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): **August 7, 2020**

TREVENA, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-36193**	**26-1469215**
(State or other jurisdiction of incorporation)	(Commission File No.)	(IRS Employer Identification No.)

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

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

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 August 10, 2020, Trevena, Inc. (the "Company") issued a press release announcing that the U.S. Food and Drug Administration has approved its lead drug candidate, OLINVYK (oliceridine) injection, that is indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternate treatments are inadequate. The press release also announced certain financial information for the quarter ended June 30, 2020. A copy of the press release is furnished hereto as Exhibit 99.1.

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 (the "Securities Act"), or the Exchange Act whether made before or after the date of this Current Report on Form 8-K, except as shall be expressly set forth by specific reference in such a filing.

Item 7.01 Regulation FD Disclosure

On August 10, 2020, the Company updated its website to include an updated corporate presentation deck. A copy of the updated corporate deck is attached hereto as Exhibit 99.2.

Additionally, on August 10, 2020, the Company filed its Quarterly Report on Form 10-Q for the quarter ended June 30, 2020 with the Securities and Exchange Commission.

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, and is not incorporated by reference into any of the Company’s filings under the Securities Act or the Exchange Act, whether made before or after the date hereof, except as shall be expressly set forth by specific reference in any such filing.

Item 8.01 Other Events

The information contained in Item 2.02 is incorporated in its entirety into this Item 8.01.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release dated August 10, 2020
99.2	Updated Corporate Presentation Deck dated August 10, 2020
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: August 10, 2020

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

Exhibit 99.1

Trevena Announces FDA Approval of OLINVYK™ (oliceridine) injection

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OLINVYK is a new chemical entity approved in adults for the management of acute pain severe enough to require an IV opioid analgesic

OLINVYK product availability expected in fourth quarter of 2020

Company funded through year-end 2021, including OLINVYK commercialization

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Company to host conference call at 8:30 a.m., today, August 10, 2020

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CHESTERBROOK, Pa., August 10, 2020 (GLOBE NEWSWIRE) --**Trevena, Inc. (Nasdaq: TRVN)**, a biopharmaceutical company focused on the development and commercialization of novel medicines for patients with central nervous system (CNS) disorders, today announced that the U.S. Food and Drug Administration (FDA) has approved OLINVYK in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate. OLINVYK will be commercially available when the U.S. Drug Enforcement Administration (DEA) issues its controlled substance schedule in approximately 90 days.

"The approval of OLINVYK marks an exciting step forward in Trevena's mission of translating cutting-edge scientific discovery into therapeutic benefit for patients in need. I would like to thank all of the patients, investigators, and our employees who helped us achieve this important milestone," said Carrie L. Bourdow, President and Chief Executive Officer. "We will work quickly to bring this novel IV analgesic to patients and healthcare providers in need of alternative treatment options."

Each year, approximately 45 million hospital patients in the United States receive an IV opioid to treat their acute pain. Many of these patients are complex and difficult to treat, such as the elderly, obese, or renally-impaired. Current hospital trends suggest that the number of these complex patients is growing, representing an increasing burden on the healthcare system.

OLINVYK is an opioid agonist that is the first new chemical entity in this IV drug class in decades and offers a differentiated profile that addresses a significant unmet need in the acute pain management landscape. OLINVYK delivers IV opioid efficacy with a rapid 2-5 minute onset of action. In addition, OLINVYK requires no dosage adjustments in patients with renal impairment, a large patient population with significant medical complications.

The FDA approval of OLINVYK was based on results from the Phase 3 development program, which evaluated OLINVYK in over 1,500 patients with moderate to severe acute pain. In two pivotal efficacy studies in hard- and soft-tissue surgical models, OLINVYK demonstrated rapid analgesic efficacy statistically significant vs. placebo. In a large, open-label, "real world" safety study, OLINVYK was safe and well-tolerated in a medically complex patient population, including the elderly, obese, and patients with comorbid conditions such as diabetes and sleep apnea.

"Complex patients present unique challenges in the management of their postoperative acute pain, due to the presence of medical comorbidities that can complicate dosing," said Gregory Hammer, M.D., Professor of Anesthesiology, Perioperative and Pain Medicine, and of Pediatrics at Stanford University. "OLINVYK represents a new alternative for clinicians, due to its rapid onset of action, effective pain relief, and unique profile."

The Company expects to make OLINVYK available in the fourth quarter of 2020 following scheduling by the DEA, which may take up to 90 days. The Company is committed to an ethical and responsible marketing campaign for OLINVYK and will have safeguards in place to monitor for and mitigate the risk of non-medical uses of OLINVYK.

The Company also today announced $54.8 million in cash and cash equivalents as of June 30, 2020, which the Company expects will be sufficient to fund operating expenses, including the commercialization of OLINVYK, through year-end 2021.

Conference Call and Webcast Information

The Company will host a conference call and webcast with the investment community on August 10, 2020, at 8:30 a.m. Eastern Time featuring remarks by Carrie Bourdow, President and Chief Executive Officer, Mark Demitrack, M.D., Chief Medical Officer, Robert Yoder, Chief Business Officer, and Barry Shin, Chief Financial Officer.

Title:	Conference Call to Provide Update Following Recent FDA Approval of OLINVYK
Date:	Monday, August 10, 2020
Time:	8:30 a.m. ET
Conference Call Details:	Toll-Free: 855-465-0180 International: 484-756-4313 Conference ID: 4976734
Webcast:	https://www.trevena.com/investors/events-presentations/ir-calendar

OLINVYK Efficacy and Safety Data

The efficacy of OLINVYK was established in two randomized, double-blind, placebo- and morphine-controlled studies which enrolled 790 patients with moderate to severe acute pain (pain intensity of ≥4 on a 0-10 numeric rating scale) after orthopedic surgery-bunionectomy or plastic surgery-abdominoplasty.

In each study, patients were randomized to one of three OLINVYK treatment regimens, a placebo-control regimen, or a morphine-control regimen. The loading dose for all OLINVYK treatment regimens was 1.5 mg; demand doses were 0.1, 0.35, or 0.5 mg, according to the assigned treatment group; supplemental doses were 0.75 mg. A lockout interval of 6 minutes was used for all PCA regimens. Etodolac 200 mg was available as rescue medication. Patients using the approved OLINVYK doses of 0.35 and 0.5 mg had a statistically significantly greater SPID-48/24 than patients using placebo.

