration, which may decrease efficacy, and may require supplemental doses.
- Cases of adrenal insufficiency have been reported with opioid use (usually greater than one month). Presentation and symptoms may be nonspecific and include nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If confirmed, treat with physiologic replacement doses of corticosteroids and wean patient from the opioid.
- OLINVYK may cause severe hypotension, including orthostatic hypotension and syncope in ambulatory patients. There is increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (e.g., phenothiazines or general anesthetics). Monitor these patients for signs of hypotension. In patients with circulatory shock, avoid the use of OLINVYK as it may cause vasodilation that can further reduce cardiac output and blood pressure.
- Avoid the use of OLINVYK in patients with impaired consciousness or coma. OLINVYK should be used with caution in patients who may be susceptible to the intracranial effects of CO_2 retention, such as those with evidence of increased intracranial pressure or brain tumors, as a reduction in respiratory drive and the resultant CO_2 retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy.
- As with all opioids, OLINVYK may cause spasm of the sphincter of Oddi, and may cause increases in serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis, for worsening symptoms.
- OLINVYK may increase the frequency of seizures in patients with seizure disorders and may increase the risk of seizures in vulnerable patients. Monitor patients with a history of seizure disorders for worsened seizure control.
- Do not abruptly discontinue OLINVYK in a patient physically dependent on opioids. Gradually taper the dosage to avoid a withdrawal syndrome and return of pain. Avoid the use of mixed agonist/antagonist (e.g., pentazocine, nalbuphine, and butorphanol) or partial agonist (e.g., buprenorphine) analgesics in patients who are receiving OLINVYK, as they may reduce the analgesic effect and/or precipitate withdrawal symptoms.
- OLINVYK may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery.
- Although self-administration of opioids by patient-controlled analgesia (PCA) may allow each patient to individually titrate to an acceptable level of analgesia, PCA administration has resulted in adverse outcomes and episodes of respiratory depression. Health care providers and family members monitoring patients receiving PCA analgesia should be instructed in the need for appropriate monitoring for excessive sedation, respiratory depression, or other adverse effects of opioid medications.

ADVERSE REACTIONS

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

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

MEDICAL INFORMATION

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

You are encouraged to report suspected adverse events of prescription drugs to the FDA. Visit **www.fda.gov/medwatch** or call **1-800-FDA-1088**.

Please see Full Prescribing Information, including Boxed Warning.

About TRV045

TRV045 is a novel, selective sphingosine-1-phosphate subtype 1 ($S1P_1$) receptor modulator being developed as a potential treatment for acute and chronic neuropathic pain secondary to diabetic peripheral neuropathy. Through a collaboration with the National Institutes of Health, Trevena is also exploring TRV045 as a potential treatment for epilepsy.

S1P receptors are located throughout the body, including the central nervous system, where they are believed to play a role in modulating neurotransmission and membrane excitability.

Trevena's discovery efforts have identified a family of compounds that are highly selective for the $S1P_1$ receptor. TRV045 reversed thermal hyperalgesia, a measure of neuropathic pain, in nonclinical models of diabetic peripheral neuropathy and chemotherapy-induced peripheral neuropathy. TRV045 was not associated with lymphopenia and produced no changes in blood pressure, heart rate, or respiratory function at or above pharmacologically active doses in nonclinical studies. TRV045 is an investigational product and is not yet approved by the FDA.

About Trevena

Trevena, Inc. is a biopharmaceutical company focused on the development and commercialization of innovative medicines for patients with CNS disorders. The Company has one approved product in the United States, OLINVYK® (oliceridine) injection, indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate. The Company's novel pipeline is based on Nobel Prize winning research and includes three differentiated investigational drug candidates: TRV045 for diabetic neuropathic pain and epilepsy, TRV250 for the acute treatment of migraine and TRV734 for maintenance treatment of opioid use disorder.

For more information, please visit www.Trevena.com

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).

Forward-Looking Statements

Any statements in this press release about future expectations, plans and prospects for the Company, including statements about the Company's strategy, future operations, clinical development and trials of its therapeutic candidates, plans for potential future product candidates and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "suggest," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the status, timing, costs, results and interpretation of the Company's clinical trials or any future trials of any of the Company's investigational drug candidates; the uncertainties inherent in conducting clinical trials; expectations for regulatory interactions, submissions and approvals, including the Company's assessment of discussions with FDA; available funding; uncertainties related to the Company's intellectual property; uncertainties related to the ongoing COVID-19 pandemic, other matters that could affect the availability or commercial potential of the Company's therapeutic candidates and approved product; and other factors discussed in the Risk Factors set forth in the Company's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q filed with the Securities and Exchange Commission (SEC) and in other filings the Company makes with the SEC from time to time. In addition, the forward-looking statements included in this press release represent the Company's views only as of the date hereof. The Company anticipates that subsequent events and developments may cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so, except as may be required by law.

For more information, please contact:

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Dan Ferry

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(617) 430-7576

Company Contact:

Bob Yoder

SVP and Chief Business Officer

Trevena, Inc.

(610) 354-8840

TREVENA, INC.
Condensed Statements of Operations
(Unaudited, in thousands except share and per share data)

	Three Months Ended Dec 31,		Year Ended Dec 31,	
	2022	**2021**	**2022**	**2021**
Product revenue	$ -	$ (1)	$ (438)	$ 498
License revenue	-	-	20	69
Total revenue	-	(1)	(418)	567
Operating expenses:				
Cost of goods sold	228	334	3,018	954
Selling, general and administrative	5,723	9,761	34,728	38,112
Research and development	3,396	3,937	18,211	13,426
Total operating expenses	9,347	14,032	55,957	52,492
Loss from operations	(9,347)	(14,033)	(56,375)	(51,925)
Other income	2,342	80	2,705	337
Loss before income tax expense	(7,005)	(13,953)	(53,670)	(51,588)
Unrealized gain on marketable securities	-	-	1	-
Net loss	$ (7,005)	$ (13,953)	$ (53,669)	$ (51,588)
Per share information:				
Net loss per share of common stock, basic and diluted	$ (0.73)	$ (2.12)	$ (7.59)	$ (7.90)
Weighted average shares outstanding, basic and diluted	9,594,072	6,586,251	7,072,362	6,529,074

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

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 38,320	$ 66,923
Inventories	906	2,352
Prepaid expenses and other current assets	1,782	1,448
Total current assets	41,008	70,723
Restricted cash	1,960	1,311
Property and equipment, net	1,488	1,841
Right-of-use lease assets	4,224	4,706
Other assets	-	1,543
Total assets	$ 48,680	$ 80,124
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable, net	$ 2,372	$ 4,547
Accrued expenses and other current liabilities	5,461	3,847
Current portion of lease liabilities	899	792
Total current liabilities	8,732	9,186
Loans payable, net	13,430	-
Leases, net of current portion	5,436	6,309
Warrant liability	5,483	-
Total liabilities	33,081	15,495
Common stock	8	7
Additional paid-in capital	563,362	558,724
Accumulated deficit	(547,772)	(494,102)
Accumulated other comprehensive income (loss)	1	-
Total stockholders' equity	15,599	64,629
Total liabilities and stockholders' equity	$ 48,680	$ 80,124

Exhibit 99.2

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; uncertainties related to the ongoing COVID-19 pandemic, 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
Scott Braunstein, M.D.	MARINUS PHARMACEUTICALS, AISLING CAPITAL, PACIRA BIOSCIENCES	**Anne M. Phillips, M.D.**	novo nordisk, GSK GlaxoSmithKline
Michael R. Dougherty	Adolor, centocor	**Barbara Yanni**	MERCK

