
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): **November 2, 2020**

TREVENA, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation)

001-36193
(Commission
File No.)

26-1469215
(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 7.01 Regulation FD Disclosure

On November 2, 2020, Trevena, Inc. (the "Company") updated its website to include an updated corporate presentation deck. A copy of the updated corporate deck is attached hereto as Exhibit 99.1.

Additionally, on November 2, 2020, the Company filed its Quarterly Report on Form 10-Q for the quarter ended September 30, 2020 with the Securities and Exchange Commission.

The information set forth on this Item 7.01 and furnished hereto as Exhibit 99.1 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 9.01 Financial Statements and Exhibits.**(d) Exhibits.****Exhibit**

No.	Description
<u>99.1</u>	<u>Updated Corporate Presentation Deck dated November 2, 2020</u>
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: November 2, 2020

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



Nasdaq TRVN | November 2020



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	 
Scott Applebaum	SVP, Chief Legal & Regulatory Officer	  
Mark A. Demitrack, M.D.	SVP, Chief Medical Officer	  
Barry Shin	SVP, Chief Financial Officer	  
Robert T. Yoder	SVP, Chief Commercial Officer	 

BOARD OF DIRECTORS

Leon O. Moulder, Jr. <i>Chairman</i>	 		
Carrie L. Bourdow		Julie H. McHugh	  
Scott Braunstein, M.D.	  	Jake R. Nunn	
Michael R. Dougherty	 	Anne M. Phillips, M.D.	 
Maxine Gowen, Ph.D.	 	Barbara Yanni	

Trevena: Innovative CNS Company

IV OLINVYK: Differentiated profile	NCE approved for the management of acute pain in adults Product availability in November; commercial launch in Q1 2021
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 Q1 2021
Strong financial position	\$112.7M cash and cash equivalents as of 9/30/2020 Funds operations through Q4 2022

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

	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	NDA	EXPECTED CATALYSTS
OLINVYK™ New chemical entity (mu-opioid receptor)	Acute pain IV APPROVED					Q4 20: Product available Q1 21: Commercial launch
TRV027 Novel AT ₁ receptor selective agonist	ARDS / abnormal clotting (COVID-19) IV Collaboration with Imperial College London					Q1 21: Topline data (ICL)
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TRV045 Novel S1P receptor modulator	CNS disorders oral Collaboration with National Institutes of Health					1H 21: IND filing

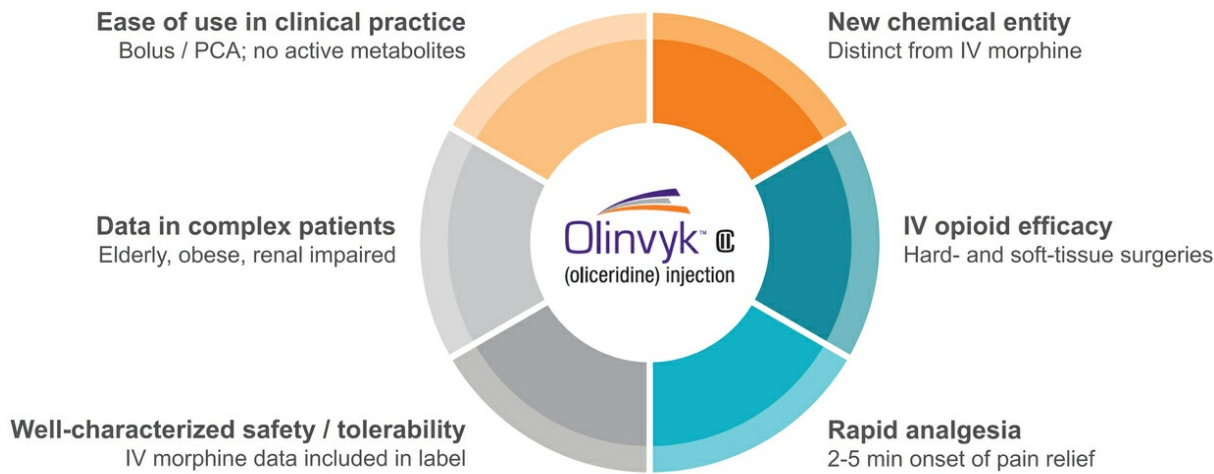
Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.



