CAM2038 for Treatment of Opioid Use Disorder

November 1, 2017

Braeburn Pharmaceuticals, Inc.

Joint Meeting of the Psychopharmacologic Drugs and Drug Safety and Risk Management Advisory Committees

Introduction

Susan Franks, MS

Senior Vice President, Regulatory Affairs

Braeburn Pharmaceuticals, Inc.

CAM2038: Subcutaneous Buprenorphine Depot with Sustained Release Formulation

- Weekly or monthly injection
  - Multiple dose strengths
- Administered by healthcare provider (HCP)
  - Ensures medication adherence and exposure
  - Minimizes risk of misuse, abuse, diversion and accidental pediatric exposure
- Allows for individualized dosing
  - Aligns with treatment guidelines

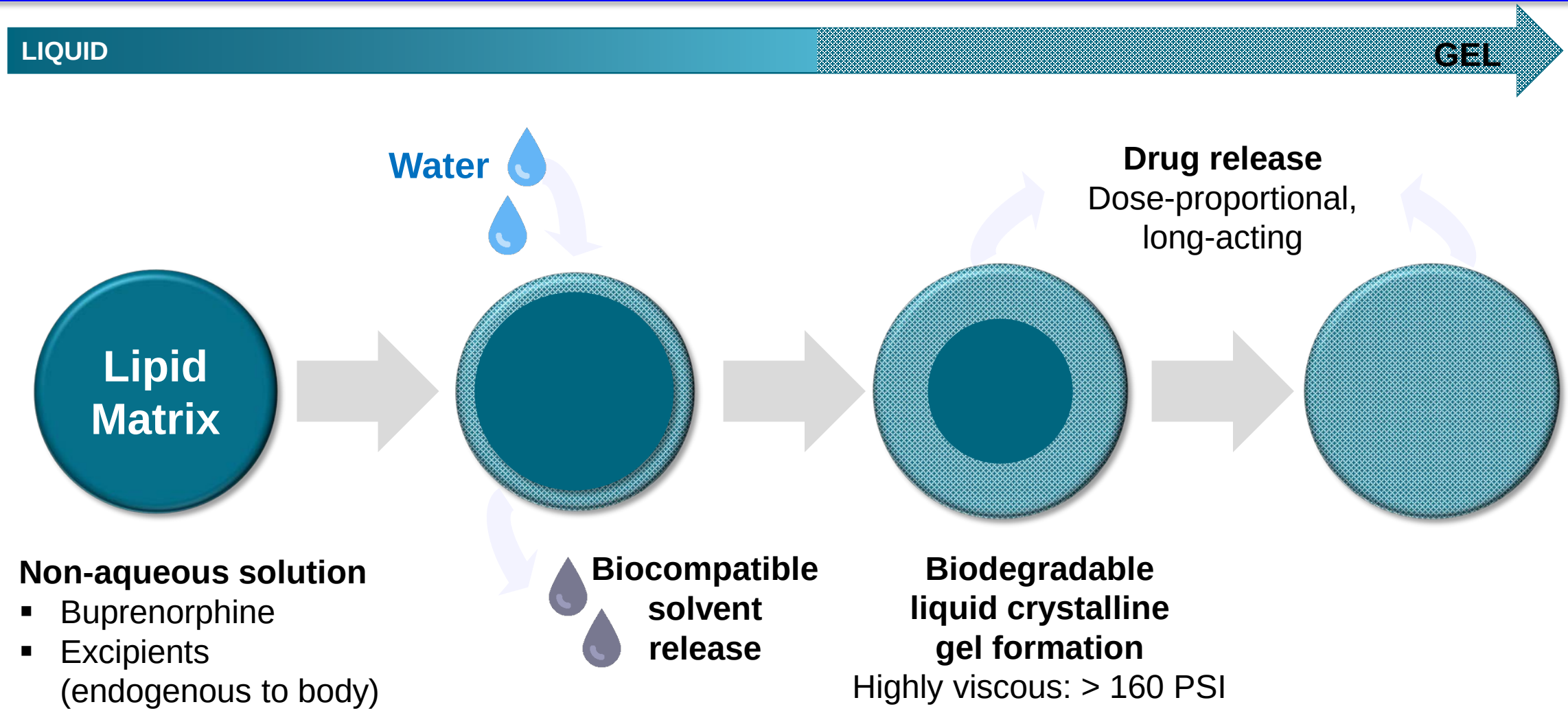
CAM2038 Proposed Indication

- For treatment of Opioid Use Disorder (OUD)
  - Including treatment initiation
  - Used as part of complete treatment plan to include counseling and psychosocial support
- Dosage strengths
  - Weekly (q1w): 8, 16, 24 and 32 mg/injection
  - Monthly (q4w): 64, 96, 128 and 160 mg/injection