The most common adverse reactions (≥10%) in these controlled trials were nausea, vomiting, dizziness, headache, constipation, pruritus, and hypoxia. When stratified by the 27 mg daily dosing limit, discontinuation of OLINVYK due to adverse reactions occurred in 4% of patients who received a daily dose ≤ 27 mg, and less than 1% of patients who received a daily dose >27 mg.

In an open-label safety study of patients with moderate to severe acute pain following a surgical procedure or due to a medical condition, a total of 768 patients received at least one dose of OLINVYK. OLINVYK was administered via clinician-administered bolus dosing, PCA, or a combination of the two. Bolus dosing was initiated at 1 to 2 mg, with supplemental doses of 1 to 3 mg every 1 to 3 hours, as needed, based on individual patient need and previous response to OLINVYK. If OLINVYK was administered via PCA, the loading dose was 1.5 mg, the demand dose was 0.5 mg, and the lockout interval was 6 minutes. Supplemental doses of 1 mg were given as needed, taking into account the patient's utilization of PCA demand doses, individual patient need, and previous response to OLINVYK.

The most frequent condition treated in the open-label safety study was postsurgical acute pain, and included (in order of decreasing frequency): orthopedic, gynecologic, colorectal, general, plastic, urologic, neurologic (including spinal), bariatric, and cardiothoracic surgical procedures. Of the 768 patients treated with OLINVYK, 32% were age 65 years or older and 78% had a Body Mass Index ≥ 25 kg/m^2. OLINVYK was administered as needed; 55% of patients received OLINVYK via clinician bolus administration only, and 45% of patients received OLINVYK via PCA self-administration or a combination of clinician bolus- and PCA self-administration. Discontinuation of OLINVYK in this study due to adverse drug reactions occurred in 3% of patients who received a daily dose ≤ 27 mg and 1% of patients who received a daily dose >27 mg.

Full Prescribing Information, including the Boxed Warning, is available 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 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 [*controlled substance schedule pending*], 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 can 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.

About OLINVYK™ (oliceridine) injection

OLINVYK is a new chemical entity approved by the FDA in August 2020. 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 will not be available for distribution until the United States Drug Enforcement Administration assigns it to its schedule of controlled substances. For more information, please visit www.OLINVYK.com.

About Trevena

Trevena, Inc. is a biopharmaceutical company focused on the development and commercialization of novel medicines for patients with CNS disorders. The Company has one approved product in the U.S., 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 also has four novel and differentiated investigational drug candidates: TRV250 for the acute treatment of migraine, TRV734 for maintenance treatment of opioid use disorder, and TRV027 for acute lung injury / abnormal blood clotting in COVID-19 patients. The Company has also identified TRV045, a novel S1P receptor modulator that may offer a new, non-opioid approach to treating a variety of CNS disorders.

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, commercialization of approved drug products and other statements containing the words "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, 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 commercialization of any approved drug product, 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 the discussions with the FDA or other regulatory agencies about any and all of its programs; uncertainties related to the commercialization of OLINVYK; 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 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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Bob Yoder
SVP and Chief Business Officer
Trevena, Inc.
(610) 354-8840

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, MERCK
Scott Applebaum	SVP, Chief Legal & Regulatory Officer	context, vitae, Shire
Mark A. Demitrack, M.D.	SVP, Chief Medical Officer	NEURONETICS, Lilly, ROIVANT
Barry Shin	SVP, Chief Financial Officer	MIZUHO, GUGGENHEIM, PiperJaffray
Robert T. Yoder	SVP, Chief Business Officer	MERCK, ORBIMED

BOARD OF DIRECTORS			
Leon O. Moulder, Jr. *Chairman*	TESARO, MGI		
Carrie L. Bourdow	Trevena	**Julie H. McHugh**	centocor, Johnson & Johnson, endo
Scott Braunstein, M.D.	MARINUS PHARMACEUTICALS, AISLING CAPITAL, PACIRA	**Jake R. Nunn**	NEA
Michael R. Dougherty	Adolor, centocor	**Anne M. Phillips, M.D.**	novo nordisk, GSK
Maxine Gowen, Ph.D.	GSK, Trevena	**Barbara Yanni**	MERCK