Trevena: Innovative CNS Company

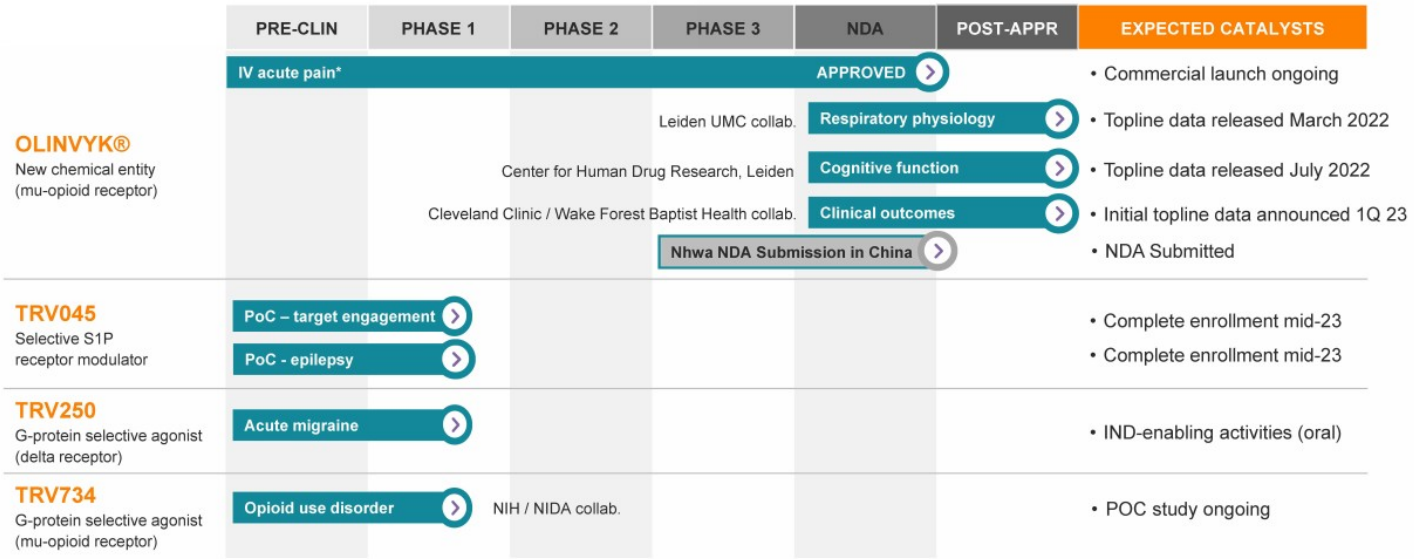
IV OLINVYK: Differentiated profile	NCE approved for the management of acute pain in adults Additional supportive studies with near-term data
Large market, targeted launch	45M+ US hospital patients; 9M procedures is initial core focus $1.5B+ market opportunity for core focus
TRV045: Selective S1PR modulator	Novel candidate for CNS disorders (with potential broader applicability) Two PoC* studies initiated (epilepsy / CNS target engagement) with near-term data
Novel CNS pipeline	New mechanisms for acute / neuropathic pain, epilepsy, acute migraine, opioid use disorder NCEs targeting significant unmet needs
Financial position	$38.3M cash / equivalents / marketable securities @ Q4

* PoC = Proof of Concept

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.

NCE = New Chemical Entity; MOA = Mechanism of Action; NIH = National Institutes of Health;

Multiple Expected Catalysts



*PoC = Proof of Concept study
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.
TRV250, TRV734 and TRV045 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

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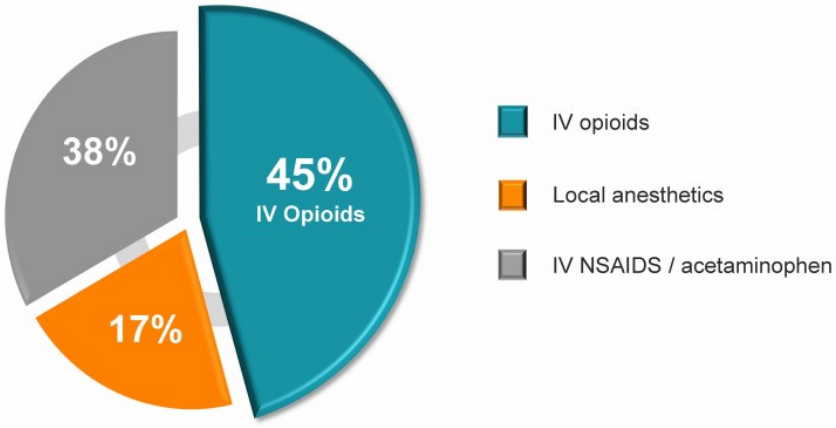
Ex-US Royalty-Based Financing Highlights

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	**$15M** upfront (received April 2022) **$10M** on commercial or financing milestone **$15M** on first commercial sale in China **$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 • Negative pledge only until Chinese approval • Flexibility for additional business development opportunities

*Potential increase to 7% (with combined US/China cap) if not approved by YE-23

Large Market Opportunity – Acute Pain

US injectable analgesic hospital market unit volume[1]



45M patients receive IV opioids annually to treat acute pain[1]

IV opioids have unrivalled analgesic efficacy

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

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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.
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

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

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

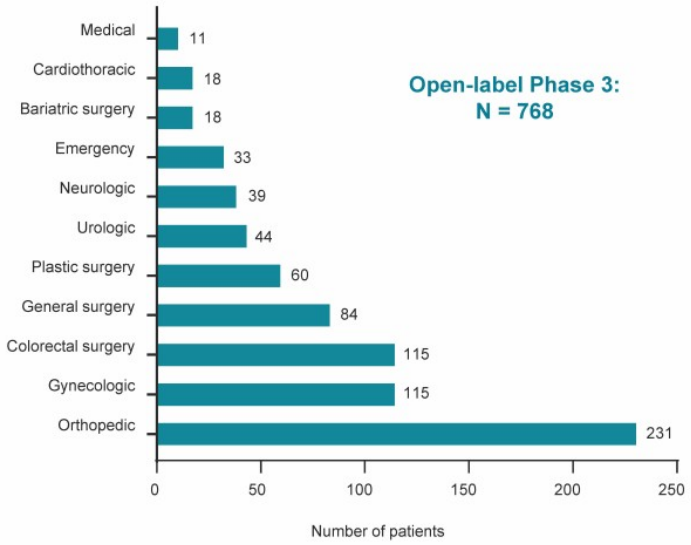
New chemical entity
Distinct from IV morphine

IV opioid efficacy
Hard- and soft-tissue surgeries

Rapid analgesia
1-3 min median onset of pain relief

OLINVYK Studied in Complex Surgeries & Patients

Broad range of surgeries / medical procedures



Complex patients included

- 32% ≥ 65 years; 46% BMI ≥ 30
- Co-morbidities: diabetes, obstructive sleep apnea, COPD, chronic / cancer pain
- Concomitant medications: antiemetics, antibiotics

Multiple inpatient and hosp outpatient settings

- Hospital recovery
- Critical care
- Emergency department
- Ambulatory surgical centers

Low discontinuation for AEs / lack of efficacy

- 2% for adverse events
- 4% for lack of efficacy

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Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.
Bergese SD et al. J Pain Research, 2019. Trial modeled real-world use: usual patient care with OLINVYK instead of standard IV opioid.
See FDA draft guidance for Industry Distributing Scientific and Medical Publications on Unapproved New Uses.

OLINVYK: Well-Characterized Safety / Tolerability

Adverse drug reactions reported in ≥5% of OLINVYK-treated patients stratified by daily dose (Phase 3 pivotal trials pooled)[1]

	Placebo (N = 162)	OLINVYK ≤ 27 mg (N = 316)	Morphine (N = 158)
Patients with any TEAE (%)	73	86	96
Nausea	35	52	70
Vomiting	10	26	52
Headache	30	26	30
Dizziness	11	18	25
Constipation	9	14	14
Hypoxia	3	12	17
Pruritus	6	9	19
Sedation	5	7	13
Somnolence	4	6	10
Back pain	4	6	6
Hot flush	4	4	8
Pruritus gen.	1	2	10

Not an adequate basis for comparison of rates between the OLINVYK treatment group and the morphine treatment group.

Key cost-drivers associated with IV opioids:

Vomiting
Can result in significant health risks and compromise recovery

Somnolence
Significant patient safety concern, can lead to respiratory depression

O_2 saturation < 90%
Independent predictor of early post-op respiratory complications

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

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 mid-2023)

GI Tolerability

52.2% Complete GI Response[1]

(Defined as no vomiting and 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 – 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

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ARTEMIS – EMR Clinical Outcomes Study

OLINVYK electronic medical records (EMR) study at VOLITION site: Wake Forest Baptist Health

- **96 OLINVYK-treated patients** at Wake Forest Baptist Health VOLITION site
- **457 matched patients** undergoing similar surgical procedures, treated with other IV opioids, at same site 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=457	OLINVYK-Treated VOLITION Patients N=96	
Hospital Length of Stay (avg)	**5.9 days**	**4.3 days** (1.6 day reduction)	P=0.0001
Post-Anesthesia Care Unit (PACU) (avg)	**2.4 hours**	**2.4 hours**	P=0.8174
ICD-Coded Delirium*	**4.4%** (20 patients)	**1.0%** (1 patient)	P=0.27

* ICD-coding used as 3D-CAM (VOLITION endpoint) is not generally used in the general patient population

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

Respiratory Physiology Study

Head-to-Head Comparison of OLINVYK and IV morphine in Elderly/Overweight Subjects (N=18)

Assessment of Respiratory Function:

- Increase inhaled CO_2 to experimentally induce respiratory drive
- Impact of drug measured as change in minute ventilation
- Greater reductions in minute ventilation indicate more respiratory depression
- Validated method to estimate the impact of a drug on respiratory drive

Ventilatory Response to Hypercapnia

Assessment of Pain Threshold:

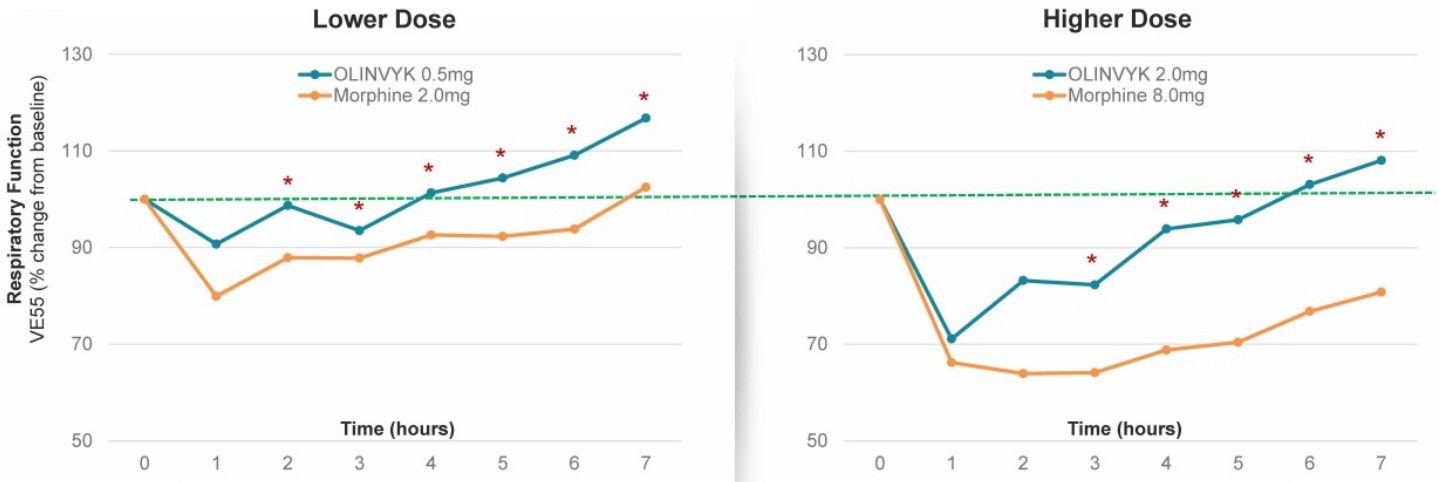
- Analgesic comparison measured using valid models of induced cold and electrical pain

Analgesia Assessment

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

Respiratory Physiology Study: Elderly / Overweight Subjects

OLINVYK demonstrated reduced impact on respiratory function vs IV morphine



* Represents P < 0.05 (statistically significant) in pairwise comparison between treatments
Treatments differ over time: main effect P < 0.0001 using a linear mixed effects model

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

Respiratory Physiology Study Observations

- Study population comprised elderly individuals (56 to 87 years, mean = 71.2) with BMI ranging from 20 to 34 (mean = 26.3)
- Both OLINVYK and IV morphine achieved comparable levels of pain relief. A statistically significant reduced impact on respiratory function was observed in patients treated with OLINVYK as measured by the mean respiratory ventilation profiles over time (P<0.0001)
- The study replicates the results from the earlier study in younger subjects using a similar methodology[1]. The findings extend our knowledge to patients who are at higher risk for the development of respiratory depression with the use of opioids, namely the elderly and overweight patients

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

1. *Soergel DG, et al. Pain. 2014;155:1829-1835*

Top Line Data: OLINVYK vs IV Morphine Cognitive Function Study

Clinical assessment of OLINVYK's potential impact on cognitive function vs. IV morphine

- Randomized, double-blind, placebo-controlled, crossover study
- N = 23 subjects, 19-53 years old (median age 26), 13 females & 10 males
- Topline data received July 2022

Cognitive function assessment: NeuroCart

CHDR
Centre for Human Drug Research

- Comprehensive CNS test battery, used in testing a wide range of CNS drugs for 30 years
- Cognitive outcome measures include major domains of motor performance, attention, reaction time, memory, and executive function

Study will also include pain model testing (cold pressor test) and PK assessment

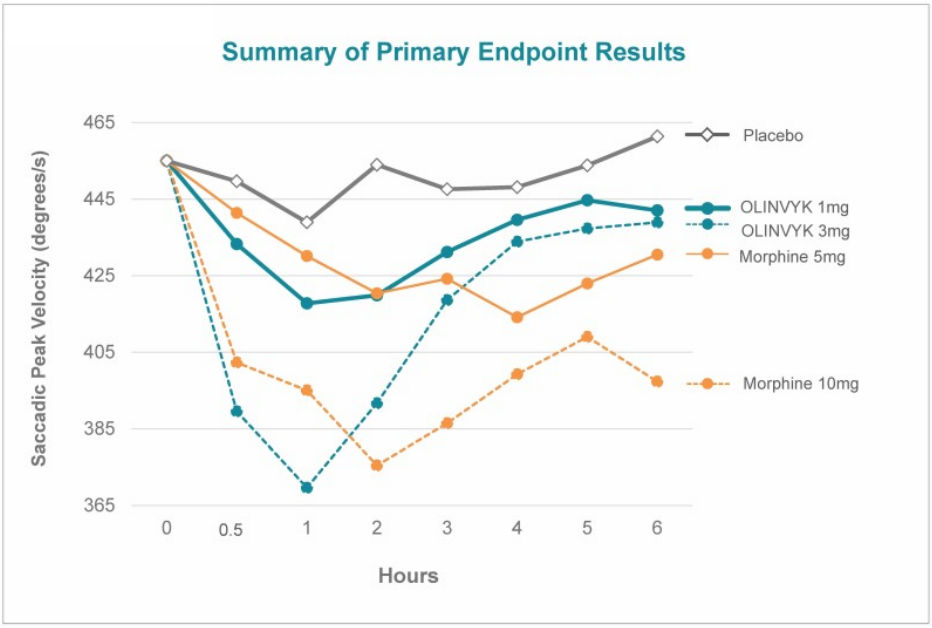
OLINVYK Showed Evidence of Reduced Impact on Neurocognitive Function Compared to IV Morphine

OLINVYK showed a statistically significant reduction in sedation versus IV morphine

- Measured by saccadic eye movement peak velocity (a sensitive measure of sedating action of medications)

The prespecified mixed-model repeated measures ANOVA highlighted a difference between treatments:

- Main effect of treatment: P<0.0001
- OLINVYK versus IV morphine: P=0.0236



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Secondary Endpoint Results

OLINVYK showed a statistically significant difference or trend (vs IV morphine) on several prespecified secondary endpoints, despite the relatively small sample size, across a range of neurocognitive measures and motor performance:

- ***Reaction Time.*** Reduced impact on saccadic eye movement reaction time
  - Main effect, P=0.0201 OLINVYK vs IV morphine, P=0.0273
- ***Postural Stability (Motor Function).*** Reduced body sway, a measure of motor function
  - Main effect, P=0.0314 OLINVYK vs IV morphine, P=0.0951
- ***Eye-Hand Coordination.*** Reduced performance accuracy on the adaptive tracking test, a measure of eye-hand coordination
  - Main effect, P=0.0011 OLINVYK vs IV morphine, P=0.1303
- Neurocognitive function including impaired sedation and postural instability may have potentially important consequences in clinical care settings with the use of opioid medications, and consequent benefits in length of stay and other health economic outcomes
- Other secondary outcome measures, including visual tracking and higher-order cognitive processing did not show statistical differences between OLINVYK and IV morphine
- No serious adverse events were observed in the study, and adverse events were generally assessed as mild

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)

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

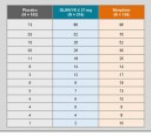
OLINVYK vs IV Morphine Health Economic Models

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 lable, 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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Customer Engagement Strategy

Targeted Account Launch

Health Care Practitioners (HCPs)
Anesthesiology, Colorectal, Critical Care physicians

1. OLINVYK: NCE, distinct from IV morphine
2. 1-3 min onset & no active metabolites
3. Safety data in complex patients / surgeries

Targeted Accounts
Over 50% of IV opioid volume covered by customer facing team

1. OLINVYK published safety data
2. Published health economic / cost offset data

Expanded Targets: ~150 Burn Center Accounts

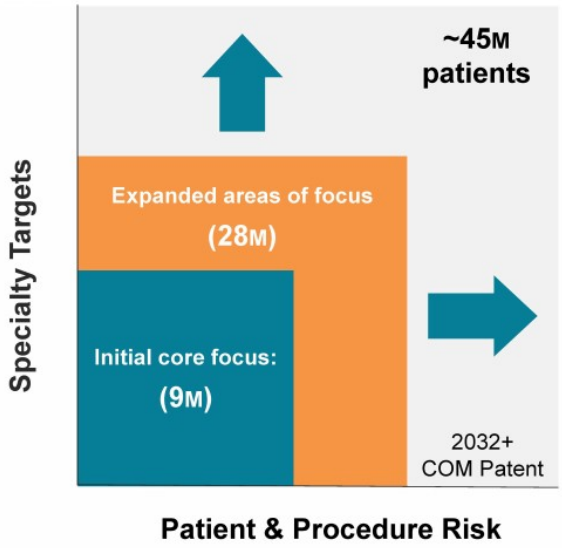
Critical care / burn patients experience severe pain and are at higher risk for AEs