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: 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

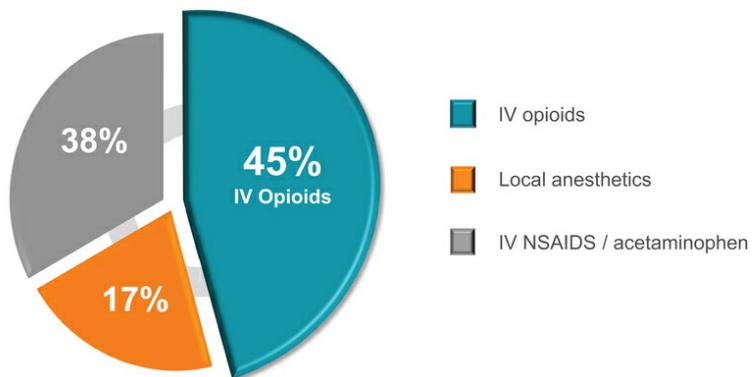


Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.

OLINVYK: Broad Indication for Acute Pain

Large acute market opportunity

US injectable analgesic
hospital market unit volume¹



45M patients receive IV opioids annually to treat acute pain¹

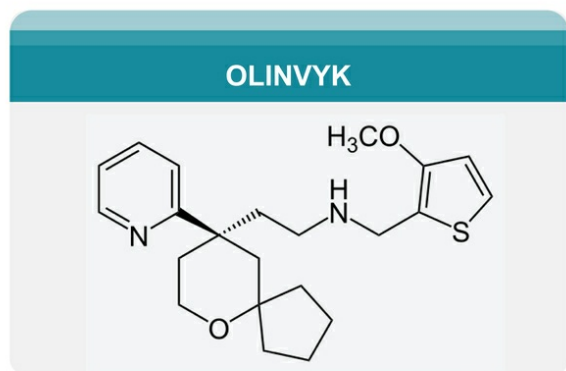
- Unrivalled analgesic efficacy
- Top surgeries: Total knee arthroplasty, colectomy, hernia repair, spine fusion, C-section²



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.

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

OLINVYK: Distinct From IV Morphine / Hydromorphone

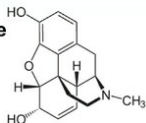


Studied in >1,900 individuals

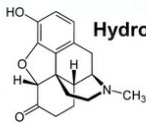
IV morphine included as active comparator

NCE with 2032+ COM patent¹

Morphine



Hydromorphone



OLINVYK: IV Opioid Efficacy and Rapid Onset



Hard Tissue (SPID-48)

Superior pain relief vs.
placebo ($p < 0.01$)

Soft Tissue (SPID-24)

Superior pain relief vs.
placebo ($p < 0.02$)



**Rapid onset (2-5 min)
& ~3 hour duration**

- 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



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.

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
- **O₂ saturation < 90%**
 - Independent predictor of early post-op respiratory complications



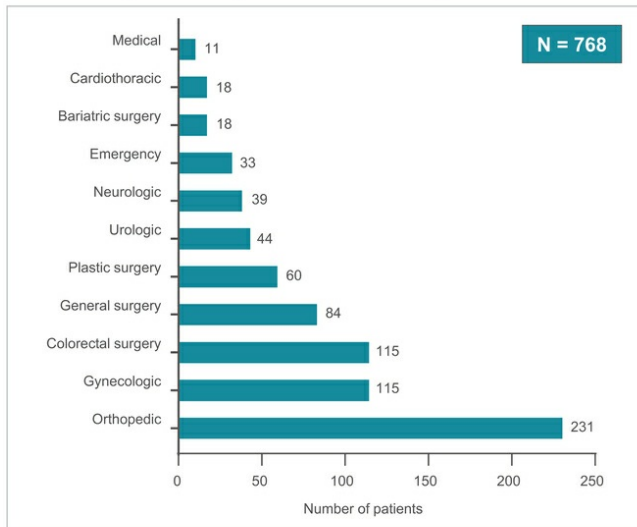
Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.