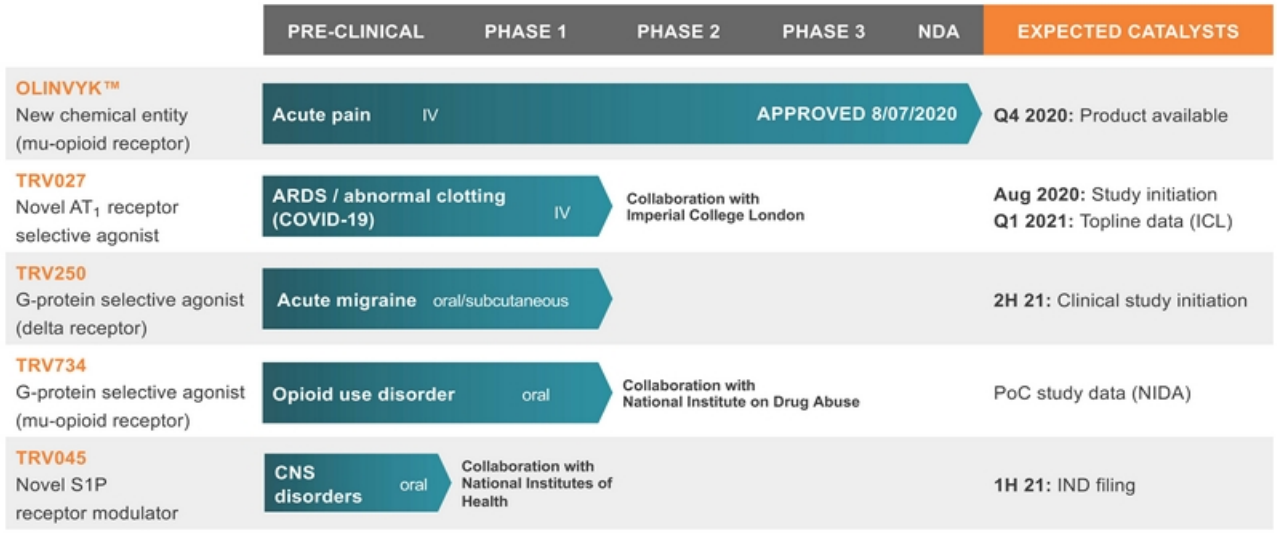
Trevena: Innovative CNS Company

OLINVYK™ approved by FDA	NCE approved for the management of acute pain in adults DEA scheduling pending; product availability in Q4 2020
Large market, targeted launch	45M+ US hospital patients; 9M procedures is initial core focus $1.5B+ market opportunity for core focus
Novel CNS pipeline	New mechanisms for acute migraine, opioid use disorder, epilepsy, pain NCEs targeting significant unmet needs
TRV027 for COVID-19	Novel MOA to treat COVID-19 acute lung injury / abnormal clotting PoC study in collaboration with Imperial College London; topline data expected in ~6 months
Solid financial position	$54.8M in cash as of 6/30/2020 Funds operations through year-end 2021

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; PoC = Proof-of-Concept

Multiple Expected Catalysts

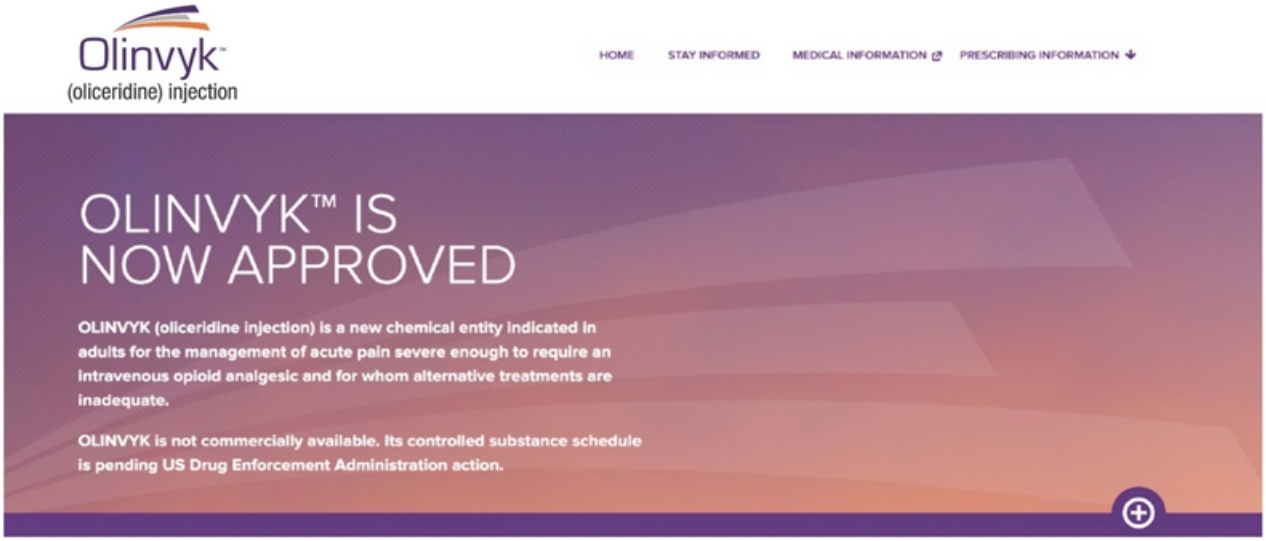


Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.

Trevena

TRV250, TRV734, TRV027, and TRV045 are investigational products and are not approved by the FDA or any other regulatory agency.
ARDS = Acute Respiratory Distress Syndrome; IND = Investigational New Drug; PoC = Proof-of-Concept

OLINVYK™ (oliceridine) injection: Now Approved



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

Ease of use in clinical practice
Bolus / PCA; no active metabolites

New chemical entity
Distinct from IV morphine

Data in complex patients
Elderly, obese, renal impaired

IV opioid efficacy
Hard- and soft-tissue surgeries

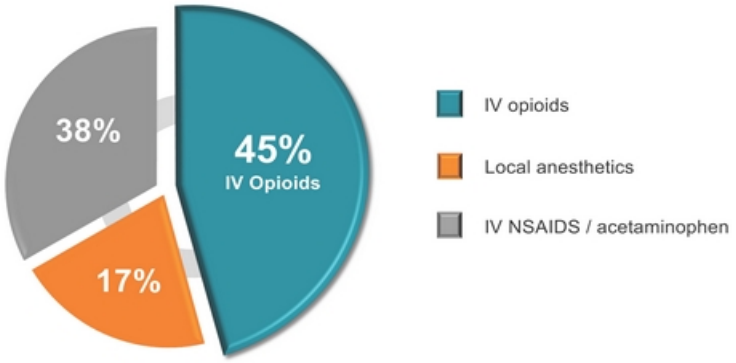
Well-characterized safety / tolerability
IV morphine data included in label

Rapid analgesia
2-5 min onset of pain relief

OLINVYK: Broad Indication for Acute Pain

Large acute market opportunity

US injectable analgesic hospital market unit volume[1]



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

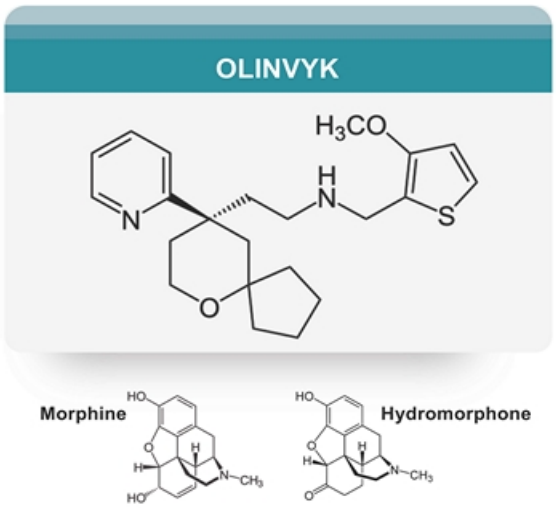
- Unrivalled analgesic efficacy
- Top surgeries: Total knee arthroplasty, colectomy, hernia repair, spine fusion, C-section[2]

OLINVYK is indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate.
Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.

