UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 23, 2015

KEMPHARM, INC.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-36913**	**20-5894398**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

2656 Crosspark Road, Suite 100 **Coralville, IA**	**52241**
(Address of Principal Executive Offices)	(Zip Code)

Registrant's Telephone Number, Including Area Code: (319) 665-2575

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instructions A.2. below):

☐ 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))

Item 8.01 Other Events.

On September 23, 2015, Dr. Sven Guenther, the Executive Vice President of Research and Development of KemPharm, Inc., or the Company, will present at the 9th Pain and Migraine Therapeutics Summit on, among other things, different approaches for finding new pain drugs with improved side effect and abuse profiles, including the Company's most advanced pain product candidates, KP201/APAP, a prodrug of hydrocodone in combination with acetaminophen, and KP511, a prodrug of hydromorphone. A copy of this presentation is available on the Company's website at www.kempharm.com, and is filed as Exhibit 99.1 to this Current Report on Form 8-K, the contents of which are incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Presentation titled "The Search for New Pain Therapeutics with Low Inherent Abuse Potential – A Case for Prodrugs" dated September 23, 2015.

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 thereunto duly authorized.

KEMPHARM, INC.

Date: September 23, 2015

By: /s/ R. LaDuane Clifton
R. LaDuane Clifton
Chief Financial Officer

Exhibit Index

Exhibit No.	Description
99.1	Presentation titled “The Search for New Pain Therapeutics with Low Inherent Abuse Potential – A Case for Prodrugs” dated September 23, 2015.

Exhibit 99.1

KemPharm

The 9th Pain & Migraine Therapeutics Summit

The Search for New Pain Therapeutics with Low Inherent Abuse Potential — A Case for Prodrugs

Sven Guenther, Ph.D.

September 23, 2015

Cautionary Note Regarding Presentation Information

This presentation has been prepared by KemPharm, Inc. (the "Company") for informational purposes only and for only the actual attendees of this presentation. Nothing contained in this presentation is, or should be construed as, a recommendation, promise, or representation by the presenter, the Company or any director, employee, agent, or adviser of the Company. Without limiting the forgoing, no representation or warranty, express or implied, is made as to the accuracy, fairness or completeness of the information or statements contained in the presentation. Certain information and statements contained in this presentation and/or made orally during this presentation relate to or are based on studies, publications, surveys and other data obtained from third-party sources, the accuracy, completeness or reasonableness of which the Company makes no representation. In addition, certain information and statements in this presentation and/or made orally during this presentation relate to internal estimates or research by the Company, the reasonableness or accuracy of which have not been evaluated by an independent source. The information and statements contained in this presentation and/or made orally during the presentation are integrally related and, as such, are intended to be delivered and understood together.

This presentation includes expressed and implied forward-looking statements concerning the Company's intent, belief and current expectations, which may be identified by words such as "believe", "expect", "estimate", "project", "may," "will," variations of such words and similar words. Such forward-looking statements are not statements of fact and are subject to risks, uncertainties and assumptions about the Company, and, as a result, the Company's actual results may materially differ from such statements.

Information and statements contained in this presentation speak only as of the date hereof. The Company assumes no obligation to update any statement after the date of this presentation as a result of new information, subsequent events or any other circumstances.

Disclosure Statement

I have relevant financial relationship(s) with some of the products described, reviewed, evaluated, or compared in this presentation.

- Financial
  - Executive Vice President of Research and Development at KemPharm, Inc.

- Nonfinancial
  - No relevant relationship(s) to disclose.