¹) OLINVYK Prescribing Information. 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
- Emergency department
- Critical care
- 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.



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 allow for flexible and tailored IV dosing

- **Bolus Dosing:** 1 mg and 2 mg vials (single dose)
- **PCA Dosing:** 30 mg vial (single patient use)
- **OLINVYK 1 mg \approx morphine 5 mg¹**

27 mg cumulative daily dose limit

Single doses over 3 mg have not been evaluated

No refrigeration / reconstitution



1 mg /
1 mL

2 mg /
2 mL

30 mg /
30 mL

WAC:	\$17.50	\$25.75	\$110.00
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~\$100 / day

(estimated avg cost across procedures)



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

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

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*

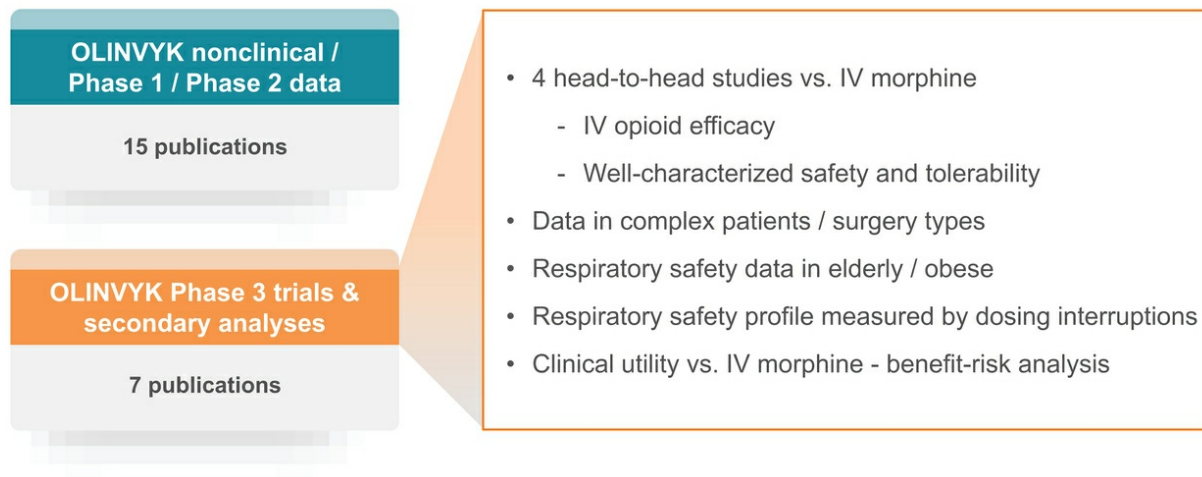


Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.

*Expected to be published at time of launch

Robust Set of Peer-Reviewed Publications

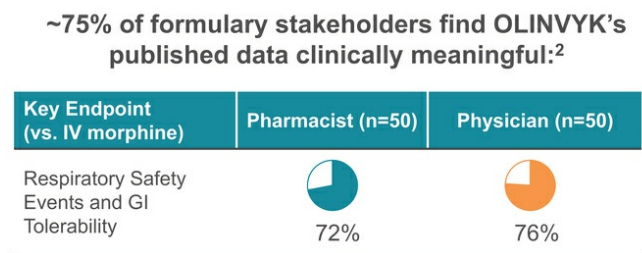
Comprehensive overview of OLINVYK development program



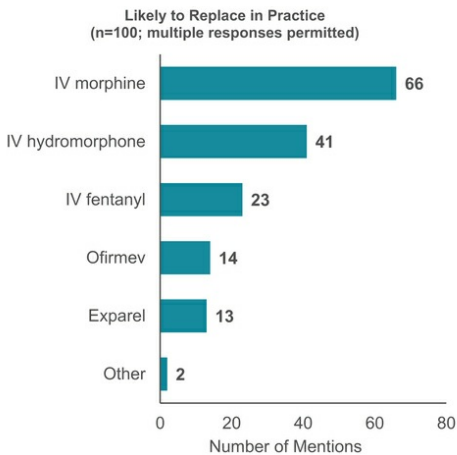
Please see Important Safety Information including BOXED WARNING at the end of presentation. Full Prescribing Information at www.OLINVYK.com.