Buprenorphine (BPN) is Well-Established Treatment for Opioid Use Disorder

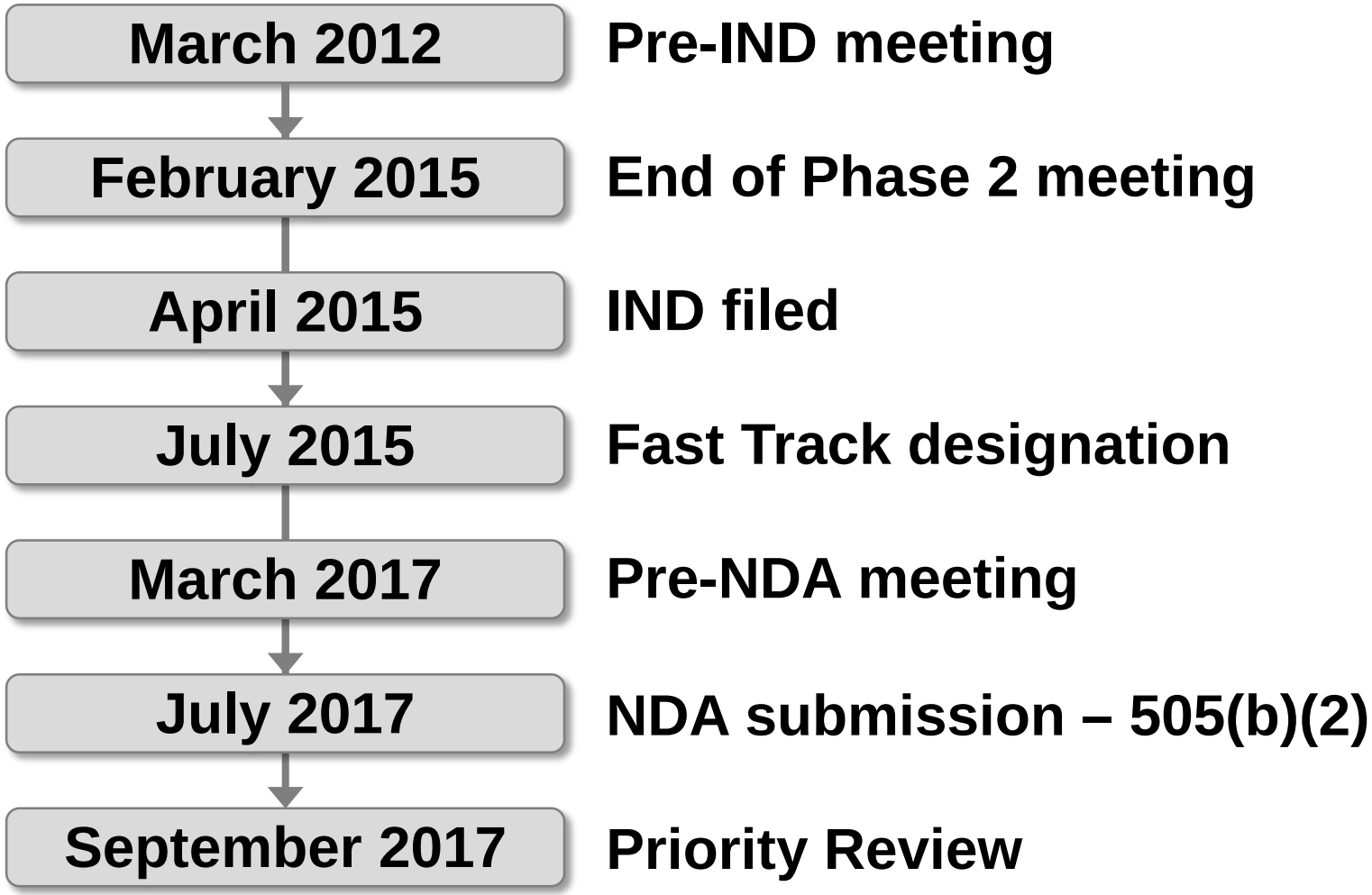
- First approved for OUD in 2002 as oral sublingual tablet
- Partial agonist for mu-opioid receptor
  - High affinity and slow rate of dissociation
  - Long half-life
  - Better safety profile vs. full mu-opioid agonist
- BPN acts at kappa-opioid and ORL-1 receptors
- Current formulations susceptible to misuse, abuse, diversion and accidental pediatric exposure

Sustained-Release Formulation Based on FluidCrystal® Technology



Episil: 510(k) cleared device using FluidCrystal technology

Regulatory History



Robust Clinical Development Program

Study	Enrolled (N)	Study Design	Tx Duration
HS-11-**426**	**60**	Phase 1, randomized, open-label, single dose	**1 Week**
HS-13-**487**	**87**	Phase 1, randomized, open-label, single- and repeated-dose	**4 Weeks**
HS-07-**307**	**41**	Phase 1/2, single-blind, single-center, single-dose, dose-escalation	**1 Week**
HS-15-**549**	**66**	Phase 2, randomized, open-label, multicenter, different injection sites	**7–22 Weeks**
HS-13-**478**	**47**	Phase 2, randomized, double-blind, multicenter, repeated-dose (Opioid Challenge Study)	**2 Weeks**
HS-11-**421**	**428**	Phase 3, randomized, double-blind, double-dummy, active-controlled, parallel group, multicenter	**24 Weeks**
HS-14-**499**	**227**	Phase 3, open-label, multicenter	**48 Weeks**

Unique Characteristics of CAM2038

- Weekly and monthly dosing
- Pre-filled syringe
- Range of fixed doses
- Delivered in any subcutaneous tissue
  - Multiple injection sites
- No refrigeration
- No reconstitution or mixing
- Small volume (0.16 – 0.64 mL)
- 23G, ½” needle
  - Ease of administration
  - Needle stick safety device

CAM2038 Allows for Individualized Dosing

- Effectively treat broad patient population
- Initiation phase through maintenance
- Flexibility to adjust dosing based on clinical response and tolerability*
- Potential to improve medication adherence

*As recommended by Substance Abuse and Mental Health Services Administration (SAMHSA), 2016

Agenda

Unmet Need	**Michelle Lofwall, MD, DFASAM** University of Kentucky
Clinical Pharmacokinetics	**Fredrik Tiberg, PhD** Camurus AB
Efficacy: **Opioid Challenge Study**	**Sharon Walsh, PhD** University of Kentucky
Efficacy and Safety: **Phase 3 Studies**	**Sonnie Kim, PharmD** Braeburn Pharmaceuticals, Inc.
Clinical Perspective	**Michael Frost, MD, FACP, FASAM, CMRO** The Frost Medical Group

Additional Subject Matter Experts

- **Genie Bailey, MD, FASAM**
  Associate Clinical Professor
  Psychiatry and Human Behavior
  Brown University

- **William Brock, PhD**
  Principal
  Brock Scientific Consulting

- **Michael Chen, PhD**
  Biostatistical Consultant
  President
  TCM Groups, Inc.