Opioid Analgesics

Anatomy of Opioid Receptors[1-13]

- Four types of opioid receptors: μ (MOP), δ (DOP), κ (KOP), nociceptin/orphanin (NOP)
- Pharmacological evidence and binding studies suggest subtypes
  - Appear to have different functions/effects
  - Example
    - μ_1: analgesia
    - μ_2: analgesia, GI transit, respiratory depression, itching
- Only 4 receptor genes
- How to explain subtype functions?
  - Splice variants (changes introduced during transcription)
  - Receptor oligomerization (different selectivity/function)
  - Biased agonism (e.g., ligand-dependent receptor function)
  - Receptor-receptor interactions

Opioid Receptor Subtype Functions[14]

Receptor	Subtype	Function
MOP	μ_1	analgesia
	μ_2	analgesia, GI transit, respiratory depression, itching
	μ_3	various including NO release
DOP	δ_1	analgesia, cardioprotection
	δ_2	analgesia, cardioprotection, thermoregulation
KOP	κ_{1a}	analgesia, feeding
	κ_{1b}	
	κ_{2a}	analgesia, diuresis, neuroendocrine
	κ_{2b}	
	κ_3	spinal analgesia, peripheral effect

Binding Profiles of Common Opioid Agonists[15]

Opioid	Receptor Binding
Morphine	μ, κ (weak)
Hydrocodone	μ
Oxycodone	μ
Buprenorphine	μ (partial agonist), κ (antagonist)
Hydromorphone	μ, κ (weak), δ (weak)
Oxymorphone	μ
Levorphanol	μ, κ, δ, NMDA (antagonist)
Tapentadol	μ, 5-HT, NE
Fentanyl	μ, κ (weak)
Methadone	μ, NMDA (antagonist)

- Most current opioid analgesics have some cross-receptor activity
- Mixed modes of action can have positive and negative outcomes
- Response to opioids varies by patient
  - Receptor type/subtype ratios
  - Receptor concentrations
  - Localization and receptor tissue distribution
  - Respective opioid metabolism (e.g, different CYP450 genotypes)
- Opioid rotation can reduce side-effects and/or tolerance

Opioid Receptor Biased Agonism[16,17]

- Opioid receptors are G-protein coupled receptors (GPCR)
- G-proteins are heterotrimeric (trimer of G_{α} and $G_{\beta\gamma}$ subunits)
- Inactive receptor is bound (coupled) to $G_{\alpha\beta\gamma}$
- Binding of agonist to receptor activates G-protein
  - G_{α} dissociates and both subunits activate effector proteins which mediate secondary messengers to perpetuate signal
  - While still activated the receptor may subsequently recruit β-arrestin which can activate additional effectors
  - Agonist binding can induce rapid phosphorylation of the receptor and thus change its G-protein/β-arrestin interactions and their respective signal pathways
- The type of agonist determines receptor activation of G-proteins, kinase interaction (phosphorylation), and β-arrestin recruitment
- Involvement of each G-proteins and β-arrestin affects signal pathways and thus receptor functions (desired/undesired)

Possible Improvements[18-21]

- Targeting specific opioid receptor subtypes with desired functions only
- Find biased opioid agonist that suppress undesired signal pathways
- Find new opioids with mixed mechanism of action to allow for lower doses with equal efficacy (e.g., opioid receptor agonist plus NMDA receptor or NK1 antagonist)
- Potentiation of antinociceptive function of μ-opioid receptor agonist by addition of ultra-low dose antagonist?

Case Studies – New Opioid Agonists

Selective Opioid Receptor Agonist – CR845

- Developed by CARA® Therapeutics
- CR845
  - Selective agonist which binds to κ-opioid receptors located on peripheral, pain-sensing nerves
  - Does not effectively cross blood-brain-barrier
  - Route of administration: IV
- Potential benefits
  - Peripheral analgesia
  - No euphoria/addiction
  - No respiratory depression
  - Localized administration prevents dysphoria/hallucination (associated with central κ-opioid receptor agonists)
- Status: post-phase 2

"Pipeline & Technologies", CARA® Therapeutics, accessed September 18, 2015, http://www.caratherapeutics.com/index.shtml.