See www.trevena.com for full manuscripts and abstracts. These publications will be used in a manner consistent with FDAMA sections 114 and 401 and the FDA Guidances thereunder.

Positive Feedback from Formulary Stakeholders¹



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 Formulary Considerations for New Products

Cost Burden of Adverse Events

\$8,826 in hospital costs per patient for nausea / vomiting¹

\$28,000 per critical respiratory event / sequelae²

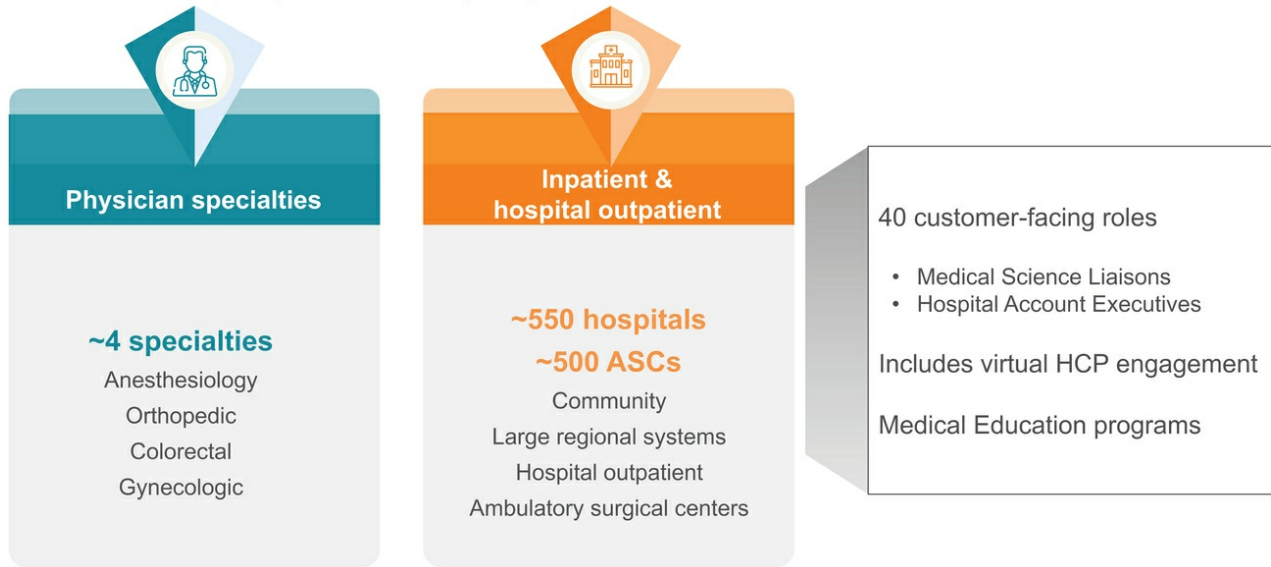
Increased hospital length of stay:
~7 additional days²

Why OLINVYK?

- ✓ Compelling clinical data
 - Differentiated acute pain profile
 - Head-to-head peer-reviewed clinical evidence versus IV morphine³
- ✓ Compelling health economic model
 - >10x net savings for hospitals⁴

Targeted Account Launch

Initial focus: complex patients in 3 key surgical areas



Customer Facing Organization

Partnering with Syneos Health to provide “best in class” commercial support



- Allows for execution speed and flexibility in deployment
- Full range support: source, hire, train and deploy customer-facing roles
- Provides infrastructure, sales operations and compliance support
- Ability to flex as business needs evolve