Targeted market opportunity

- ~40k burn-related hospitalizations each year across 150 burn centers in US
- Longer average in-patient stay: 8-9 days
- Burn guidelines recommend use of IV opioids

Key considerations	OLINVYK attributes
Need for rapid, long-lasting acute pain relief	1-3 minute onset of action ~3 hour duration
Many patients have renal injury	No dose adjustment for patients with renal impairment
Need to avoid dose-stacking	No active metabolites

OLINVYK: Significant Opportunity in Acute Pain Market



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

Initial core focus

- Hospitals / ambulatory surgical centers
- Burn (6-8 days) / critical care & colorectal (3-5 days)

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.
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

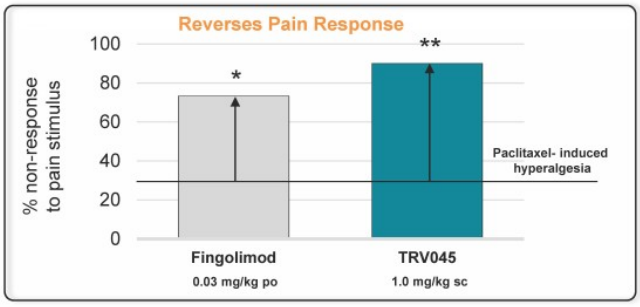
- Inhibits pain sensation[1]
- Inhibits excitatory neuronal signaling[2]

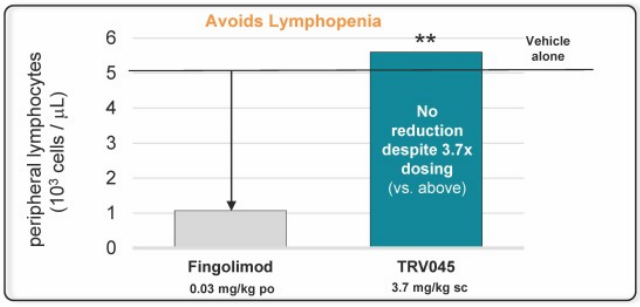
Existing S1PR-targeted drugs, however, are ill-suited for CNS indications due to known:

Lymphopenia
Cardiac AEs
Pulmonary AEs
Ophthalmologic AEs

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: Novel MOA, Selective S1PR





- In animals, TRV045 reversed neuropathic pain without immune-suppressing activity[1]
- Novel mechanism with broad potential for CNS indications
  - Phase 1 study completed
  - Targeted proof-of-concept study initiated

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 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)

Targeted CNS proof-of-concept study initiated

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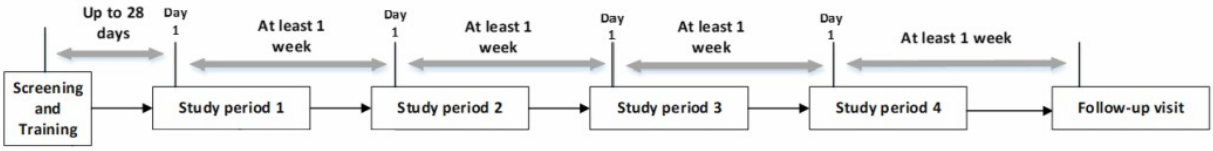
[1] Based on nonclinical measures of in vitro and in vivo PD

POC Study: Single-dose Target Engagement (Ph 1)

Enrollment completion expected mid-2023

- **Design:** Randomized, double-blind, placebo-controlled, four-way cross-over study (n~24)
  - Placebo or TRV045 (50/150/300mg)

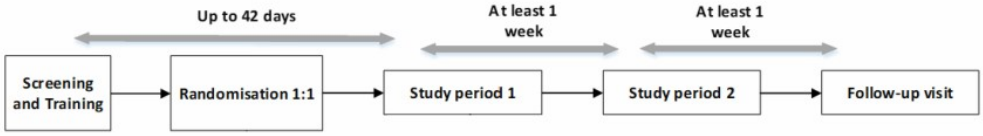


Pharmacodynamic Endpoint	Test and Outcome	Pain Type
Cold Pressor	Pain detection (PDT), pain tolerance (PTT), post-test VAS	Nociceptive (thermal)
Electrical Pain	Burst: PDT, PTT, PT-VAS Stair: PDT, PTT, PT-VAS	Nociceptive (electrical)
Conditioned Pain Modulation Resp	Change in elec. stair pre- / post- cold pressor test: PDT, PTT	Nociceptive (central mod)
Heat Pain	Volar forearm: PDT Back: PDT	Nociceptive (thermal, inflam)
Pressure Pain	Gastrocnemius tourniquet: PDT, PTT	Nociceptive (mechanical)
Secondary Allodynia (post-capsaicin)	Volar forearm: PDT	Neuropathic (central sens)

POC Study: Repeat-dose TMS study (Ph 1)

Enrollment completion expected mid-2023

- **Design:** Randomized, double-blind, placebo-controlled, multiple dose, two-way cross-over study (n~24)
  - Placebo or TRV045 (250mg) for 4 days

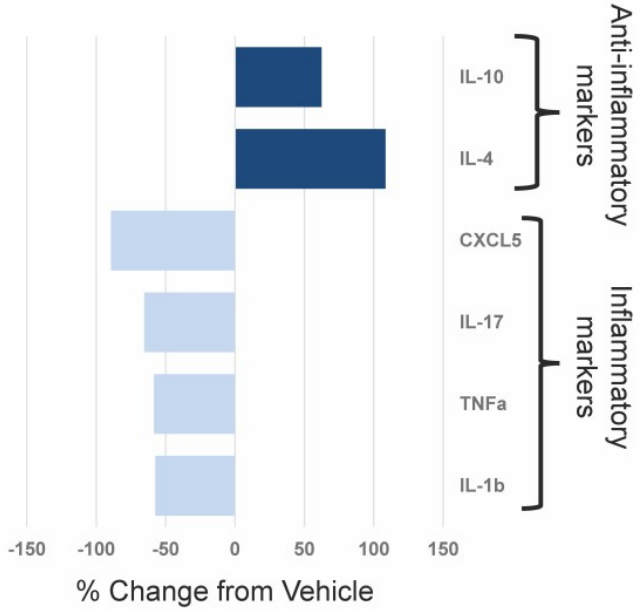


Pharmacodynamic Endpoint	Test and Outcome
Resting Motor Threshold	% maximal machine output
MEP Amplitude	Peak-to-peak amplitude (P-PA)
Short Intracortical Inhibition	% ratio of the mean P-PA of un-/conditioned pulse at ISI of 2 msec
Intracortical Facilitation	% ratio of the mean P-PA of un-/conditioned pulse at ISI of 15 msec
Long Intracortical Inhibition	% ratio of the mean P-PA of un-/conditioned pulses at ISI of 100 / 300 msec
Single- / Paired-Pulse TMS EEG Evoked Potentials	TOIs: N15, P30, N45, P60, N100, P180

Effect of TRV045 on Cytokine / Chemokine Release

Anti-inflammatory actions on astrocytes in cell culture

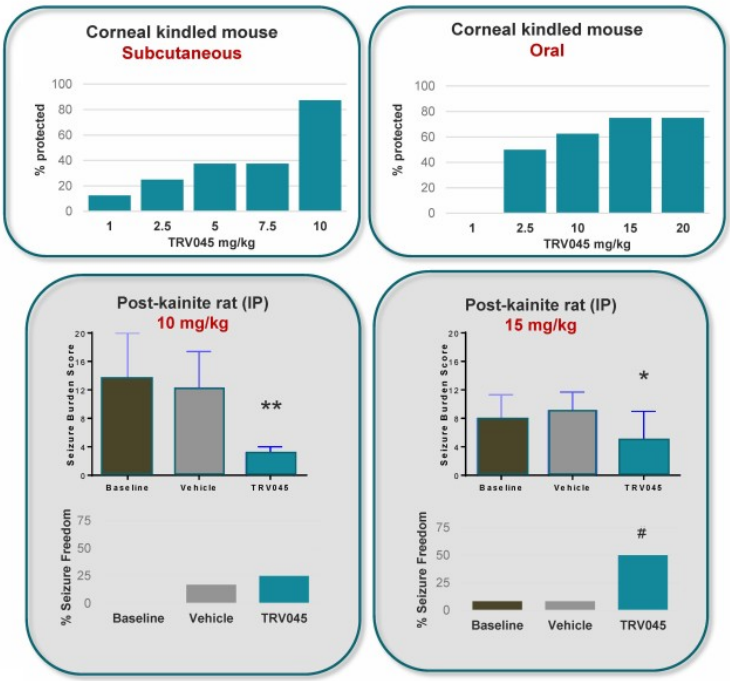
- Methods:
  - Primary mouse astrocytes in monolayer cell culture; incubated for 24 hrs w/ 5 μM TRV045
  - Panel of 17 cytokines / chemokines * assessed by ELISA
- Main Findings:
  - Net anti-inflammatory action on astrocyte cytokine / chemokine release in culture
    - Increase in release of all anti-inflammatory cytokines measured (P<0.05 v vehicle)
    - Reduction in release of all inflammatory cytokines measured (P<0.05 v vehicle)