Novel Opioid Modulator for Pain – ALKS 7106

- Developed by Alkermes®, plc
- ALKS 7106
  - Opioid modulator without abuse-deterrent formulation
  - Specific intrinsic receptor activity (subtype specific?)
  - Rapid entry into CNS
  - ~ 30-fold more potent than morphine
- Potential benefits
  - Ceiling effect on neurotransmitter release
  - Low potential for abuse and overdose death
- Status: abandoned due to missing endpoints in phase 1 trial

"Press Releases", Alkermes®, plc, accessed September 18, 2015, http://investor.alkermes.com/phoenix.zhtml?c=92211&p=irol-news&nyo=0

New μ-Opioid Receptor Agonist – NKTR-181

- Developed by Nektar® Therapeutics
- NKTR-181
  - Known μ-opioid agonist conjugated with polymer to form new molecular entity
  - Addition of polymer slows entry into the brain
- Potential benefits
  - Similar analgesia to oxycodone
  - Less Drug Liking in human abuse potential study compared to oxycodone (in solution)
  - Inherent extended release profile
- Status: phase 3 trial ongoing (chronic pain)

"NKTR-181", Nektar® Therapeutics, accessed September 18, 2015, http://www.nektar.com/product_pipeline/cns_pain_nktr-181.html

μ-Opioid Receptor Biased Agonist – TRV130

- Developed by Trevana
- TRV130
  - Biased binding to μ-opioid receptor
  - Activates G-protein signal pathway
  - Reduced β-arrestin recruitment and associated signals
- β-arrestin mediated signal pathways may be responsible for certain side-effects of non-biased agonists (e.g., morphine)
- Potential benefits
  - Reduced constipation
  - Reduced respiratory depression
  - Reduced analgesic tolerance
- Does not alter abuse potential
- Status: phase 2b trial completed (acute postoperative pain)

"Products", Trevana, accessed September 18, 2015, http://www.trevenainc.com/products.php

Status – Opioid Analgesics

- Many different opioids identified and available
- Multiple opioid receptor functions and mechanisms explored to decouple side-effects (e.g., respiratory depression and euphoria) from analgesic effects
- Despite considerable research no significantly improved products available
- Opioids with reduced abuse potential associated with lower potency
- Outlook
  - Expect incremental improvement, no immediate breakthrough

Prodrugs

Definitions

- Prodrug: inactive molecule that releases an effective moiety (or “prometabolite”) after administration
- “Effective moiety”: molecule which participates directly in the pharmacological action (binding) responsible for efficacy
- “Prometabolite”: active precursor of an effective moiety

Drug Metabolism

Possible Prodrug Properties

- Involves a chemical modification of an effective moiety that is reversed in vivo
- Examples of properties prodrugs can modify/improve compared to original effective moiety
  - Bioavailability
  - Pharmacokinetics
  - Metabolism
  - Physicochemical properties
    - Solubility
    - Stability
  - Tissue targeted delivery
  - Others (e.g., CMC)
- End results are typically improved efficacy and/or safety

Case Studies – Prodrugs

Ligand Activated Therapy (LAT) Platform Technology

1) Select FDA-approved and widely prescribed drug for improvement

2) Chemically modify using a ligand to create an NME prodrug
   - Ligands – GRAS or demonstrated to be safe
   - NME prodrugs generate composition-based patents

3) Following ingestion, normal human metabolic processes cleave the ligand and release the active drug

Prodrugs as an Abuse Deterrent Platform

- Inert molecule selectively metabolized in the GI tract can potentially eliminate non-oral routes of abuse
  - Enzyme profile present in GI tract not found elsewhere
  - Prodrugs have different metabolic stability via non-oral routes
- New molecule requires chemical manipulation in order to release the effective moiety from the prodrug
  - Harsh, chemical reactions
  - Multiple steps of additional neutralization and isolation
  - Loss of yield
- Prodrugs have the ability to potentially reduce oral routes of abuse through a saturation of any number of steps in the metabolic process
  - Overconsumption
  - Oral drug liking and exposure at high doses
  - Overdose protection
- Other benefits beyond abuse are possible with prodrugs

Prodrugs in Development

- KemPharm has generated a number of prodrugs of highly abused opioids and advanced those candidates into development
- KP201 (benzhydrocodone hydrochloride)
  - Currently formulated as IR product with APAP
  - Standalone KP201 next logical product to best utilize prodrug properties
- KP511 (prodrug of hydromorphone)
  - Preclinical stage