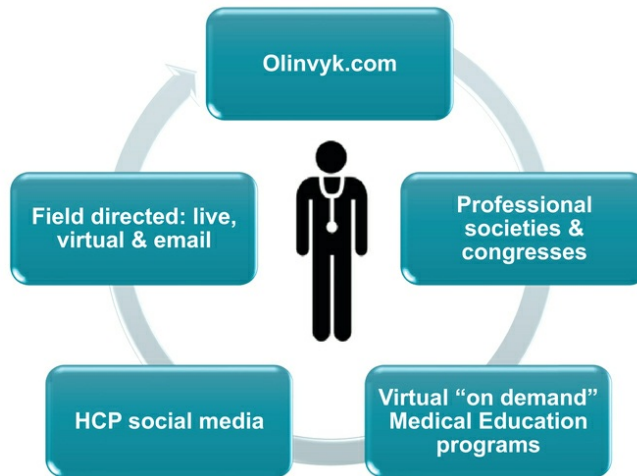
40 Customer Facing Roles

- **Sales:** Institutional Account Managers
- **Trade & Access:** Regional Account Managers
- **Medical:** Medical Science Liaisons

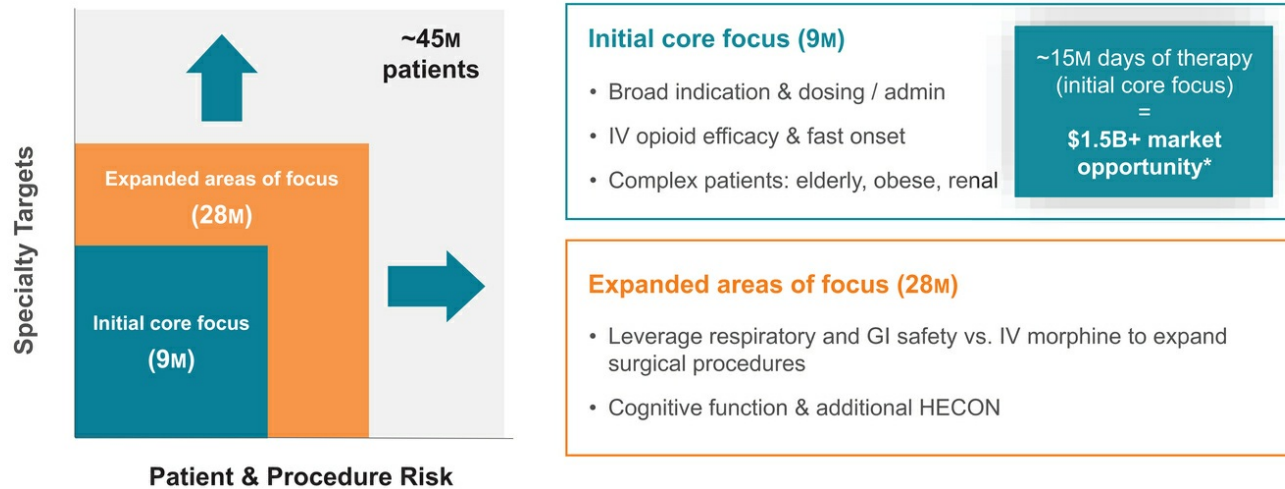
Omni-Channel Strategy for HCP Engagement