Trevena

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: Distinct From IV Morphine / Hydromorphone

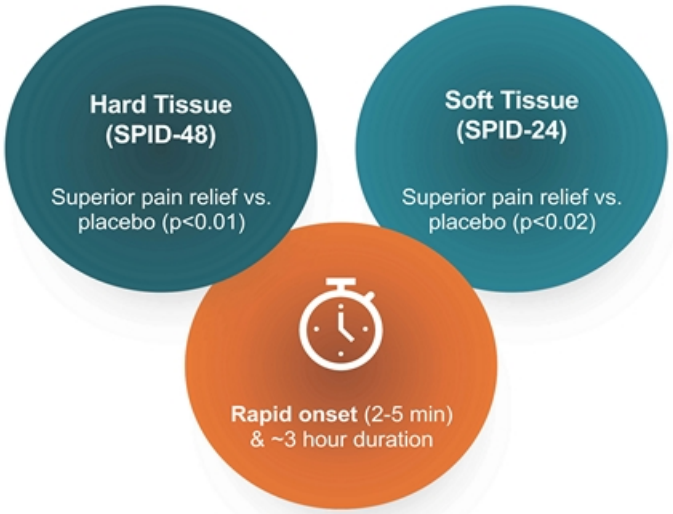


Studied in >1,900 individuals

IV morphine included as active comparator

NCE with 2032+ COM patent[1]

OLINVYK: IV Opioid Efficacy and Rapid Onset



- Efficacy achieved in hard tissue & soft tissue models
- Rapid onset: perceptible pain relief within 2-5 minutes
- OLINVYK efficacy data in peer-reviewed journals
  The Journal of Pain Research[1] and *Pain Practice*[2]

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

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

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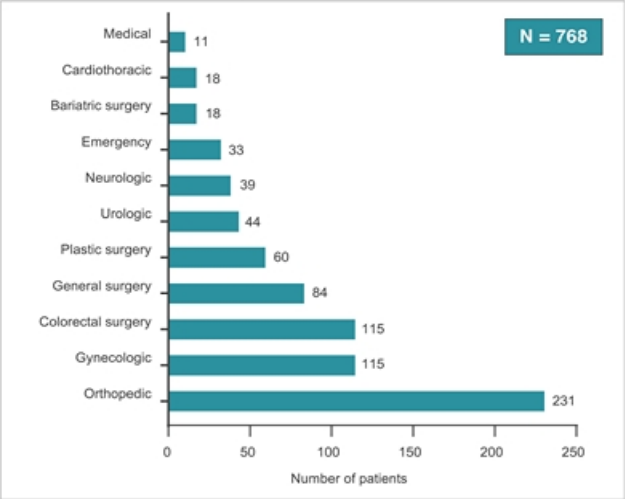
Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.

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

Data in “Real World Use”: Complex Surgeries & Patients

Broad range of surgeries / medical procedures



Complex patients were included

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

Multiple inpatient and 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

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

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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: Ease of Dosing and Administration

3 vials to allow for flexible dose adjustment tailored to patient needs

Bolus Dosing: 1 mg and 2 mg vials

- Initial 1.5 mg dose
- Single doses over 3 mg have not been evaluated

PCA Dosing: 30 mg vial

- Initial 1.5 mg dose
- 0.35 mg / 0.5 mg demand doses with 6-minute lock-out
- 0.75 mg supplemental doses at 1 hour and hourly as needed

- OLINVYK 1 mg ≈ morphine 5 mg
- 27 mg cumulative daily dose limit

Vials are illustrative only

3 presentations:

1 mg/mL	single-dose vial
2 mg/2mL (1mg/ml)	single-dose vial
30 mg/30mL (1mg/ml)	single-pt-use vial

For IV administration only
No refrigeration / reconstitution

Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.
OLINVYK is not commercially available and its controlled substance schedule is pending U.S. DEA action.

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PCA = Patient-Controlled Analgesia

Customer Engagement Strategy

Comprehensive Data Available at Launch

Will support future commercialization and hospital formulary uptake

Health Care Practitioners (HCPs)

- New chemical entity
- Fast, effective IV opioid pain relief
- Clinical data in complex patients / targeted surgeries

Hospital Formulary Committees

- Published head-to-head trials vs. IV morphine
- Published health economic / cost offset data*

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OLINVYK is not commercially available and its controlled substance schedule is pending U.S. DEA action.

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*Expected to be published at time of launch

Robust Set of Peer-Reviewed Publications

Comprehensive overview of OLINVYK development program

OLINVYK nonclinical / Phase 1 / Phase 2 data

15 publications

OLINVYK Phase 3 trials & secondary analyses

7 publications

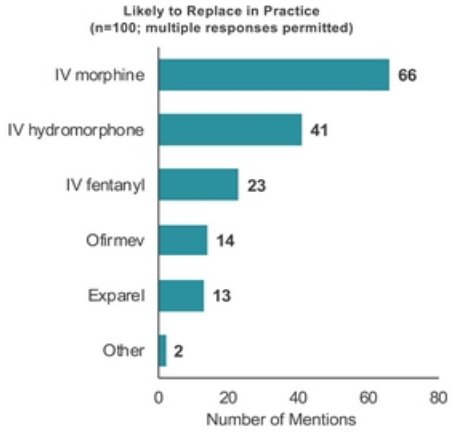
- 4 head-to-head studies vs. IV morphine
  - IV opioid efficacy
  - Well-characterized safety and tolerability
- Data in complex patients / surgery types
- Respiratory safety data in elderly / obese
- Respiratory safety profile measured by dosing interruptions
- Clinical utility vs. IV morphine - benefit-risk analysis

Positive Feedback from Formulary Stakeholders[1]

74% of formulary stakeholders find OLINVYK's published data clinically meaningful:[2]

Key Endpoint (vs. IV morphine)	Pharmacist (n=50)	Physician (n=50)
Respiratory Safety Events and GI Tolerability	 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.