KP201/APAP Overview

Treatment of Acute Moderate to Moderately Severe Pain

KP201 Product Features

- Prodrug composed of hydrocodone and benzoic acid
- Entirely new chemical entity: benzhydrocodone
- First commercial product is intended to be IR with APAP
- KP201 potentially provides
  - High tamper resistance
  - Resistance to non-oral routes of abuse
- Expedited 505(b)(2) regulatory pathway
- NDA filing expected in 2H 2015

KP201 μ-Opioid Receptor Pharmacology

- KP201 has very poor binding affinities to all opioid receptors
- Intact KP201 does not impart clinical opioid effects
  - Not an effective moiety
  - Does not produce euphoria
- Effective moiety hydrocodone (μ-opioid receptor agonist), is "cloaked" by prodrug

Binding affinity at μ-opioid receptor	
Compound	**K_i [nM]**
Hydromorphone	0.6
Hydrocodone	19.8
KP201	191.0

KP201/APAP Tamper Resistant Properties – In Vitro Studies

- Extraction of API (KP201) only yields inactive prodrug
- Hydrocodone not released through
  - Physical manipulation (e.g., grinding)
  - Common solvent extraction (e.g., “alcohol dose dumping”, “cold water extraction”)
- KP201 is chemically stable under commonly applied “extraction methods”
- Hydrolysis under very harsh conditions is not practical
  - KP201 partially hydrolyzes under highly basic/acidic conditions
- Poor solubility in blood and water render it unsuitable for IV administration

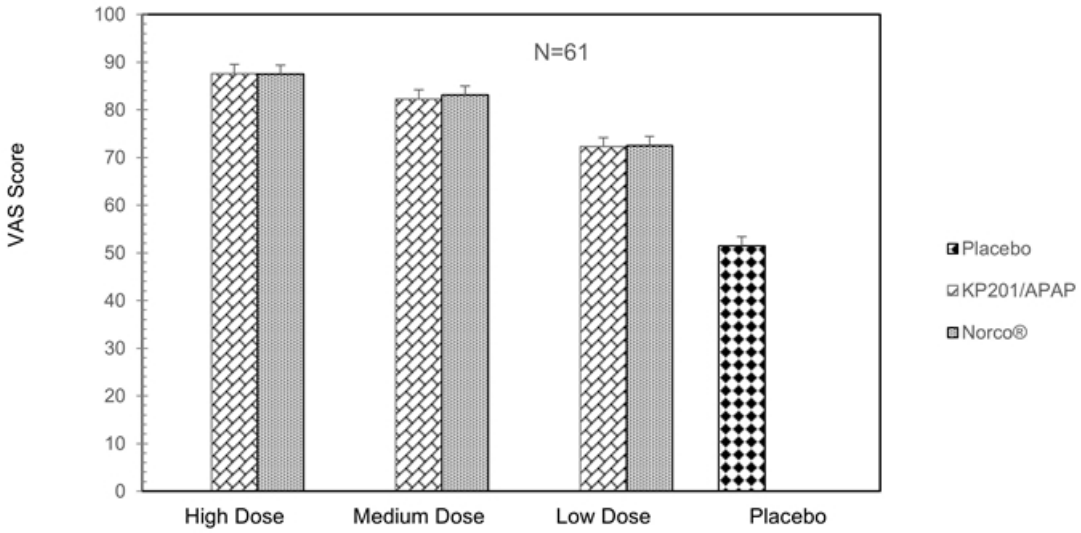
Ongoing Tampering Studies

- KP201.T01
  - Designed to determine the extractability of KP201 from the IR formulation and to evaluate conditions that may potentially hydrolyze the prodrug to hydrocodone
  - to demonstrate the stability KP201 compared to the little effort required to isolate hydrocodone from current IR combination products
- KP201.T02
  - Simulated injection study to show the poor solubility of KP201 at physiological pH in blood and plasma
  - IV abuse potential studies are not feasible to due potential health risks to subjects
- KP201.T03
  - Designed to demonstrate KP201 is not suitable for smoking