Communication across a full range of channels to maximize reach and impact

Customize mix across channels with targeted HCPs



OLINVYK Approval Strategy Allows for Growth



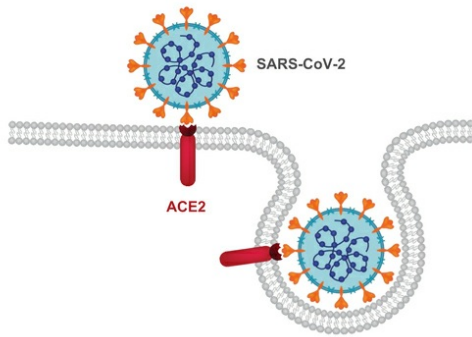
TRV027

NCE targeting the AT₁ receptor in COVID-19

Multi-Organ Damage From Coronavirus

Elimination of ACE2 protein leads to critical hormonal imbalances

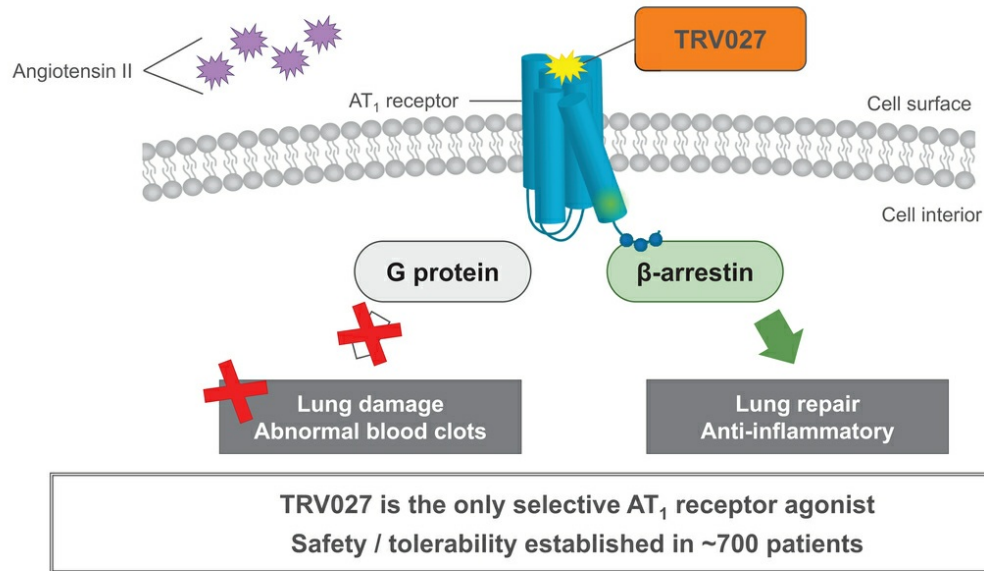
Coronavirus binds to and eliminates ACE2¹



- 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 complications³

TRV027: New MOA for COVID-19

Mechanism targeted to improve lung function and prevent abnormal clotting



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)
- Study currently ongoing, topline data expected Q1 2021

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

Multiple Expected Catalysts

	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	NDA	EXPECTED CATALYSTS
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TRV045 Novel S1P receptor modulator	CNS disorders oral		Collaboration with National Institutes of Health			1H 21: IND filing

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26

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 US¹:



650M migraines
treated each year



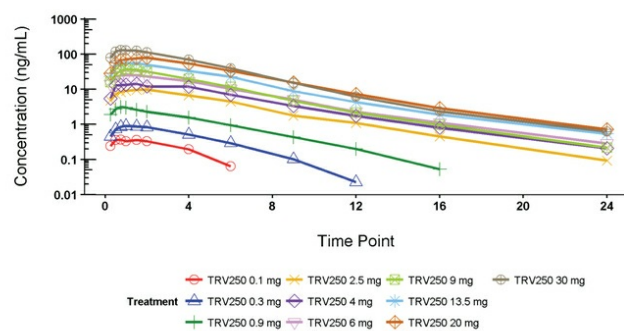
1.2M ER visits
due to migraines

- 20-30% of migraine sufferers do not respond to / cannot tolerate the market-leading triptan drug class
- Approx. 50% of migraineurs also suffer from anxiety²

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

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)

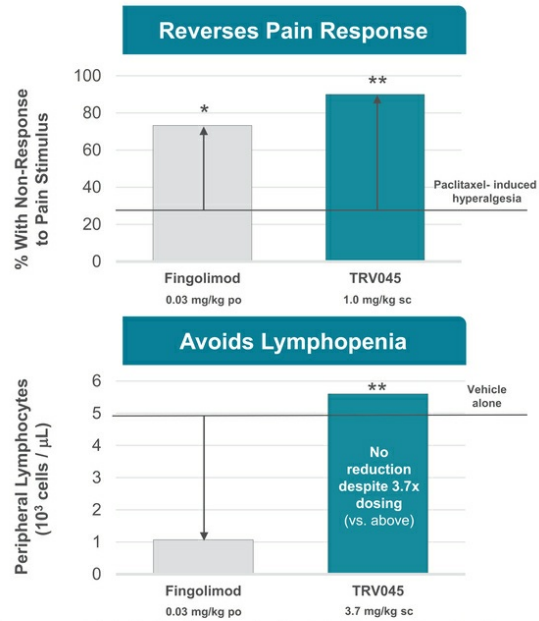
- Nonclinical evidence of improved tolerability with TRV734
- NIDA study demonstrated reduced drug-seeking behavior in animal model of relapse²
- Current therapies not well tolerated, can hinder patient adherence