- **Joga Gobburu, PhD**
  Professor/Executive Director
  Center for Translational Medicine
  University of Maryland

- **Peter Kowey, MD, FACC, FHRS, FAHA**
  Professor of Medicine and Clin. Pharm.
  Jefferson Medical College
  Emeritus Chief, Division of CV Diseases
  Lankenau Heart Institute

- **Lee-Jen Wei, PhD**
  Professor of Biostatistics,
  Department of Biostatistics
  School of Public Health, Harvard University

Unmet Need

Michelle Lofwall, MD, DFASAM

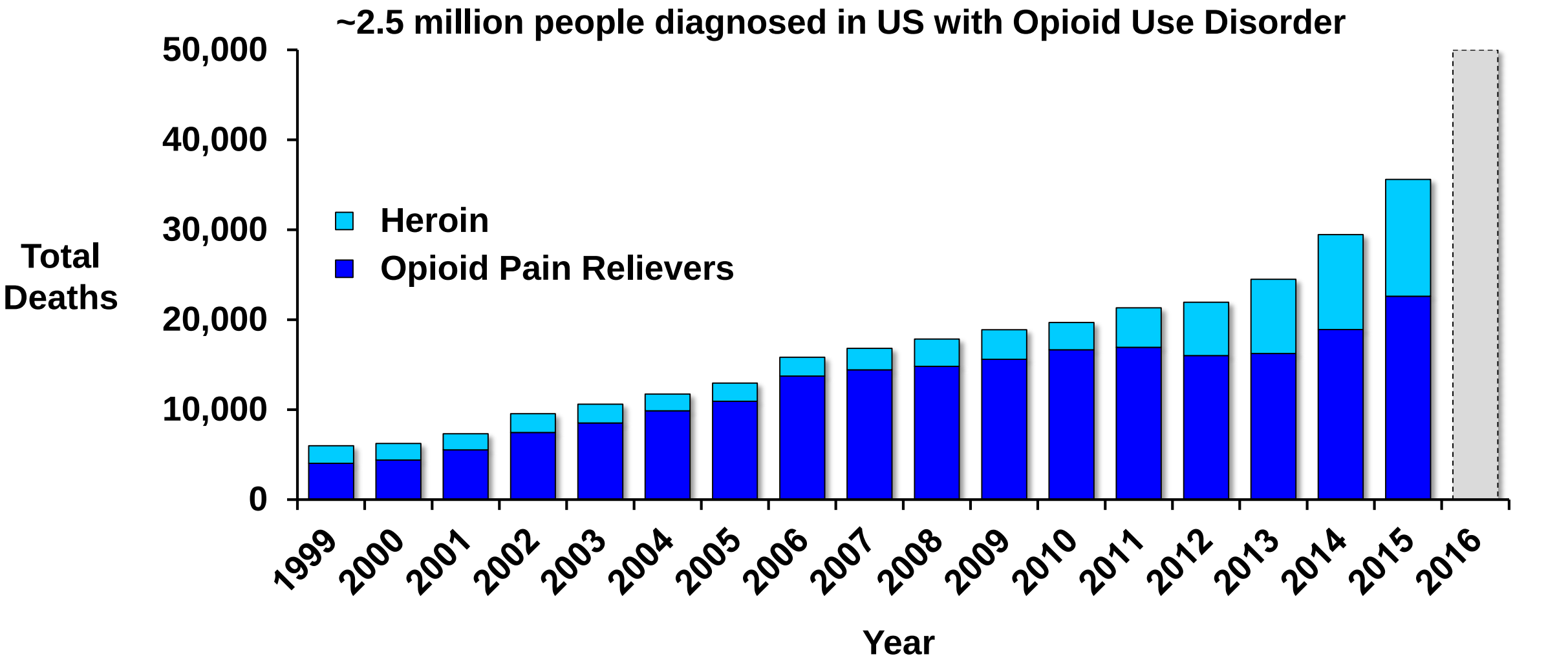
Associate Professor
Behavioral Science and Psychiatry
Center on Drug and Alcohol Research
University of Kentucky

Moderate to Severe Opioid Use Disorder: Chronic and Life-Threatening

- Compulsive opioid use
  - Overwhelming cravings and changes in brain function
  - Opioid withdrawal syndrome
- Causes significant mental, physical and social problems
  - Contraction / transmission of infectious diseases
  - Unintentional overdose
  - Criminal activity and incarceration
- Majority Americans not in treatment although treatment saves lives
- More options can decrease treatment gap

Schwartz, 2007; Strathdee, 2015; Surya Prasad, 2014; Schwartz, 2013

Public Health Epidemic:
> 35,000 Opioid-Related Overdoses in 2015



National Center for Health Statistics, CDC, 2017

Goal of OUD Treatment: Reduce Opioid Use, Put OUD into Remission

- Treatment path is not linear or same from patient to patient
  - Some may initiate treatment and go into remission
  - Others may struggle with intermittent use of illicit opioids
- Patients can benefit from treatment without perfection
  - Less withdrawal, cravings and illicit opioid use
  - Fulfilling responsibilities, healthy relationships
  - Less risky behaviors like injection use
- Treatment works and can save lives

Schwartz, 2013; Dupuoy, 2017; Auriacombe, 2001; Sordo, 2017

Treatment History for OUD

- Methadone approved in early 1970s but restricted to federal clinics
- Naltrexone approved in 1984 (oral tablets) and 2006 (monthly depot)
  - Indicated for relapse prevention
  - Must not be physically dependent on opioids
- BPN tablets approved for OUD in 2002[1]
  - BPN film approved in 2010
  - Sublingual and buccal formulations with increased BPN bioavailability
- Implantable buprenorphine approved in 2015[2]
  - Clinically stable patients already responsive to transmucosal BPN