Hospital Pharmacy Considerations

Improve clinical outcomes and reduce costs

$8,826 in hospital costs per patient for nausea / vomiting[1]

$28,000 per critical respiratory event / sequelae[2]

Increased hospital length of stay: **~7 additional** days[2]

OLINVYK

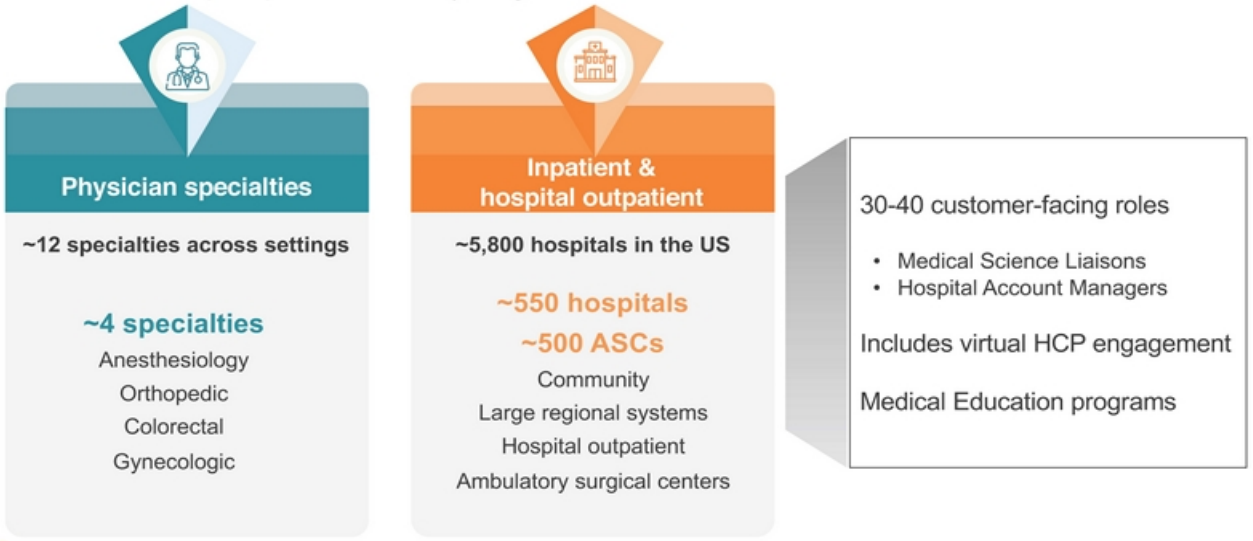
- ✓ Differentiated acute pain profile
- ✓ Safety in complex patients
- ✓ Head-to-head peer-reviewed clinical evidence[3]
- ✓ Compelling health economic model
- ✓ Formulary stakeholder feedback supports ~$100/day[4]

Trevena

1) 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. 2) Overdyk FJ, PLoS One, 2016. 3) These publications will be used in a manner consistent with FDAMA sections 114 and the FDA Guidance thereunder. 4) Based on daily dosing in ATHENA "real world" open label safety study and 2020 CRA pricing study. The price for OLINVYK has not been established.

Targeted Account Launch

Initial focus: complex patients in 3 key surgical areas



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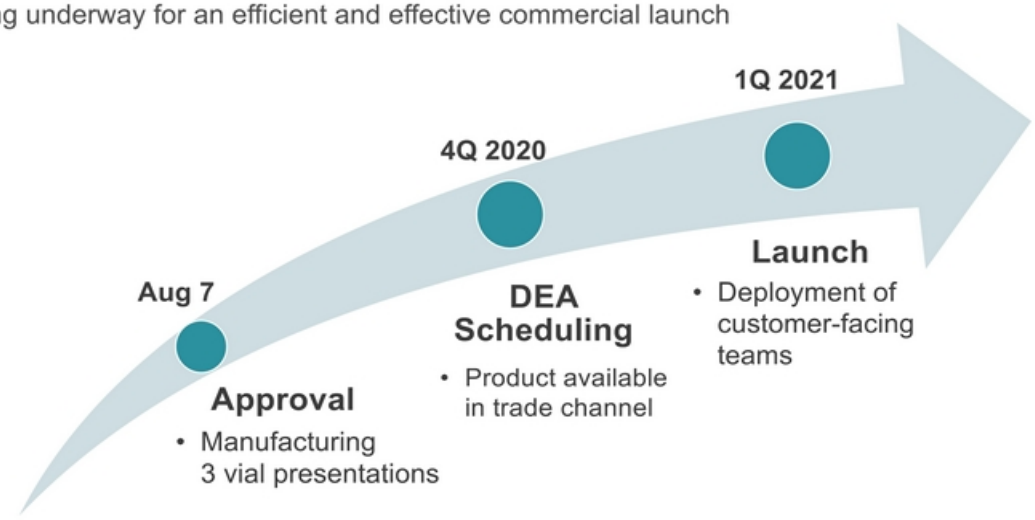
ASCs = ambulatory surgical centers

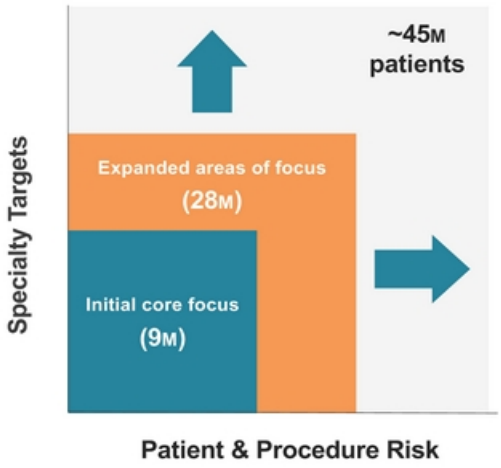
Launch Timeline

Planning underway for an efficient and effective commercial launch



Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.
OLINVYK is not commercially available and its controlled substance schedule is pending U.S. DEA action.