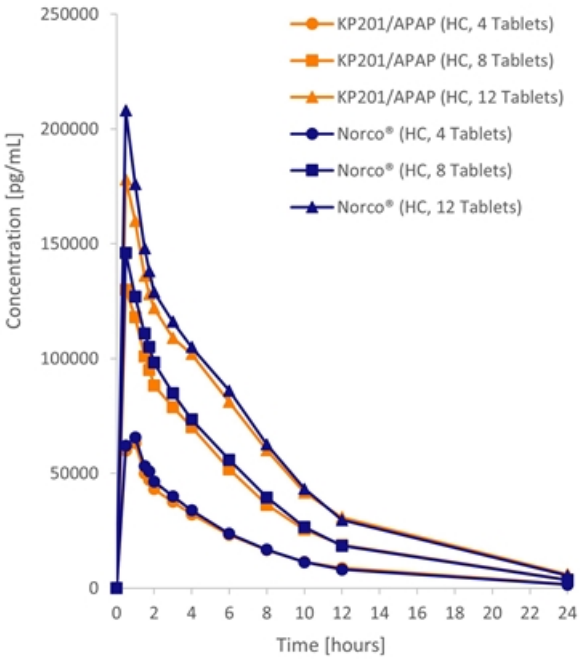
KP201.A01: Oral Abuse Potential Trial

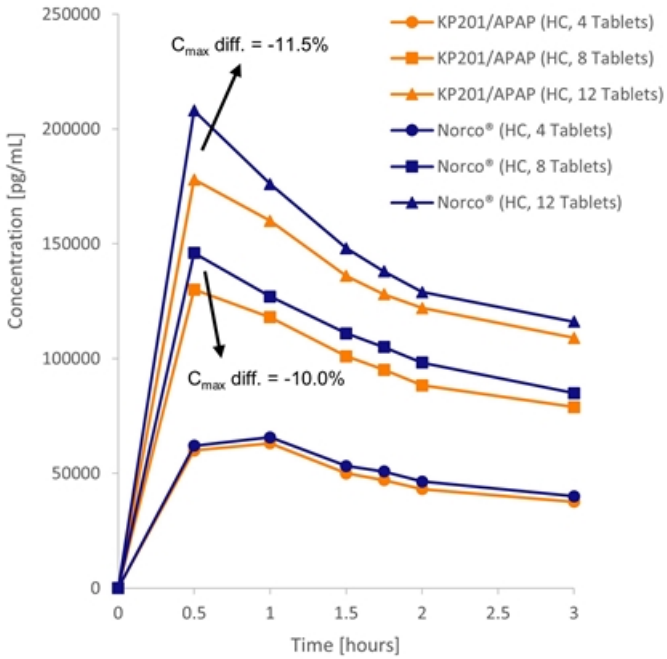
- Design
  - Assessment of Drug Liking, exposure levels and safety of KP201/APAP compared to Norco® after oral administration in nondependent, recreational opioid users (N=61)
  - Single-center, randomized, double-blind, active- and placebo-controlled crossover trial
  - KP201/APAP, 6.67 mg/325 mg vs. Norco, 7.5 mg/325 mg vs. Placebo
  - Doses: 4, 8, and 12 tablets (7 treatment arms)
- Results
  - Similar Drug Liking between KP201/APAP and comparator at equivalent doses (expected due to IR formulation)
  - Reduced hydrocodone exposure at oral doses ≥ 8 tablets
  - Reduced incidence of hypoxia at oral doses ≥ 8 tablets

KP201.A01: Drug Liking Scores (E_{max})



KP201.A01: Pharmacokinetics (Hydrocodone)