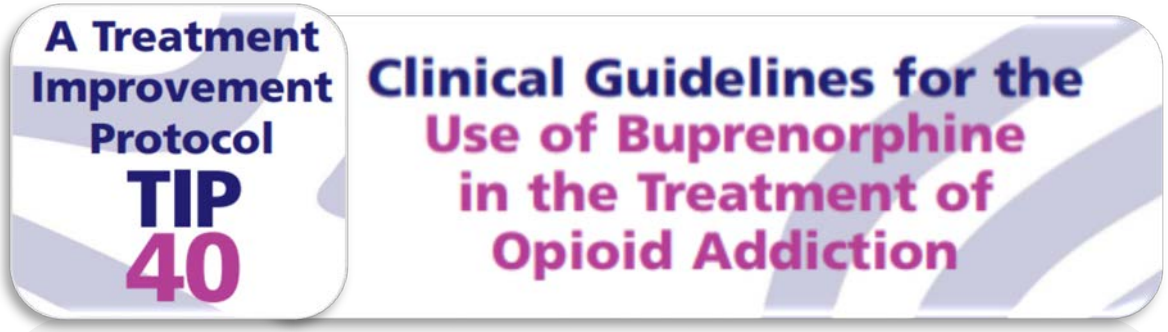
1. Subutex® (buprenorphine) and Suboxone® (buprenorphine/naloxone); 2. Probuphine® (buprenorphine)

Buprenorphine is Well-Established Treatment for Opioid Use Disorder

- Numerous studies show both efficacy and effectiveness[1-2]
- Well-known safety profile
- DATA 2000 providers can prescribe BPN in office setting
- Buprenorphine partial agonist activity
  - Opioid blockade effects decrease reinforcing effects and respiratory depressant effects of illicit opioids
  - Mitigates opioid withdrawal and craving
- Goals of buprenorphine treatment
  - Use lowest effective dose without significant side effects
  - Retain patient in treatment[3-4]

1. Federation of State Medical Boards, 2013; 2. Model policy on DATA 2000, retrieved January 20, 2016; 3. CitesMattick, 2014; 4. Johnson, 2000

Best Practice Clinical Guidelines Recommend Individualized Therapy



*"After treatment begins, the physician should **adjust drug therapy** to the **individual medical needs of each patient.**"*

Substance Abuse and Mental Health Services Administration (SAMHSA), 2004

*"**Changes to treatment** should be made on an **individual basis** and could include any combination of the following:*

- *adjusting the patient's BPN dosage,*
- *increasing the frequency of office visits,*
- *requiring supervised administration…"*

Substance Abuse and Mental Health Services Administration (SAMHSA), 2016

Phases of Buprenorphine Treatment: Initiation and Maintenance

- Initiation
  - 2 – 4 mg BPN dose repeated as needed
  - Typical day 1 dose: 8 mg SL BPN
- Maintenance
  - Doses range from 4 – 24 mg given once daily
  - Typical target dose: 16 mg SL BPN daily

Suboxone (buprenorphine and naloxone) sublingual film: Full prescribing information; retrieved January 22, 2016

Range of Buprenorphine Doses Needed to Treat Heterogeneous Patient Population with OUD

- Varying severities of OUD require different treatment plans
- Maintenance doses vary between patients and over course of treatment
- Stable patients may decrease dose over time
- Patients in sustained remission may taper off
- Patients who lapse may need to increase dose

Current Buprenorphine Formulations Have Limitations

- Suboptimal treatment retention[1-3]
  - Often ≤ 50% after 3 to 6 months
  - Dropout associated with relapse
- Issues of non-adherence[4-6]
  - Daily medication can be challenging
  - Patients think they can stop medication, use, then go back
  - Even brief non-adherence can be fatal
  - Can lead to diversion
  - Can be abused

1. Fiellin, 2006; 2. Hser, 2017; 3. Weiss, 2011; 4. Lofwall, 2014; 5. CDC, 2013; 6. Toce, 2017

Accidental Pediatric Exposure: Death, Hospitalizations and ER Visits

- Pediatric deaths reported due to BPN[1]
- 9.5% of emergency visits for drug ingestion among children age ≤ 6 years old were caused by BPN[2]
- Since 2011, focus to decrease pediatric exposure[3-4]
  - Emphasis on safe storage
  - Transition to unit dose packaging
- Some decreases in pediatric exposure but risk remains[3-4]

1. Kim, 2012; 2. CDC, 2010-2011; 3. MMWR Morb Mortal Wkly Rep., 2016; 4. Budnitz, 2015

Long-acting Depot Formulations Needed to Ensure Adherence and Reach More Patients

- Needed in hospitals and emergency rooms
  - Treatment transitions to outpatient setting
- For patients
  - New to treatment
  - Transitioning from other modalities
  - With moderate or severe disease
  - From initiation through maintenance