* *Full cytokine / chemokine panel studied: (Inflammatory markers) – TNFα, IL-6, IL-1b, IL-17, IL-23, IL-33, CCL1, CCL2, CCL20, CXCL5, CXCL12, CX3CL1, IFNγ, Csf2, Substance P; (Anti-inflammatory markers) – IL-10, IL-4. [Trevena, Inc., 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



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

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TRV250: New MOA for Acute Treatment of Migraine

TRV734: Maintenance Therapy for Opioid Use Disorder

TRV250: New MOA for Acute Treatment of Migraine

Delta receptor: Untapped potential in CNS space

Migraine represents a large market opportunity; total migraine drug market = ~$3.5B

Delta receptors have unique distribution throughout the brain

Play important role in regulation of pain, mood, and anxiety

Every year in the US[1]:

650M migraines treated each year

1.2M ER visits due to migraines

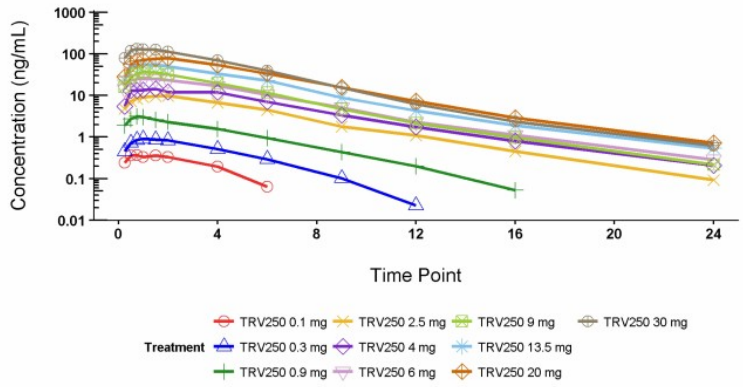
- **20-30%** of migraine sufferers do not respond to / cannot tolerate the market-leading triptan drug class
- Approx. **50%** of migraineurs also suffer from anxiety[2]

1) Data from Decision Resources, Pharmacor migraine market landscape and forecast 2018. 2) Moven et al., J Neurol Neurosurg Psychiatry, 2016.
Icons made by Freepik from www.flaticon.com

TRV250: Well-Tolerated in Ph1 Healthy Volunteer PK Study

Subcutaneous doses up to 30 mg studied; no SAEs observed

Single dose pharmacokinetics of TRV250 given by SC injection



Well tolerated, with no SAEs across broad range of doses

Predictable PK: dose-proportional between 0.1 mg to 30 mg SC

Half-life consistent across all doses

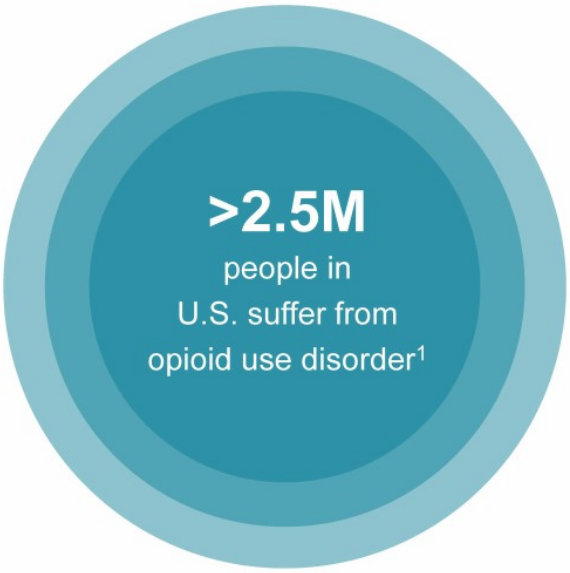
No EEG findings observed in any subject

IND-enabling activities initiated for new oral dose form

SC = subcutaneous. Fossler MJ et al., CNS Drugs, Aug 2020;34(8):853-865.

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

Trevena® 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 Real world top line data results announced in Q1 2023
Large market, targeted launch	45M+ US hospital patients; 9M procedures is initial core focus $1.5B+ market opportunity for core focus
TRV045: Selective S1PR modulator	Novel candidate for CNS disorders (with potential broader applicability) Two PoC* studies initiated (epilepsy / CNS target engagement) with near-term data
Novel CNS pipeline	New mechanisms for acute / neuropathic pain, epilepsy, acute migraine, opioid use disorder NCEs targeting significant unmet needs
Financial position	$38.3M cash / equivalents / marketable securities @ Q4

* PoC = Proof of Concept

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.

NCE = New Chemical Entity; MOA = Mechanism of Action; NIH = National Institutes of Health;

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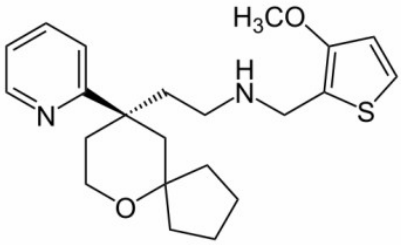
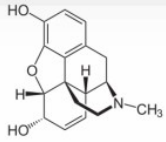
Appendix

OLINVYK: Distinct From IV Morphine / Hydromorphone

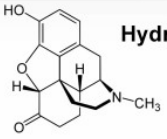
OLINVYK



Morphine



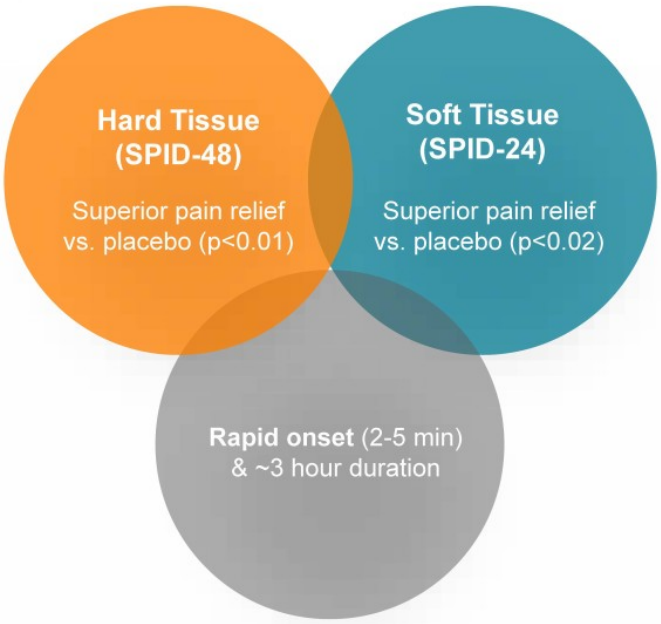
Hydromorphone



- Studied in >1,900 individuals
- IV morphine included as active comparator
- NCE with 2032+ COM patent[1]

Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.
1) 2032 composition of matter patent expiration does not include potential patent extensions.

OLINVYK: IV Opioid Efficacy and Rapid Onset



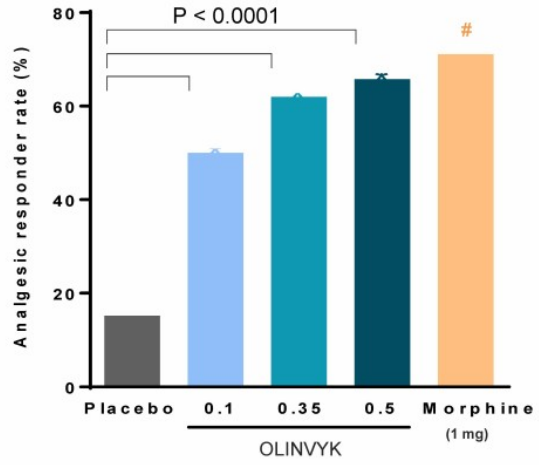
- Efficacy achieved in hard tissue & soft tissue models
- Rapid onset: perceptible pain relief within 1-3 minutes
- OLINVYK efficacy data in peer-reviewed journals *The Journal of Pain Research*[1] and *Pain Practice*[2]

Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.
1) Viscusi ER et al. J Pain Res. 2019;12:927–943. Published 2019 Mar 11. 2) Singla NK et al. Pain Pract. 2019;19:715-731. Published 2019 Jun 04.