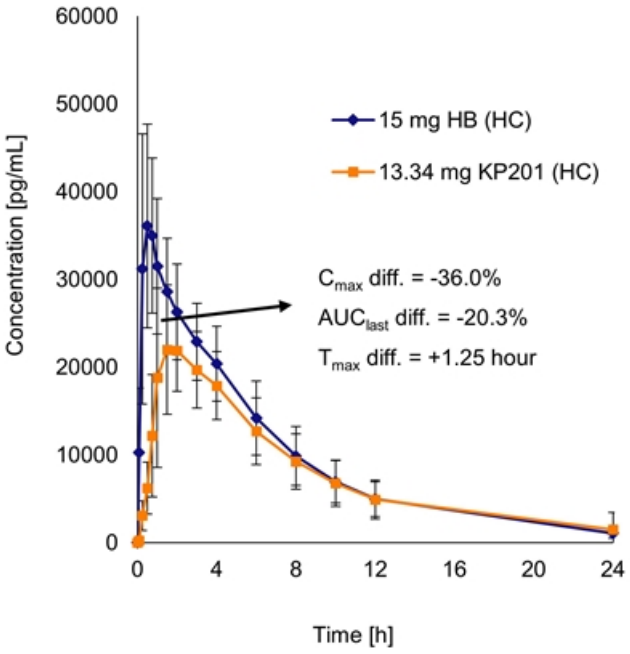


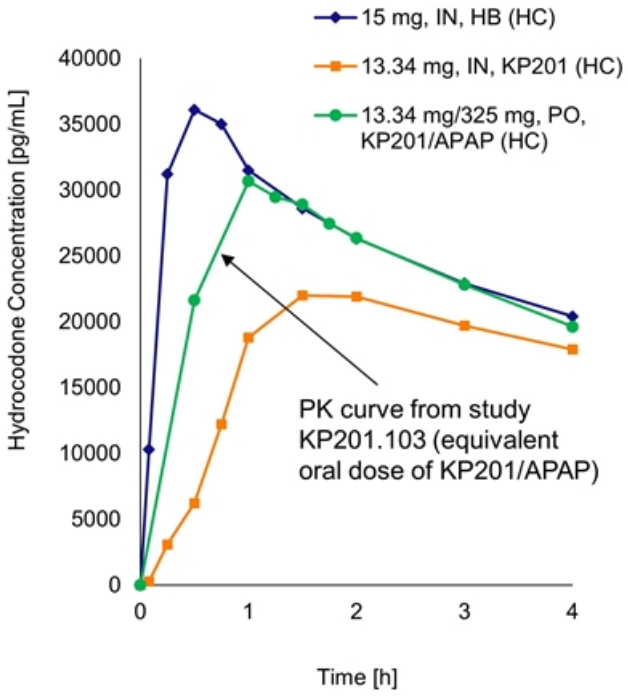
HC = hydrocodone
APAP = acetaminophen
Norco® = hydrocodone bitartrate/APAP
C_{max} diff. = difference in C_{max} comparing KP201/APAP and Norco®

KP201.A03: Intranasal Pharmacokinetic Study

- Design
  - Assessment of pharmacokinetics of KP201 API compared to hydrocodone bitartrate (HB) API in nondependent, recreational opioid users (N=24)
  - Single-center, randomized, double-blind, single-dose, 2-way crossover trial
  - KP201 API (13.34 mg) vs. HB API (15 mg) (equimolar doses)
  - Primarily a PK study. Limited PD data collected.
- Results
  - Significant reduction in hydrocodone exposure with KP201 compared to HB (> 50% reduction during first 2 hours)
  - Reduced hydrocodone exposure from IN KP201 compared to PO
  - Significant delay in median T_{max} for KP201
  - Snorting of KP201 was significantly more difficult compared to HB

KP201.A03: Intranasal Pharmacokinetics





HC = hydrocodone
HB = hydrocodone bitartrate
APAP = acetaminophen
IN = intranasal

C_{max} diff. = difference in C_{max} comparing KP201 and HB
AUC_{last} diff. = difference in AUC_{last} comparing KP201 and HB
T_{max} diff. = difference in median T_{max} comparing KP201 and HB