Clinical Pharmacokinetics

Fredrik Tiberg, PhD

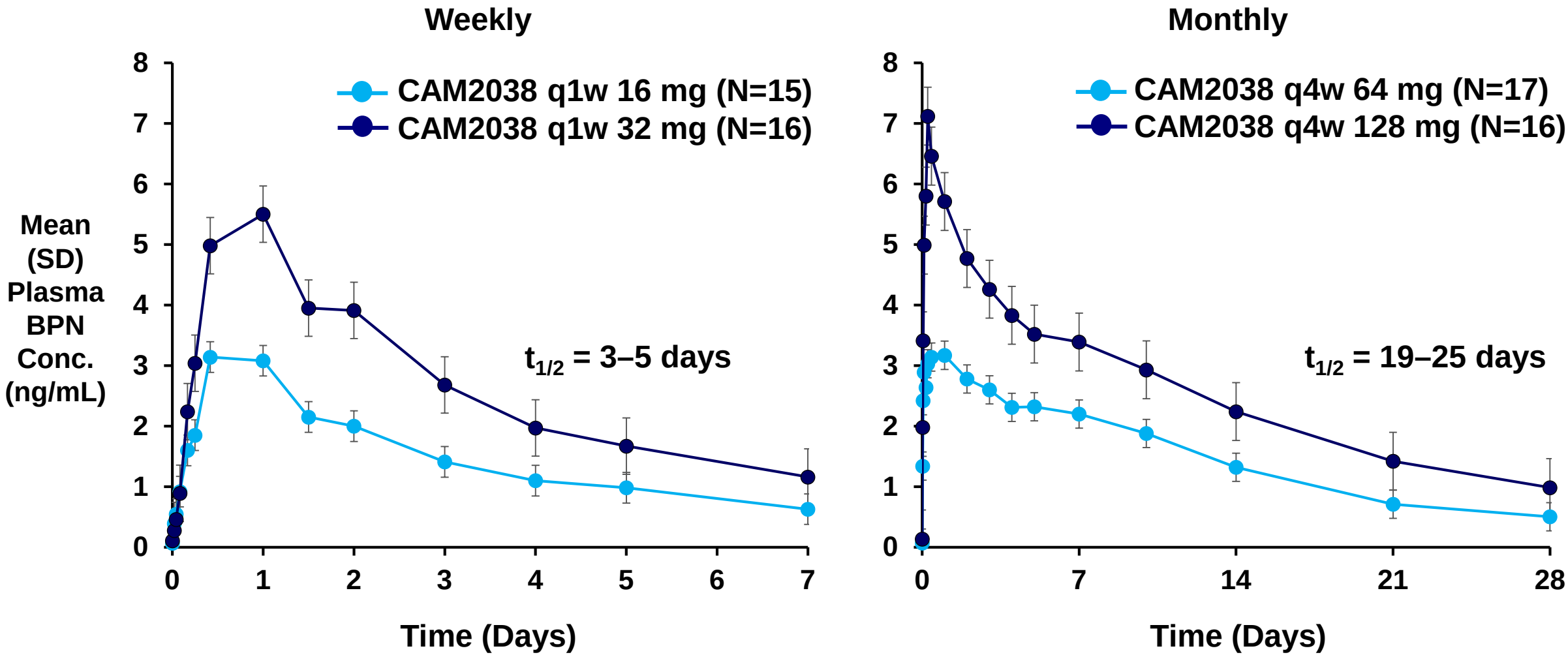
President and CEO
Camurus AB

Adjunct Professor of Physical Chemistry
Lund University, Sweden

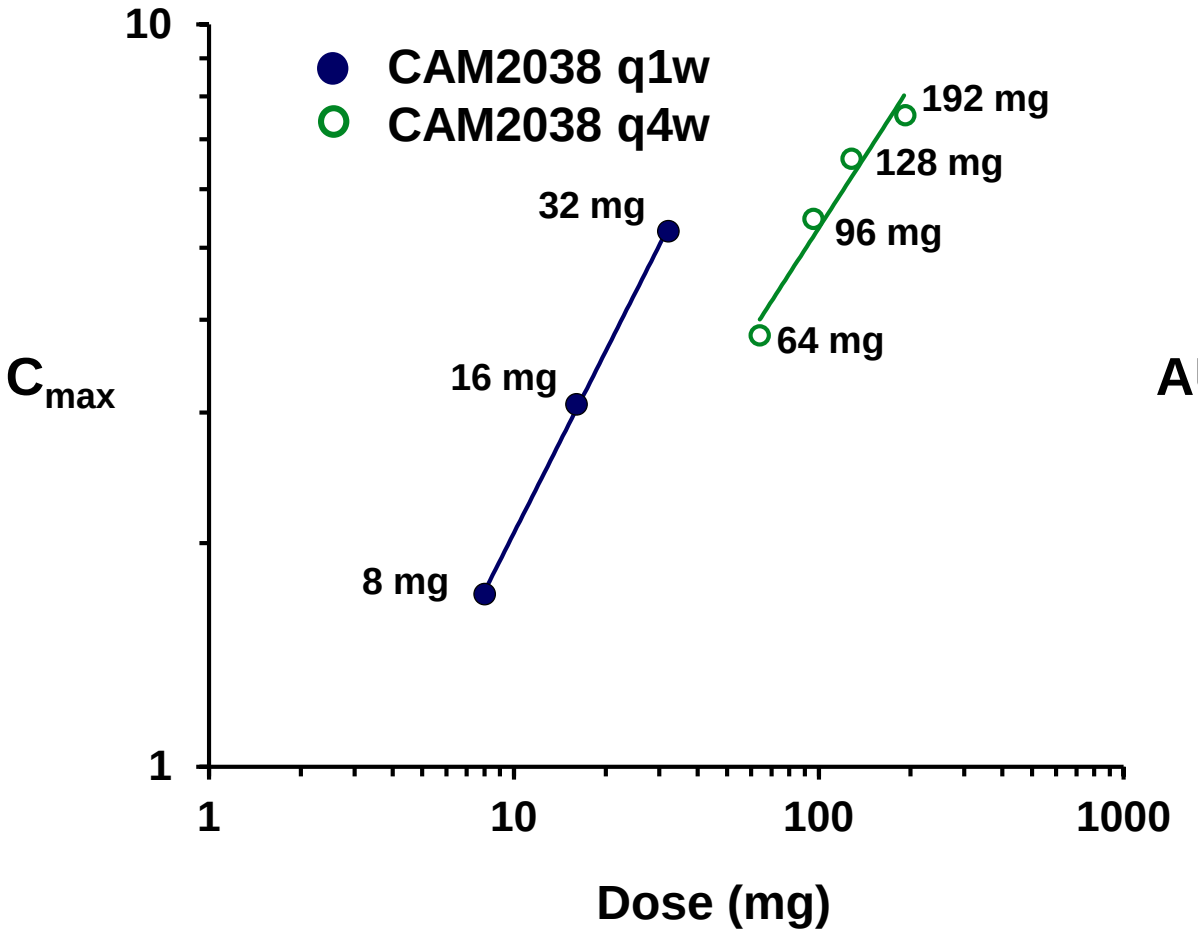
5 Clinical Pharmacokinetic Studies to Support Dosing and Bridging to Sublingual Buprenorphine