**NIDA-funded proof-of-concept
patient study initiated**

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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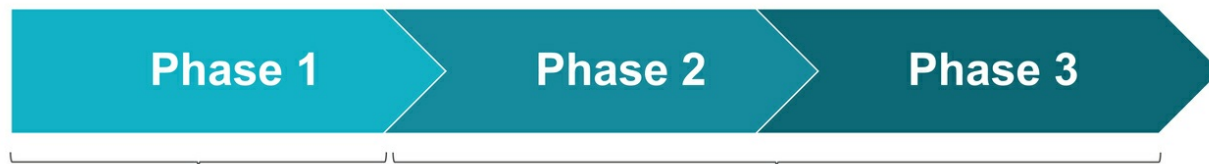


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APPENDIX

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

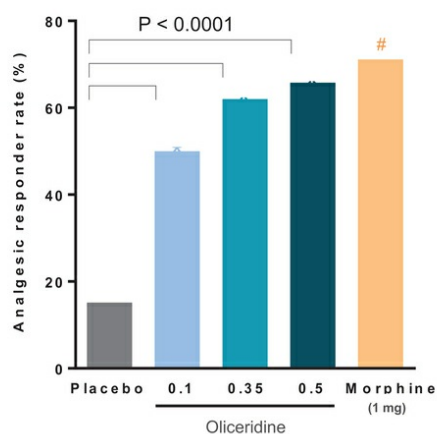


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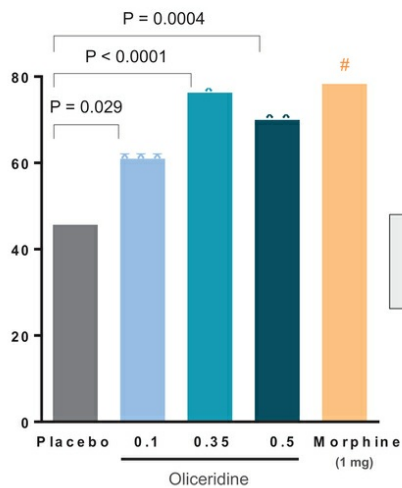
subjects exposed to OLINVYK in Ph1 = 318; # patients treated with OLINVYK in Ph2 and Ph3 = 1,535

Primary Efficacy Endpoint Achieved in Two Pivotal Studies

OLINVYK achieved IV opioid efficacy



Ph3: Hard Tissue Surgery
Mean baseline pain = 6.7



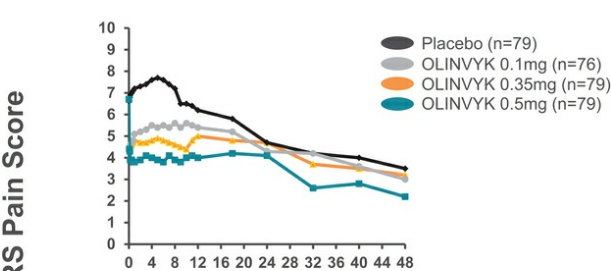
Ph3: Soft Tissue Surgery
Mean baseline pain = 7.3

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).

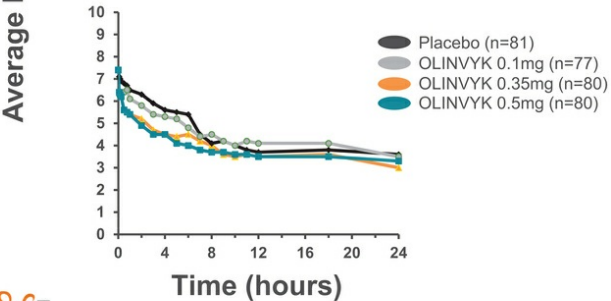
OLINVYK: IV Opioid Efficacy in 2 Phase 3 RCTs



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

Outcome	OLINVYK			Placebo
	0.1 mg	0.35 mg	0.5 mg	
% 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