KP511 Overview

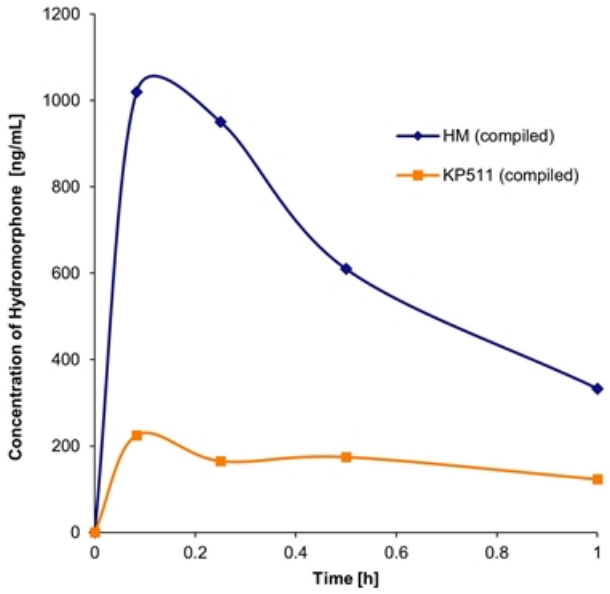
Treatment of Moderate to Severe Pain

KP511 Product Features

- KP511 is a prodrug of hydromorphone
- Bioequivalent release of hydromorphone demonstrated in rats
- Potential properties based on preclinical data
  - Significantly reduced IN and IV bioavailability (abuse deterrence)
  - Highly tamper resistant
  - Limited oral bioavailability at high doses (overdose protection)

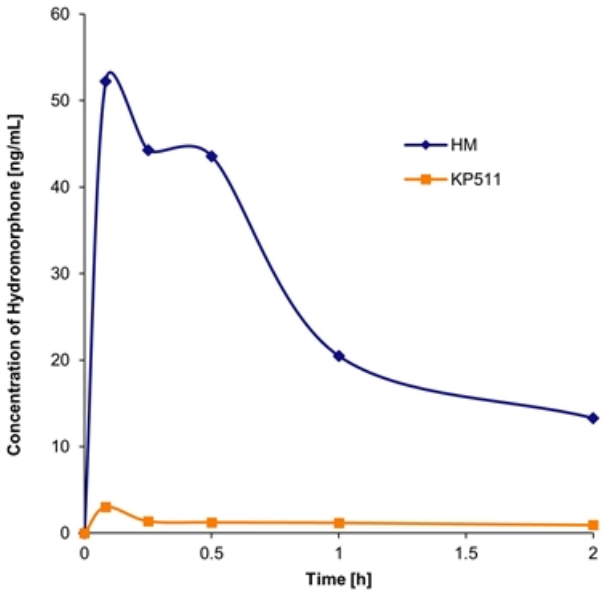
KP511 Reduced Abuse Potential

Intranasal



- 2.0 mg/kg (hydromorphone eq.)
- Average data from 2 studies (N=10)
- %-AUC = 25%
- %-C_{max} = 22%