Primary Efficacy Endpoint Achieved in Two Pivotal Studies

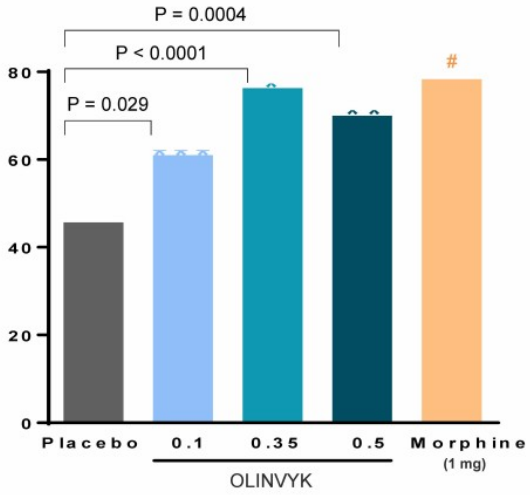
OLINVYK achieved IV opioid efficacy

Published in *The Journal of Pain Research*



Ph3: Hard Tissue Surgery
Mean baseline pain = 6.7

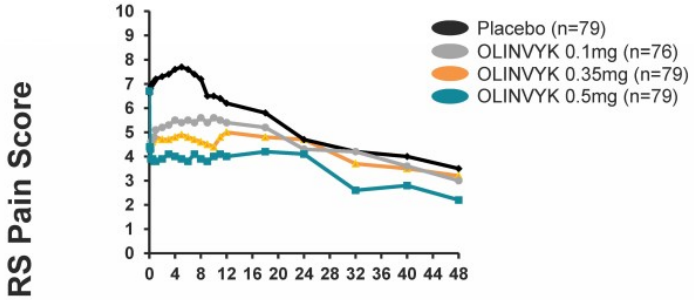
Published in *Pain Practice*



Ph3: Soft Tissue Surgery
Mean baseline pain = 7.3

Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.
These analyses were the prespecified primary endpoints for both studies. Section 14 of the Prescribing Information includes the SPID-24 and SPID-48 efficacy analyses that were the basis for approval.
Viscusi ER et al. J Pain Res. 2019;12:927–943. Published 2019 Mar 11. Singla NK et al. Pain Pract. 2019;19:715-731. Published 2019 Jun 04. #p < 0.05 vs. placebo (unadjusted).

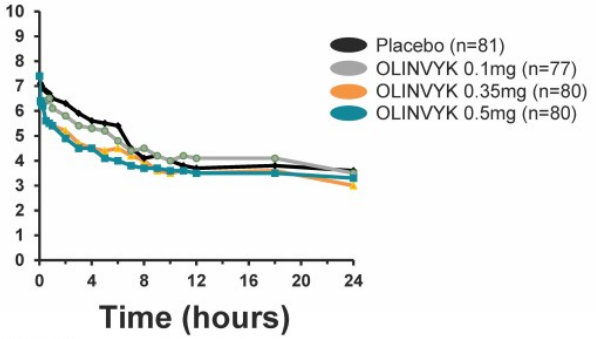
OLINVYK: IV Opioid Efficacy in 2 Phase 3 RCTs



Study 1 (Orthopedic – Hard Tissue)

3 PCA regimens studied (0.1, 0.35, 0.5 mg) vs. placebo; all doses P<0.01 vs. placebo

	OLINVYK			
Outcome	**0.1 mg**	**0.35 mg**	**0.5 mg**	**Placebo**
% Completed	83%	87%	84%	60%
% D/C LOE	9%	4%	5%	34%
% Rescue Meds	41%	20%	17%	77%



Study 2 (Plastic Surgery – Soft Tissue)

3 PCA regimens studied (0.1, 0.35, 0.5 mg) vs. placebo; 0.35 / 0.5 mg doses P<0.02 vs. placebo

	OLINVYK			
Outcome	**0.1 mg**	**0.35 mg**	**0.5 mg**	**Placebo**
% Completed	86%	90%	87%	74%
% D/C LOE	11%	3%	5%	22%
% Rescue Meds	31%	21%	18%	49%

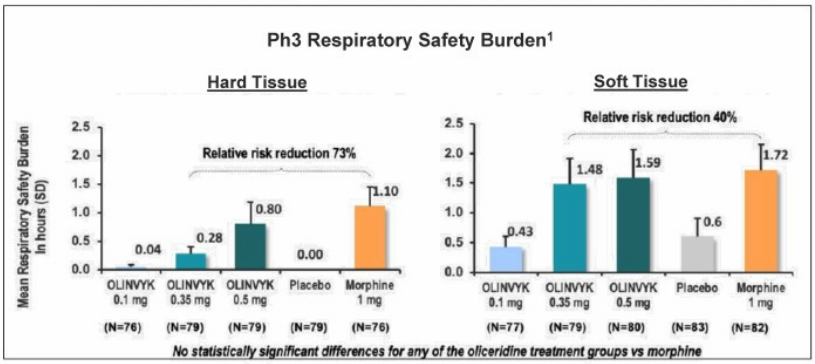
Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.

Robust Assessment of Respiratory Safety in Phase 3 RCTs

Data included in AMCP dossier used in formulary review

- Prespecified secondary endpoint: Respiratory Safety Burden (RSB)
  - Calculated based on incidence and cumulative duration of respiratory safety events
- Full characterization of respiratory safety profile has been made available to HCPs and formulary decision makers
  - Data can be found in OLINVYK AMCP dossier and published literature

Ph3 Respiratory Safety Burden[1]



No statistically significant differences for any of the oliceridine treatment groups vs morphine

Ph3 Respiratory Safety Events[2]
(Components of the RSB calculation)

Hard Tissue

Orthopedic Surgery-Bunionectomy Study	Placebo (N=79)	Demand Dose OLINVYK 0.1 mg (N=76)	OLINVYK 0.35 mg (N=79)	OLINVYK 0.5 mg (N=79)	Morphine 1 mg (N=76)
Components of the respiratory safety burden					
≥1 respiratory safety event, n (%)	0	1 (1.3)	7 (8.9)	11 (13.9)	14 (18.4)
P-value vs morphine	0.006	0.002	0.050	0.364	–
Duration of event, mean hours (SD)	0 (N/E)	2.88 (N/E)	3.21 (2.24)	5.72 (7.44)	5.96 (4.67)
P-value vs morphine	0.102	0.140	0.260	0.186	–
Respiratory safety event measures					
Oxygen saturation <90%, n (%)	1 (1.3)	3 (3.9)	8 (10.1)	11 (13.9)	15 (19.7)
P value vs morphine	0.005	0.006	0.100	0.352	–
Respiratory rate ≤8 bpm, n (%)	0	0	1 (1.3)	1 (1.3)	4 (5.3)
P value vs morphine	0.956	0.956	0.188	0.185	–
Sedation (MRPSS ≥3), n (%)	10 (2.7)	14 (18.4)	16 (20.3)	13 (16.5)	15 (19.7)
P value vs morphine	0.242	0.838	0.926	0.610	–

Soft Tissue

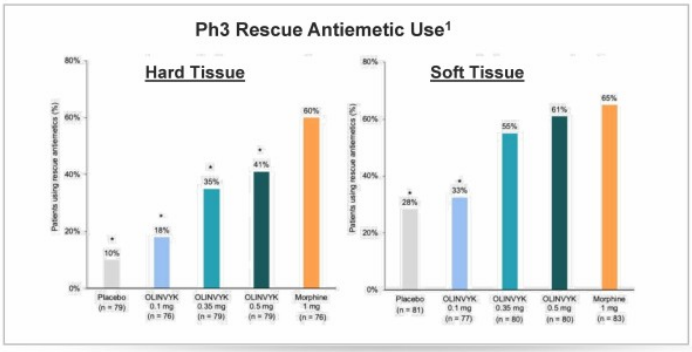
Plastic Surgery-Abdominoplasty Study	Placebo (N=83)	Demand Dose OLINVYK 0.1 mg (N=77)	OLINVYK 0.35 mg (N=79)	OLINVYK 0.5 mg (N=80)	Morphine 1 mg (N=82)
Components of the respiratory safety burden					
≥1 respiratory safety event, n (%)	5 (6.0)	6 (7.8)	17 (21.5)	18 (22.5)	22 (26.8)
Odds ratio vs morphine	0.15	0.19	0.61	0.68	—
P value vs morphine	0.0003	0.0007	0.20	0.32	
Duration of event, mean hours (SD)	9.88 (7.0)	5.51 (1.91)	6.88 (5.66)	7.07 (6.56)	6.40 (5.09)
P value vs morphine	0.52	0.29	0.78	0.76	—
Respiratory safety event measures					
Oxygen saturation <90%, n (%)	7 (8.4)	6 (7.8)	15 (19.0)	16 (20.0)	20 (24.4)
P value vs morphine	0.02	0.01	0.57	0.76	–
Respiratory rate ≤8 bpm, n (%)	1 (1.2)	0	4 (5.1)	6 (7.5)	8 (9.8)
P value vs morphine	0.054	0.95	0.38	0.84	–
Sedation (MRPSS ≥3), n (%)	15 (18.1)	8 (10.4)	19 (24.1)	18 (22.5)	21 (25.6)
P value vs morphine	0.25	0.02	0.83	0.65	–

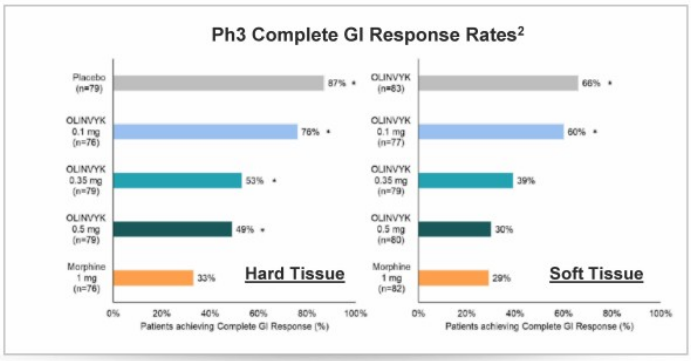
bpm = breaths per minute; MRPSS = Moline-Roberts Pharmacologic Sedation Scale