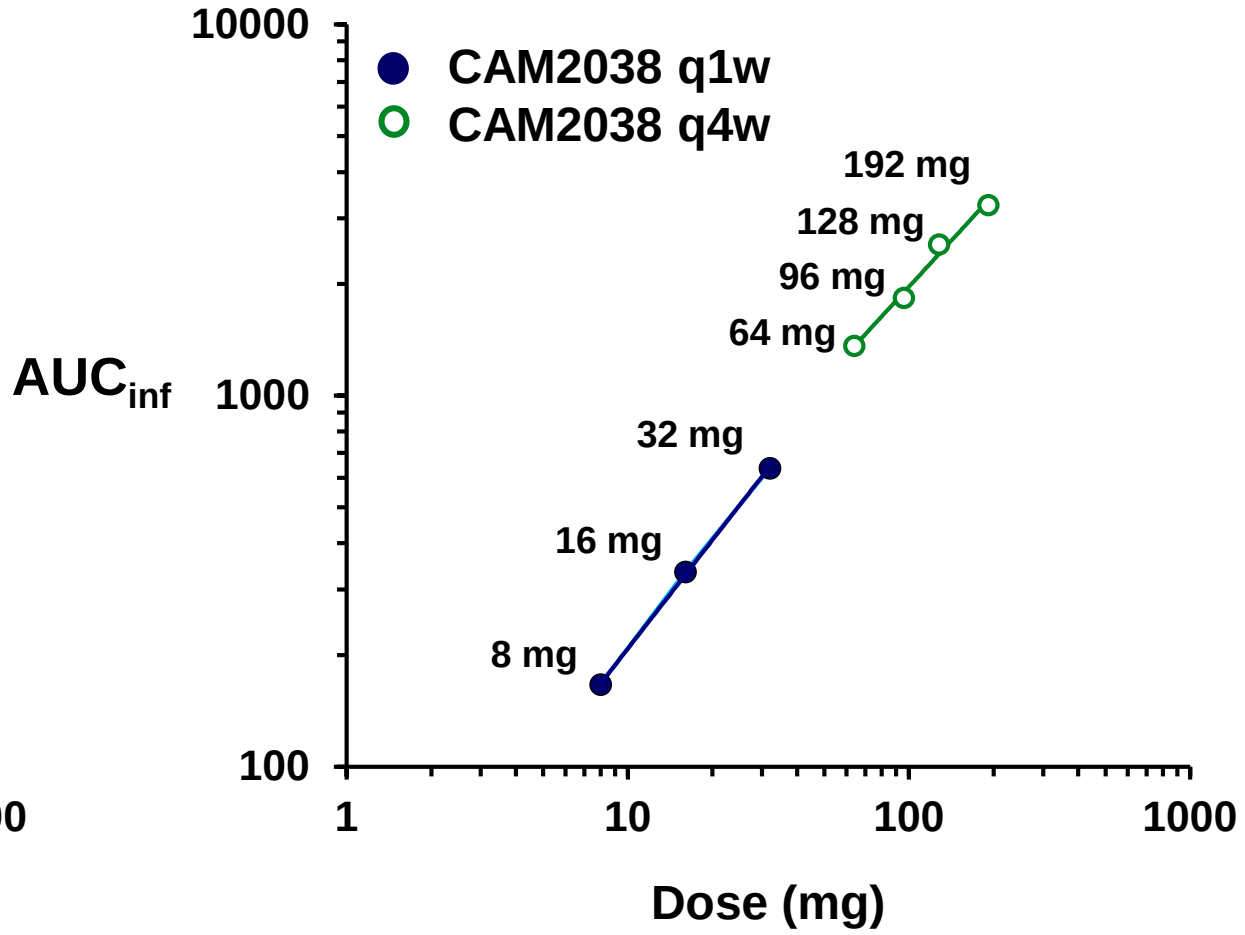
- Assess pharmacokinetic (PK) profiles for CAM2038 weekly (q1w) and monthly (q4w)
  - Dose proportionality and bioavailability
- Bridging to reference SL BPN product
  - Observed BPN plasma exposures and population PK modeling
- Selection of treatment initiation and conversion doses

Pharmacokinetic Profiles After Single Dosing of Weekly and Monthly CAM2038 Depots