Intravenous

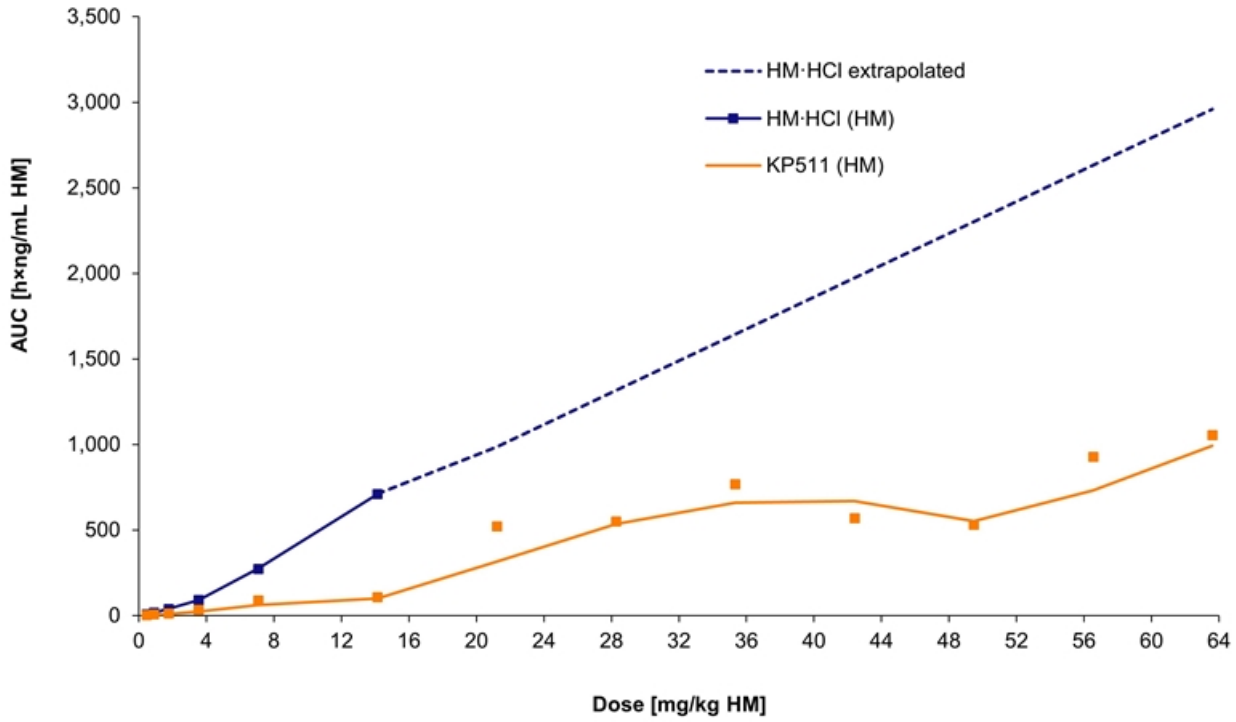


- 0.2 mg/kg (hydromorphone eq.)
- 1 study (N=5)
- %-AUC = 5%
- %-C_{max} = 6%

Note: HM refers to hydromorphone hydrochloride.
Studies conducted in rats.

KP511 Potential Oral Overdose Protection

AUC



Note: HM refers to hydromorphone hydrochloride.
Studies conducted in rats.

KP511 Tamper Resistant Properties

- Extraction of API (KP511) from formulation only yields inactive prodrug with inherent pharmacological abuse protection
- Hydromorphone cannot be released through
  - Physical manipulation (e.g., grinding)
  - Solvent extraction (e.g., “alcohol dose dumping”, “cold water extraction”)
- KP511 is chemically stable under commonly applied “extraction methods”
- Hydrolysis under extremely harsh conditions is not practical
  - KP511 partially hydrolyzes to hydromorphone only under extremely harsh conditions (e.g., conc. HCl at 100 °C)
  - Decomposition products also have reduced IN and IV abuse potential
  - Additionally, decomposition products diminish oral potency
  - Yields a complex mixture of decomposition products in highly acidic or caustic solutions
    - Extraction of hydromorphone from mixture difficult and inefficient

A Case for Prodrugs

- Known to be efficacious a priori
- Modify well-known metabolism vs complex, not completely understood mechanism of action
- Are able to effectively address abuse of IR and ER opioid products
- Reduced development path
- Flexible application allows for future improvements as abusers become more sophisticated
- Can work synergistically with other technologies (e.g., formulation)

Future Outlook Prodrugs

- Combine prodrugs with an ER-ADF could provide double barrier
- Identify prodrugs with reduced abuse potential and inherent ER properties, i.e., no ER formulation required
- Create prodrugs of more potent opioid agonists
- Add novel, advanced formulations to enhance benefits of unique prodrug pharmacology
  - Formulations that limit opioid overexposure
  - Autoinhibition of prodrug hydrolysis at supratherapeutic doses

Thank you!

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