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

Robust Assessment of GI Tolerability in Phase 3 RCTs

Data included in AMCP dossier used in formulary review





- Phase 3 pivotal trials included measurements of nausea / vomiting rates and rescue antiemetic use
- Additional exploratory post-hoc analysis was conducted using a “complete GI response” endpoint[3]
- Full characterization of GI tolerability has been made available to HCPs and formulary decision makers
  - Data can be found in OLINVYK AMCP dossier and published literature

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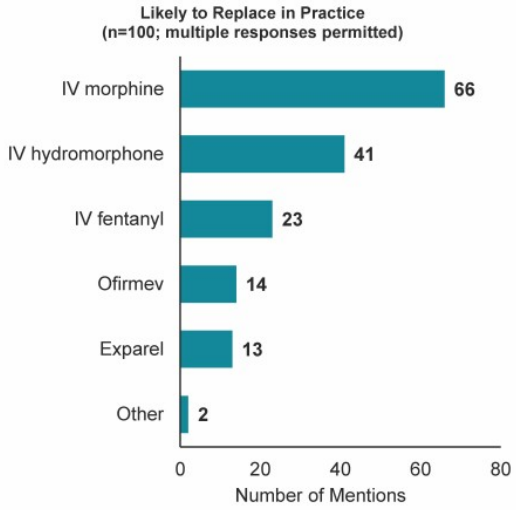
P < 0.05 vs. morphine.1) Figure 2-10, Section 2.2, OLINVYK Evidence Dossier for Formulary Consideration. 2) Figure 2-11, Section 2.2, OLINVYK Evidence Dossier for Formulary Consideration. 3) GI complete response defined as the proportion of patients who did not experience the AE of vomiting and did not use rescue antiemetic medication throughout their allocated treatment period in the study.

Positive Feedback from Formulary Stakeholders[1]

~75% of formulary stakeholders find OLINVYK's published data clinically meaningful:[2]

Pharmacist (n=50)	Physician (n=50)
	
72%	76%

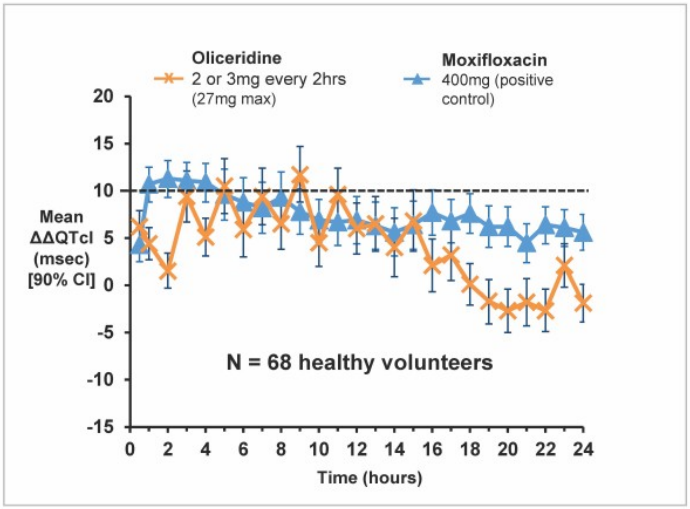
Majority of stakeholders view IV morphine as likely to be replaced by OLINVYK:



Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.
1) Qualitative Pricing research, Charles River Associates, April 2020. 2) "Are the improvements in respiratory safety events and GI tolerability clinically meaningful?" Based on OLINVYK Ph3 clinical trial data.

No Accumulation Despite Repeated Dosing

Multi-Dose tQT Study



Key results

- **No accumulation through 24 hrs**
  Mean QTcI <10ms at 22 of 24 points
- **No categorical QTc outliers**
  Δ >60 ms; >500 ms absolute
- **Well tolerated, no SAEs***
  92% reached max daily dose

*The effect on QT prolongation at total cumulative daily doses >27 mg has not been studied in a thorough QT study. Total cumulative daily doses exceeding 27 mg per day may increase the risk for QTc interval prolongation. Therefore, the cumulative total daily dose of OLINVYK should not exceed 27 mg.

Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.
3 subjects not dosed due to lack of venous access: 1 discontinuation due to a non-serious adverse event (asymptomatic non-sustained ventricular tachycardia) with confounding hypokalemia and no meaningful QT prolongation during dosing, 1 subject completed dosing but not evaluable due to equipment malfunction

VOLITION: Initial Topline Results and Study Design

Study Design

- Real-world, open-label, multi-site, post-approval clinical outcomes study in 203 adult patients undergoing major non-cardiac surgery.
- IV OLINVYK was dosed as the first-line analgesic during post-operative care, with a 1.5mg loading dose of OLINVYK at surgical closure, and 0.35mg to 0.5mg of OLINVYK, as needed, administered with a PCA device, with a 6-minute lockout period. Additional boluses (≤1 mg) of OLINVYK were available if needed as soon as 15 minutes after the initial 1.5 mg loading dose.
- The average age of patients in VOLITION was 57.1 years (range 19 to 89), with approximately equal representation of men and women.
- Approximately 85% of patients underwent an abdominal surgical intervention (e.g. partial or total colectomy, enterotomy or other open abdominal procedures).
- A majority of patients had significant morbidity at the time of surgery (ASA status), and respiratory risk was intermediate to high risk (PRODIGY risk score).
- Average surgical duration; 4.7 hours (range of 1.2 to 12.6 hours).

- **GI Complete Responder Rate** (prespecified exploratory endpoint)**.** 52.2% of OLINVYK-treated patients were classified as GI complete responders, defined as no vomiting and no antiemetic use throughout the postoperative period. As reference, in pooled data for the Company's pivotal Phase 3 studies of OLINVYK, the GI complete response rate was 46.2% (0.35mg) and 39.7% (0.5mg). As reflected in the OLINVYK label, nausea and vomiting were two of the most common adverse events reported in the controlled clinical trials.
- **Wakefulness / Sedation** (prespecified exploratory endpoint)**.** Over 90% of OLINVYK-treated patients reported feeling "alert and calm" from the morning of the first post-operative day and at every observation point thereafter, based on the Richmond Agitation-Sedation Scale. Sedation is an established risk of opioids including OLINVYK.
- **Cognition** (prespecified exploratory endpoint)**.** Only 3.9% of OLINVYK-treated patients exhibited symptoms suggestive of delirium at any point in the 48-hour post-operative period. Delirium was assessed based on the validated 3D-CAM screening tool.
- **Data from Primary, Secondary and Other Exploratory Endpoints.** Data is not yet available for other endpoints, including the primary and secondary respiratory endpoints, as well as other prespecified exploratory endpoints. The Company expects to report these data mid-2023.
- **Tolerability.** No drug-related serious adverse events (SAEs) and no deaths were reported in the VOLITION study. Data on other adverse events is not yet available, and the Company expects to report these data mid-2023.

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, and as reflected in the OLINVYK label, nausea and vomiting were two of the most common adverse events reported in the controlled clinical trials

ARTEMIS: Initial Topline Results and Study Design

Study Design

- EMR-based analysis that compared the health outcomes of VOLITION study patients with a matched population of patients, who underwent similar surgical procedures but were treated with other IV opioids, at the same institutions and during the same general time period as VOLITION.
- Matching was conducted with a greedy matching algorithm, using a propensity scoring method with eight different demographic and clinical characteristics (e.g. age, sex, type and duration of surgery, measures of overall surgical and medical morbidity, and type of hospital insurance).