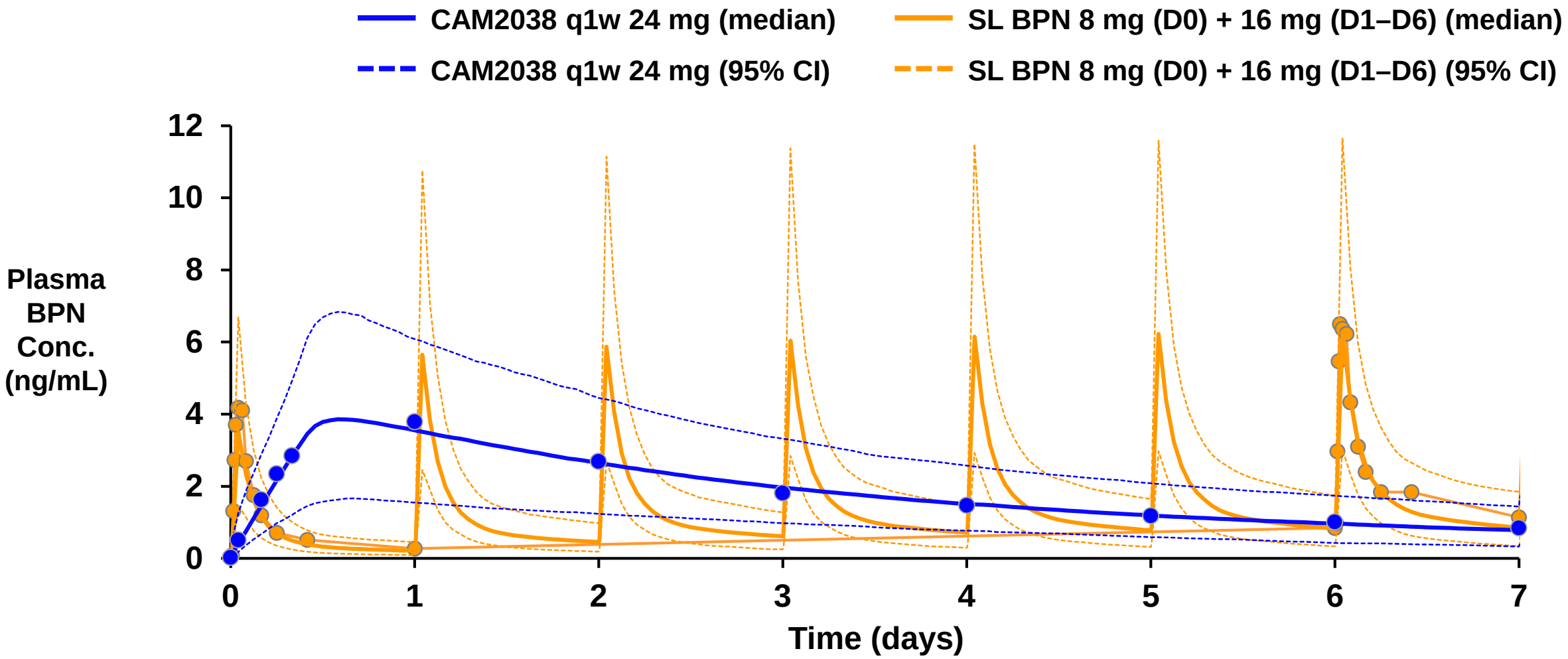


Dose Proportionality Observed Across CAM2038 Weekly and Monthly Dose-Range



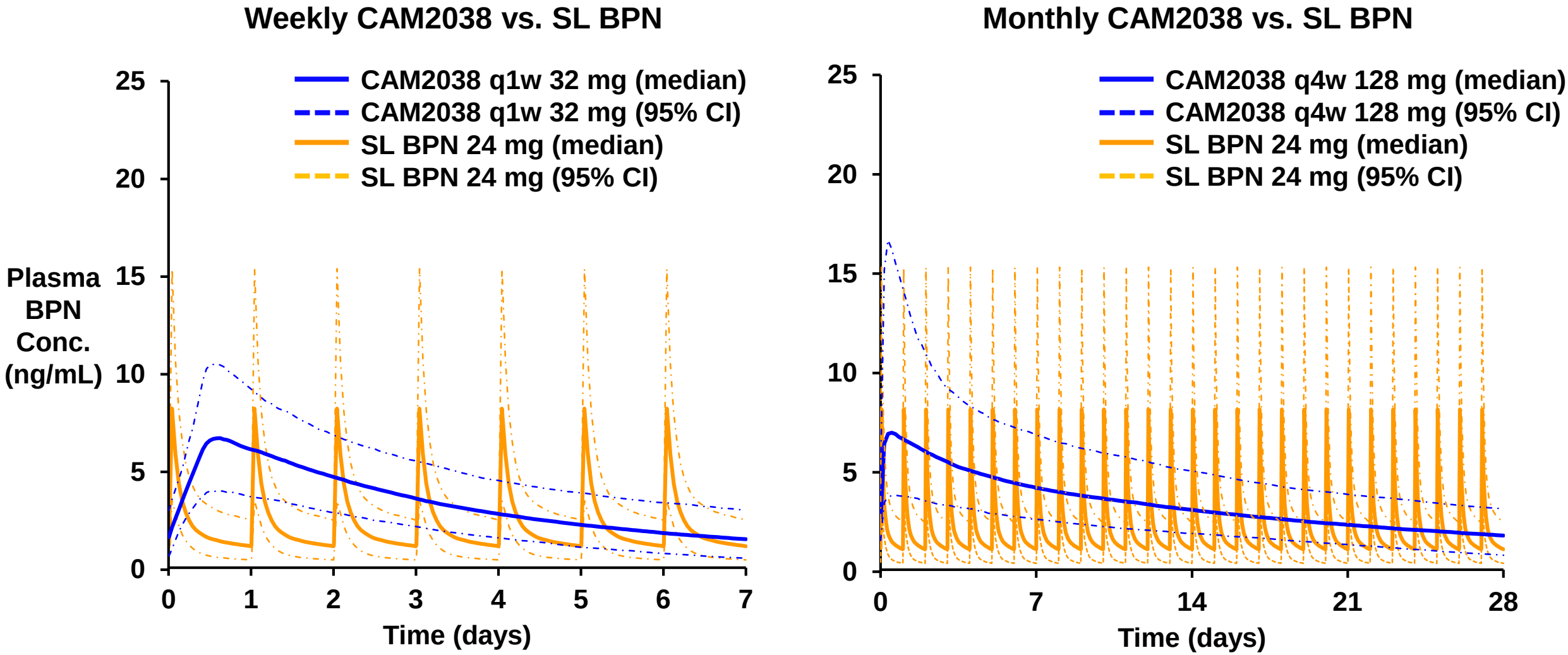


CAM2038 vs. Daily Sublingual Buprenorphine



Pop PK model based on 236 subjects and > 10000 observations; 1000 simulations used for each plasma concentration profile

Population PK Steady-State Profiles Show CAM2038 Concentration Within Range of Daily SL BPN