OLINVYK Approval Strategy Allows for Growth



Initial core focus (9M)

- Broad indication & dosing / admin
- IV opioid efficacy & fast onset
- Complex patients: elderly, obese, renal

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

Expanded areas of focus (28M)

- Leverage respiratory and GI safety vs. IV morphine to expand surgical procedures
- Cognitive function & additional HECON

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

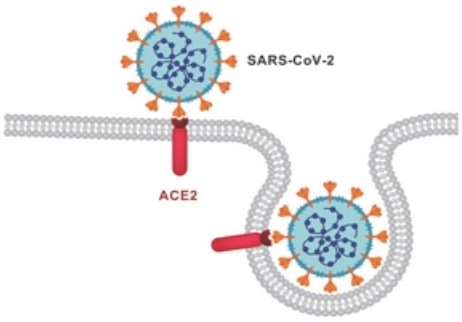
TRV027

NCE targeting the AT_1 receptor in COVID-19

Multi-Organ Damage From Coronavirus

Elimination of ACE2 protein leads to critical hormonal imbalances

Coronavirus binds to and eliminates ACE2[1]

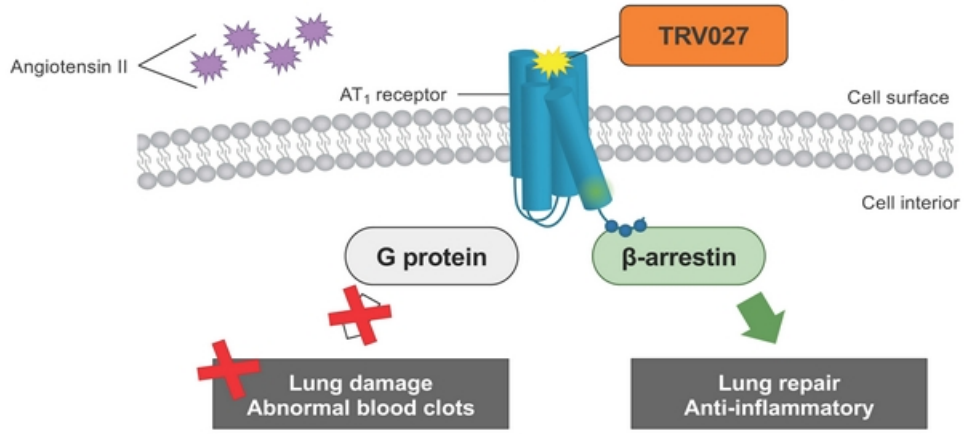


- Leads to accumulation of angiotensin II:
  - Acute lung injury and abnormal blood clots
  - Can lead to ARDS / pulmonary embolism / stroke
- 66% - 94% mortality rate for COVID-19 related ARDS[2*]
- ~1/3 of hospitalized COVID-19 patients develop clotting complications[3]

*ARDS = Acute Respiratory Distress Syndrome. 1) Kuba K et al., Nat Med, 2005. 2) Gibson PG et al, Med J Aust, 2020. *In patients requiring ventilation. 3) Klok FA et al, Thromb Res, 2020.*

TRV027: New MOA for COVID-19

Mechanism targeted to improve lung function and prevent abnormal clotting



TRV027 is the only selective AT_1 receptor agonist
Safety / tolerability established in ~700 patients

TRV027 COVID-19 Study - Imperial College London

Investigate effect of TRV027 on blood clotting, lung function, and other clinical outcomes

- Randomized, double-blind, placebo-controlled proof-of-concept study
- N = ~60 (30 per arm) COVID-19 patients
  - Hospitalized, non-ventilated
  - ≥18 years old
- IV infusion of placebo or TRV027 for 7 days (12 mg/hr)

Primary endpoint:

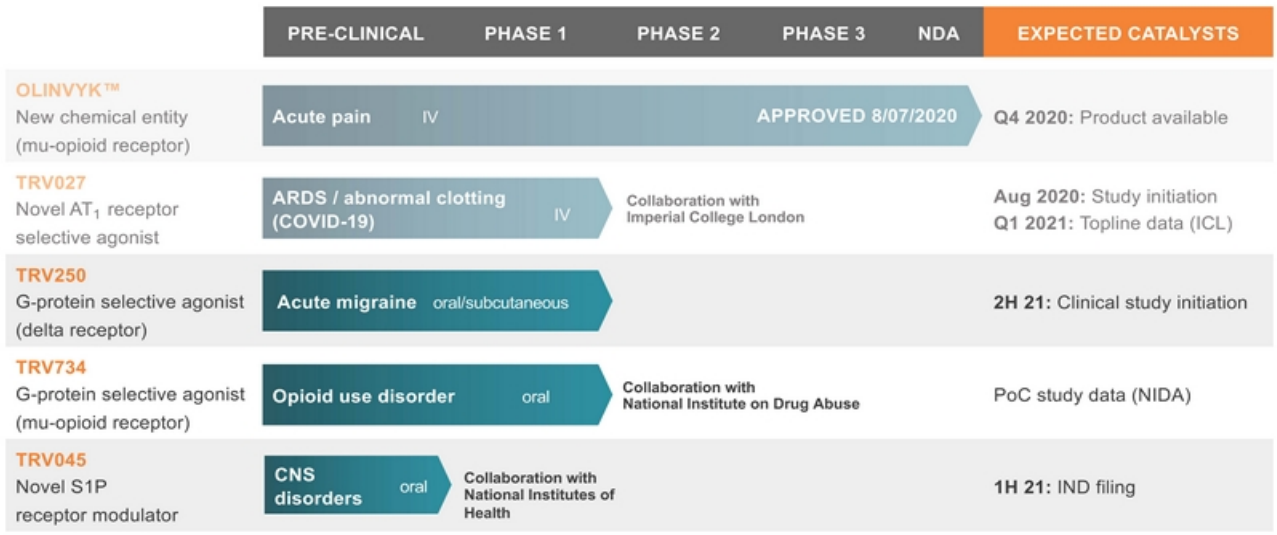
Reduction of abnormal clotting associated with COVID-19*

Indicator of TRV027's effect on health outcomes associated with increased mortality in COVID-19

Imperial College London

* Primary endpoint: D-dimer levels. https://clinicaltrials.gov/ct2/show/record/NCT04419610.