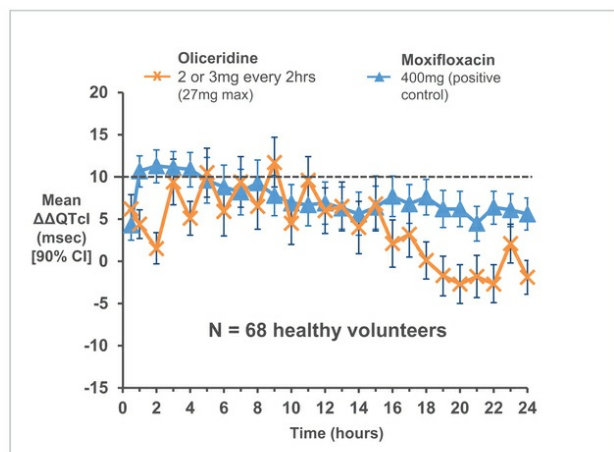
Outcome	OLINVYK			Placebo
	0.1 mg	0.35 mg	0.5 mg	
% Completed	86%	90%	87%	74%
% D/C LOE	11%	3%	5%	22%
% Rescue Meds	31%	21%	18%	49%



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

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**
 $\Delta >60$ 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.

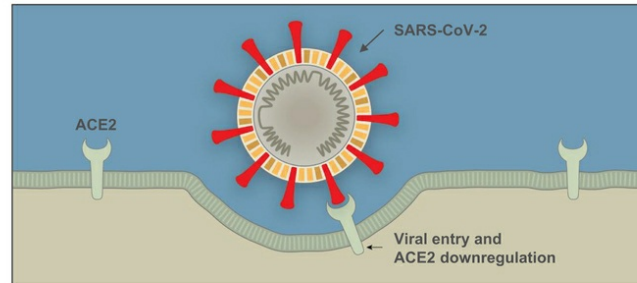


3 subjects not dosed due to lack of venous access; 1 discontinuation due to a non-serious adverse event (asymptomatic non-sustained ventricular tachycardia) with confounding hypokalemia and no meaningful QT prolongation during dosing; 1 subject completed dosing but not evaluable due to equipment malfunction

Interaction Between the AT₁ Receptor and ACE2 in COVID-19

Downregulation of ACE2 by coronavirus indirectly promotes activation of the AT₁ receptor

- Coronavirus binds to and downregulates angiotensin converting enzyme 2 (ACE2)¹
- Decrease in ACE2 elevates angiotensin II levels
 - Angiotensin II activates AT₁ receptor
 - No breakdown of angiotensin II into Ang(1-7)
 - Normally, Ang(1-7) acts as a β -arrestin-biased ligand at the AT₁ receptor²
 - Protective therapeutic benefits in the lungs³



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 signaling²
- 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 / impulsivity³
- Potential for broad therapeutic application

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.

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.

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.



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 inducer, or with discontinuation of a CYP3A4 inducer. These patients may require less frequent dosing and should be closely monitored for respiratory depression and sedation at frequent intervals. Concomitant use of OLINVYK with CYP3A4 inducers or discontinuation of a moderate or strong CYP3A4 inhibitor can lower the expected concentration, which may decrease efficacy, and may require supplemental doses.
- Cases of adrenal insufficiency have been reported with opioid use (usually greater than one month). Presentation and symptoms may be nonspecific and include nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If confirmed, treat with physiologic replacement doses of corticosteroids and wean patient from the opioid.
- OLINVYK may cause severe hypotension, including orthostatic hypotension and syncope in ambulatory patients.
- There is increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (e.g., phenothiazines or general anesthetics). Monitor these patients for signs of hypotension. In patients with circulatory shock, avoid the use of OLINVYK as it may cause vasodilation that can further reduce cardiac output and blood pressure.
- Avoid the use of OLINVYK in patients with impaired consciousness or coma. OLINVYK should be used with caution in patients who may be susceptible to the intracranial effects of CO₂ retention, such as those with evidence of increased intracranial pressure or brain tumors, as a reduction in respiratory drive and the resultant CO₂ retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy.
- As with all opioids, OLINVYK may cause spasm of the sphincter of Oddi, and may cause increases in serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis, for worsening symptoms.
- 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.