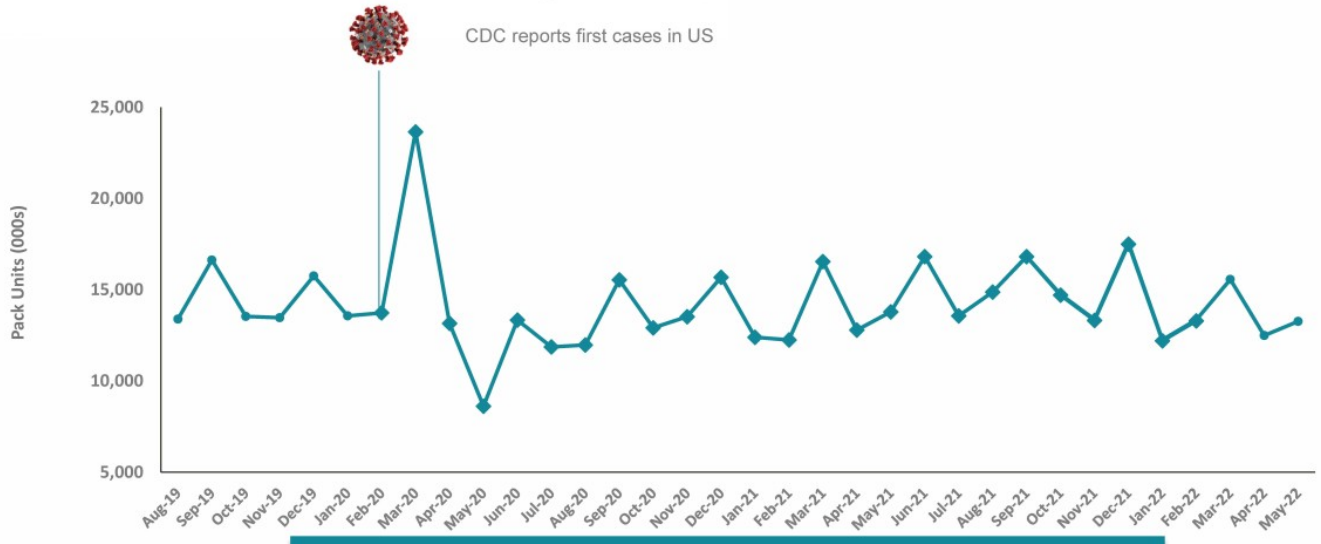
EMR analysis does not provide definitive data of group differences as seen in a prospectively randomized study

- ***Healthcare Utilization Measures.*** OLINVYK-treated patients had a statistically significant 1.6 day (~27%) reduction in average overall hospital length of stay compared to matched patients treated with other IV opioids (P=0.0001), based on preliminary EMR analysis of matched patients at the Wake Forest Baptist Health study site. There was no statistically significant difference in the average duration of time in the post-anesthesia care unit (PACU), with 2.4 hours observed for both OLINVYK-treated and matched patients (P=0.8174).
- ***Delirium.*** *Twenty (4.4%) m*atched patients experienced ICD-coded delirium or altered consciousness, compared to one patient (1.0%) with OLINVYK, though this difference was not statistically significant (P=0.27). Patients receiving any IV opioid who experienced delirium or altered consciousness in this study had an average hospital length of stay 10.5 days longer than patients who did not experience this event. ICD-coding was used for this comparative analysis as 3D-CAM is not generally used in the general patient population.
- **Initial EMR Data Set.** ARTEMIS is an electronic medical records (EMR) data analysis, with records available from the Wake Forest Baptist Health study site (n=96 OLINVYK-treated patients; n=457 matched patients on other IV opioids). While an EMR analysis does not provide definitive data of group differences as seen in a prospectively randomized study, we believe EMR data bring a unique perspective to an understanding of how drugs may perform in the real world.

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, and as reflected in the OLINVYK label, nausea and vomiting were two of the most common adverse events reported in the controlled clinical trials

Stable IV Opioid Market Performance

Despite the 20% decline in elective surgeries, IV opioid volume remained stable



Declines due to COVID-19 across top surgical procedures:
Total knee, Total hip, Hernia repair, Hysterectomy, Bariatric

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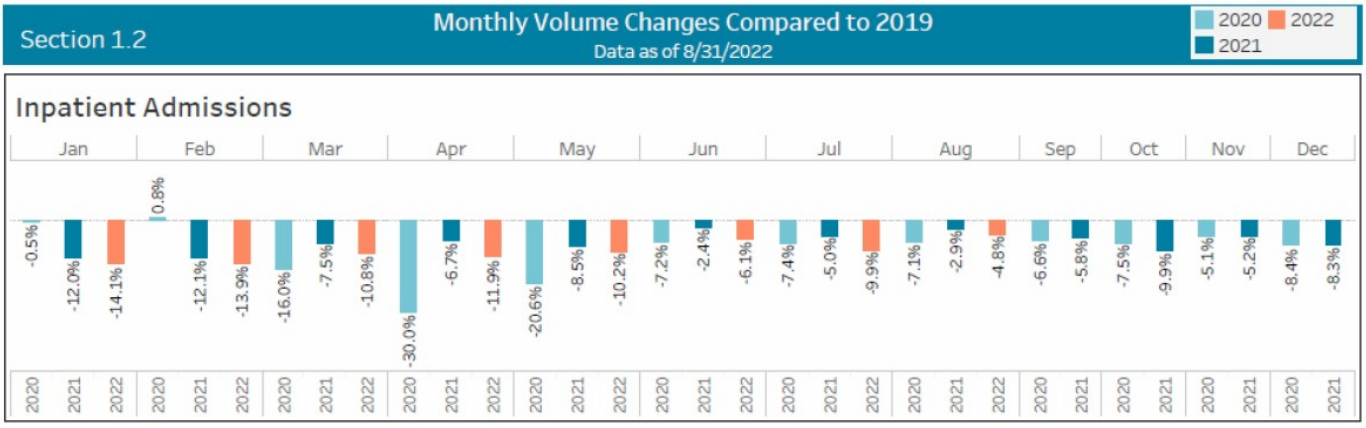
SOURCE: IQVIA DDD Data May 2022

Hospital Inpatient Visits Below Pre-Pandemic Levels

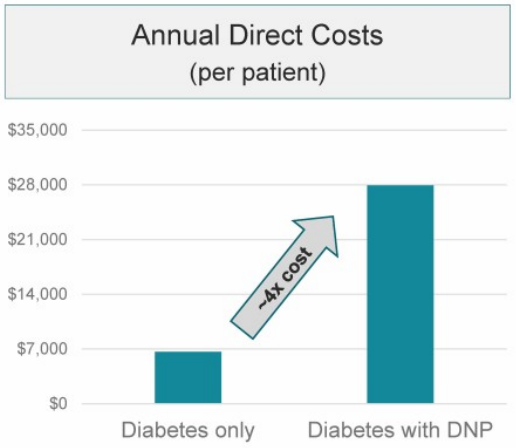


- Monthly Volume Changes in 2022 remain below 2019 levels for each month of the year.
- Through August each month in 2022 has shown a decline greater than was seen in 2021

Diabetic Neuropathic Pain

Diabetic neuropathic pain (DNP) represents a large market opportunity

- 30M+ US adults with diabetes (500M+ worldwide)[1,2]
- DNP affects up to 25% of patients with diabetes[3,8]
- Significant need for efficacious medicines for DNP [4-5]
  - Only ~50% of patients experience a clinical response with currently approved therapies
- Direct costs for patients with DNP were ~4x that of patients with only diabetes (no DNP)[6]



1) IDF, www.diabetesatlas.org 2) Economic Costs of Diabetes in the U.S. in 2017, Diabetes Care 2018;41:917–928. 3) Shillo et al., Current Diabetes Reports, 2019 4) Pritchett, YL et al. Pain Medicine 2007 5) Freeman R et al., Diabetes Care 2008 6) Sadosky et. al., J Diabetes Complications 2015. 7) Datamonitor 8) Hicks, et al. Current Diabetes Reports, 2019

Epilepsy

One of the most common neurological diseases in the world[1]

Disease Overview

- Epilepsy is a chronic disorder characterized by recurrent seizures[1].
- 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[2].
  - A seizure is a sudden surge of electrical activity in the brain caused by complex chemical changes that occur in nerve cells[3].
  - Usually, there is a balance of cells that either encourage or stop other brain cells from sending messages[3].
  - A seizure occurs when there may be too much or too little electrical activity in the brain causing an imbalance[3].
  - Seizures are a symptom of many different disorders that can affect the brain[3].

Market Opportunity

- Nearly 50 million people suffer from epilepsy worldwide, including 3 million adults and 470,000 children in the U.S[1,4,5].
- 150,000 new cases of epilepsy are reported in the United States each year[6].
- According to the CDC, 56% of adults living with diagnosed epilepsy continue to have seizures[7].

1. World Health Organization. Epilepsy. https://www.who.int/news-room/fact-sheets/detail/epilepsy. Accessed November, 2021. 2. Epilepsy Foundation. About Epilepsy: The Basics. https://www.epilepsy.com/learn/about-epilepsy-basics. Accessed November, 2021. 3. Epilepsy Foundation. What is a Seizure? https://www.epilepsy.com/learn/about-epilepsy-basics/what-seizure. Accessed November, 2021.4. CURE Epilepsy. What is epilepsy? https://www.cureepilepsy.org/about-epilepsy/what-is-epilepsy. Accessed November, 2021. 5. Zack MM, Kobau R. National and state estimates of the numbers of adults and children with active epilepsy—United States, 2015. MMWR Morb Mortal Wkly Rep. 2017;66(31):821-825. 6. Epilepsy Foundation. What is Epilepsy? https://www.epilepsy.com/learn/about-epilepsy-basics/what-epilepsy. Accessed November, 2021. 7. Tian N, Boring M, Kobau R, Zack MM, Croft JB. Active Epilepsy and Seizure Control in Adults — United States, 2013 and 2015. MMWR Morb Mortal Wkly Rep 2018; 67:437–442. DOI: http://dx.doi.org/10.15585/mmwr.mm6715a1

Trevena®

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.

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- 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.