Multiple Expected Catalysts



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TRV250, TRV734, TRV027, and TRV045 are investigational products and are not approved by the FDA or any other regulatory agency.
ARDS = Acute Respiratory Distress Syndrome; IND = Investigational New Drug; PoC = Proof-of-Concept

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

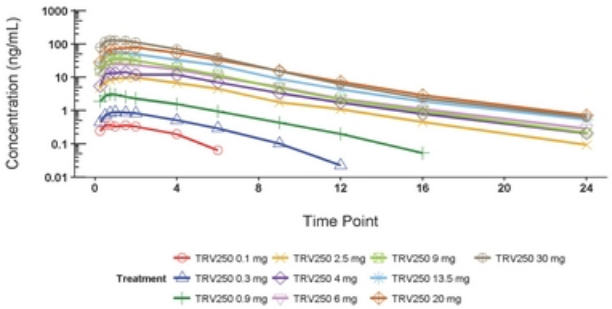
- **20-30%** of migraine sufferers do not respond to / cannot tolerate the market-leading triptan drug class
- Approx. **50%** of migraineurs also suffer from anxiety[2]

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



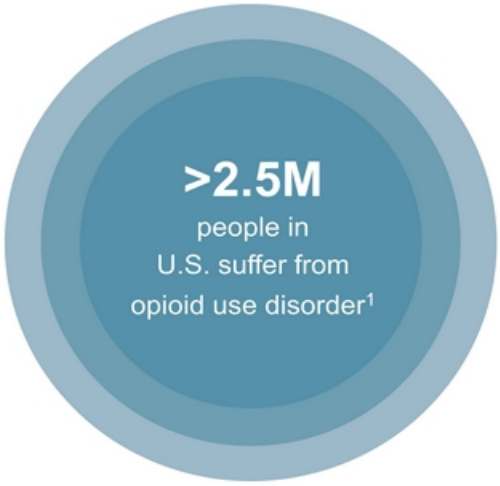
- Well tolerated, with no SAEs across broad range of doses
- Predictable PK: dose-proportional between 0.1 mg to 30 mg SC
- Half-life consistent across all doses
- No EEG findings observed in any subject

Trevena

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: Potential for improved tolerability



Ongoing collaboration with National Institute on Drug Abuse (NIDA)

- Nonclinical evidence of improved tolerability with TRV734
- NIDA study demonstrated reduced drug-seeking behavior in animal model of relapse[2]
- Current therapies not well tolerated, can hinder patient adherence

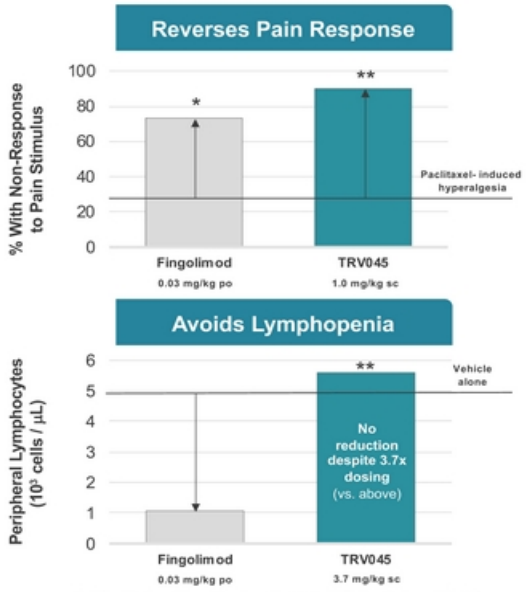
NIDA-funded proof-of-concept patient study initiated

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

TRV045: Next-Generation S1P Modulator for CNS Disorders

New MOA at S1P, without associated lymphopenia

- S1P receptors in the CNS play unique role in modulating neurotransmission / membrane excitability
- In animals, TRV045 reversed paclitaxel-induced hyperalgesia without immune-suppressing activity
  - Fingolimod reduced lymphocytes by 78%
  - TRV045 had no effect on lymphocytes
- Non-opioid MOA with broad potential for CNS indications
  - Chronic pain, CIPN, diabetic neuropathy
  - Epilepsy, acute / chronic pain evaluations underway



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*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*

Trevena: Innovative CNS Company

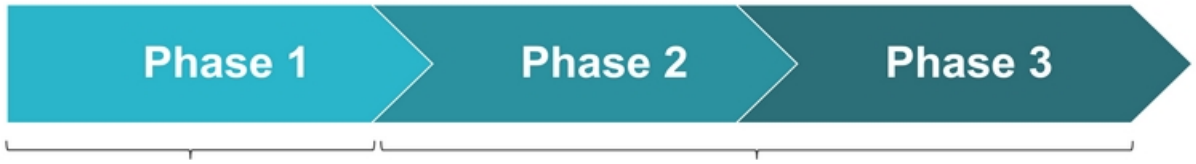
OLINVYK™ approved by FDA	NCE approved for the management of acute pain in adults DEA scheduling pending; product availability in Q4 2020
Large market, targeted launch	45M+ US hospital patients; 9M procedures is initial core focus $1.5B+ market opportunity for core focus
Novel CNS pipeline	New mechanisms for acute migraine, opioid use disorder, epilepsy, pain NCEs targeting significant unmet needs
TRV027 for COVID-19	Novel MOA to treat COVID-19 acute lung injury / abnormal clotting PoC study in collaboration with Imperial College London; topline data expected in ~6 months
Solid financial position	$54.8M in cash as of 6/30/2020 Funds operations through year-end 2021

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.

APPENDIX

Robust Clinical Development Program

OLINVYK studied in > 1,900 individuals



- **No dosage adjustments** for elderly / renally impaired
- No known active metabolites

4 head-to-head trials vs. IV morphine:

- IV opioid efficacy
- Rapid onset of action
- Well-characterized respiratory safety / GI tolerability
- Low rates of vomiting and rescue antiemetic use

Large safety study:

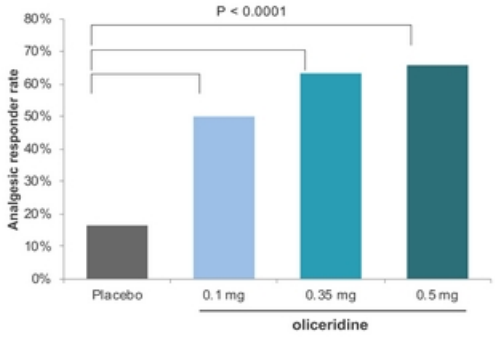
- Real-world use in complex patients and target surgeries

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

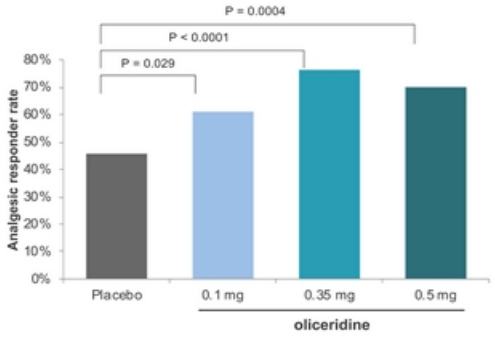
 # subjects exposed to OLINVYK in Ph1 = 318; # patients treated with OLINVYK in Ph2 and Ph3 = 1,535

Primary Efficacy Endpoint Achieved in Two Pivotal Studies

OLINVYK achieved IV opioid efficacy



Hard tissue



Soft tissue

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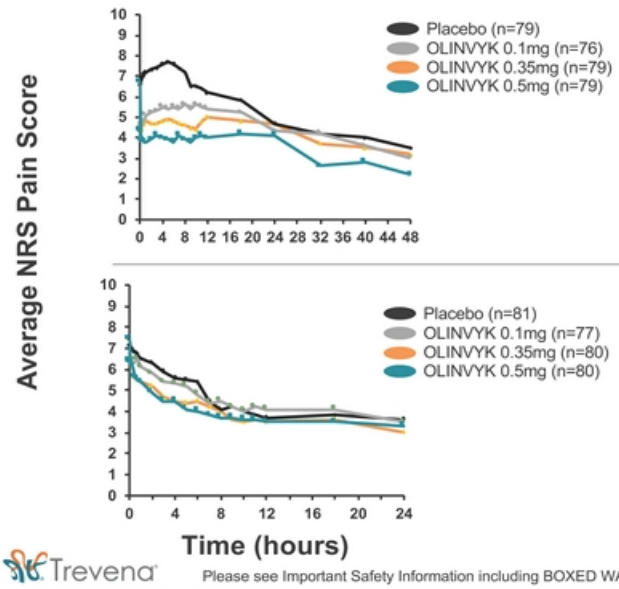
OLINVYK regimens: 1.5 mg loading bolus, with 0.1, 0.35, or 0.5 mg available on demand every 6 minutes. Displayed p-values are for OLINVYK vs. placebo with Hochberg multiplicity adjustment.

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.

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%

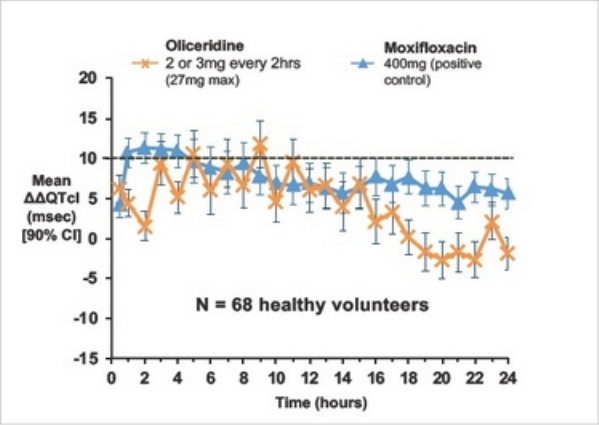
Study 2 (Plastic Surgery – Soft Tissue)

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%

No Accumulation Despite Repeated Dosing

Multi-Dose tQT Study



Key results

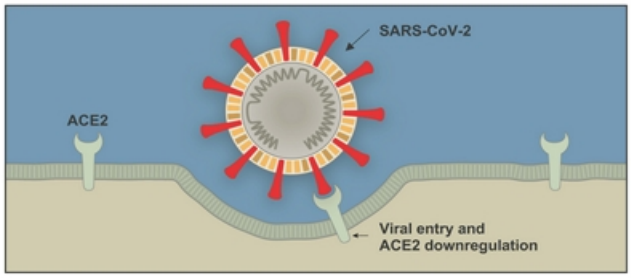
- **No accumulation through 24 hrs**
  Mean QTcI <10ms at 22 of 24 points
- **No categorical QTc outliers**
  Δ >60 ms; >500 ms absolute
- **Well tolerated, no SAEs***
  92% reached max daily dose

*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.

Interaction Between the AT_1 Receptor and ACE2 in COVID-19

Downregulation of ACE2 by coronavirus indirectly promotes activation of the AT_1 receptor

- Coronavirus binds to and downregulates angiotensin converting enzyme 2 (ACE2)[1]
- Decrease in ACE2 elevates angiotensin II levels
  - Angiotensin II activates AT_1 receptor
  - No breakdown of angiotensin II into Ang(1-7)
    - Normally, Ang(1-7) acts as a β-arrestin-biased ligand at the AT_1 receptor[2]
    - Protective therapeutic benefits in the lungs[3]



1) Kuba K et al., Nat Med, 2005. 2) Teixeira LB et al., Sci Rep, 2017. 3) Santos RAS et al., Physiol Rev, 2018.

Delta Receptor Agonists Have Unique Benefits

Potential utility for a variety of CNS indications

Triptans / Ditans

- Target: serotonin receptors → mediate vascular excitability (associated CV risk)[1]
- Migraine-specific treatment

CGRPs

- Target: CGRP receptors → regulate neuronal structures involved in pain signaling[2]
- Migraine-specific treatment

Delta receptor agonists

- Target: delta receptors → located in pain pathways; also distributed throughout brain regions associated with sensory information, emotional processing, and reward / impulsivity[3]
- Potential for broad therapeutic application

1) Rothrock JF & Friedman DI, American Headache Society website: https://americanheadachesociety.org/wp-content/uploads/2018/05/John_Rothrock_and_Deborah_Friedman_-_Triptans.pdf. 2) Durham PL, Headache, 2006. 3) Peppin JF & Raffa RB, Journal of Clinical Pharmacy and Therapeutics, 2015.

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

WARNINGS AND PRECAUTIONS

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

ADVERSE REACTIONS

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

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