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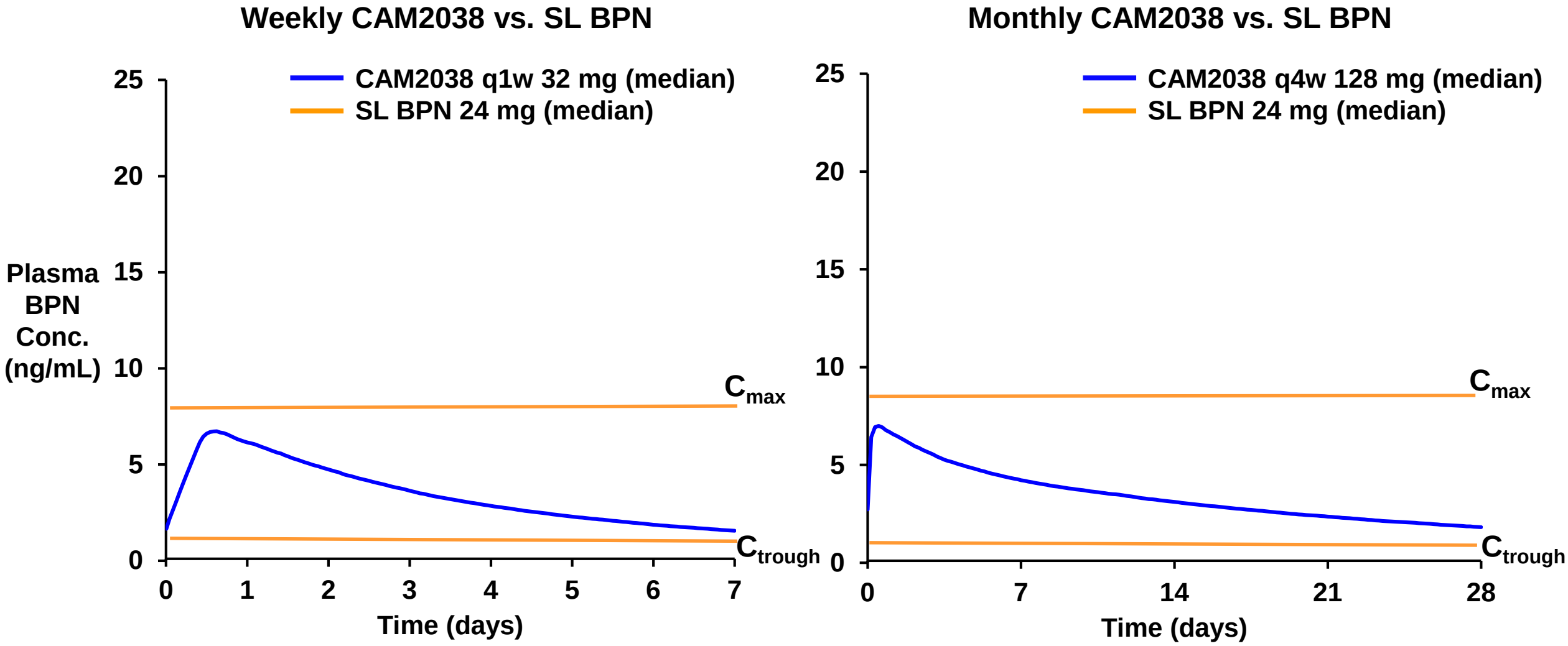


Steady-State Plasma Concentrations from Population PK Confirm Dose Conversions

	CAM2038 Dose	C_{max} (ng/mL)	C_{trough} (ng/mL)
CAM2038 q1w	8 mg	1.69	0.39
SL BPN 8 mg		3.92	0.54
CAM2038 q1w	16 mg	3.38	0.78
CAM2038 q4w	64 mg	3.81	0.92
SL BPN 16 mg		6.09	0.85
CAM2038 q1w	24 mg	4.97	1.18
CAM2038 q4w	96 mg	5.86	1.36
SL BPN 24 mg		7.94	1.10
CAM2038 q1w	32 mg	6.75	1.55
CAM2038 q4w	128 mg	7.51	1.81
CAM2038 q4w	160 mg	9.38	2.26

Proposed Dose Conversion Table for Switching Between SL BPN, Weekly or Monthly CAM2038

Daily SL BPN Dose	CAM2038 q1w	CAM2038 q4w
2 – 6 mg	8 mg	N/A
8 – 10 mg	16 mg	64 mg
12 – 16 mg	24 mg	96 mg
18 – 24 mg	32 mg	128 mg
26 – 32 mg	N/A	160 mg

Summary of PK for CAM2038

- CAM2038 provides dose proportional profiles suitable for weekly and monthly dosing
- Flexible dosing allows for individualized treatment across BPN exposure ranges of SL BPN products
- CAM2038 provides comparable BPN exposure to SL BPN with 20 – 30% total BPN dose
- Dose recommendations
  - Weekly initiation dose of 24 mg CAM2038
  - Dose conversions between SL BPN, CAM2038 q1w and q4w

Efficacy: Study 478 Opioid Challenge Study

Sharon Walsh, PhD

Director, Center on Drug and Alcohol Research

Professor of Behavioral Science, Psychiatry, Pharmacology and Pharmaceutical Sciences
University of Kentucky

Study 478: Double-Blind, Randomized, Within-Subject, Inpatient Laboratory Study

- Primary objective: assess ability of CAM2038 to block opioid effects of hydromorphone
- Primary endpoint: drug liking on visual analog scale (VAS)
  - VAS E_{max} 95% CI difference to placebo non-inferiority margin for complete blockade ≤ 11 mm[1]
- Secondary measures
  - VAS ratings of high, good effect, any effect, alertness and drowsiness, withdrawal and craving

1. Chen and Bonson, 2013

Study 478 Design: Screening and Qualification

Outpatient Screening
≤ 2 weeks

Qualification Phase
~ 1 week

Randomization

Inclusion Criteria

- **Ages 18 – 55**
- **Moderate-to-severe OUD**
- **Physical dependence on opioids**
- **Not seeking treatment for OUD**

Admitted as inpatients

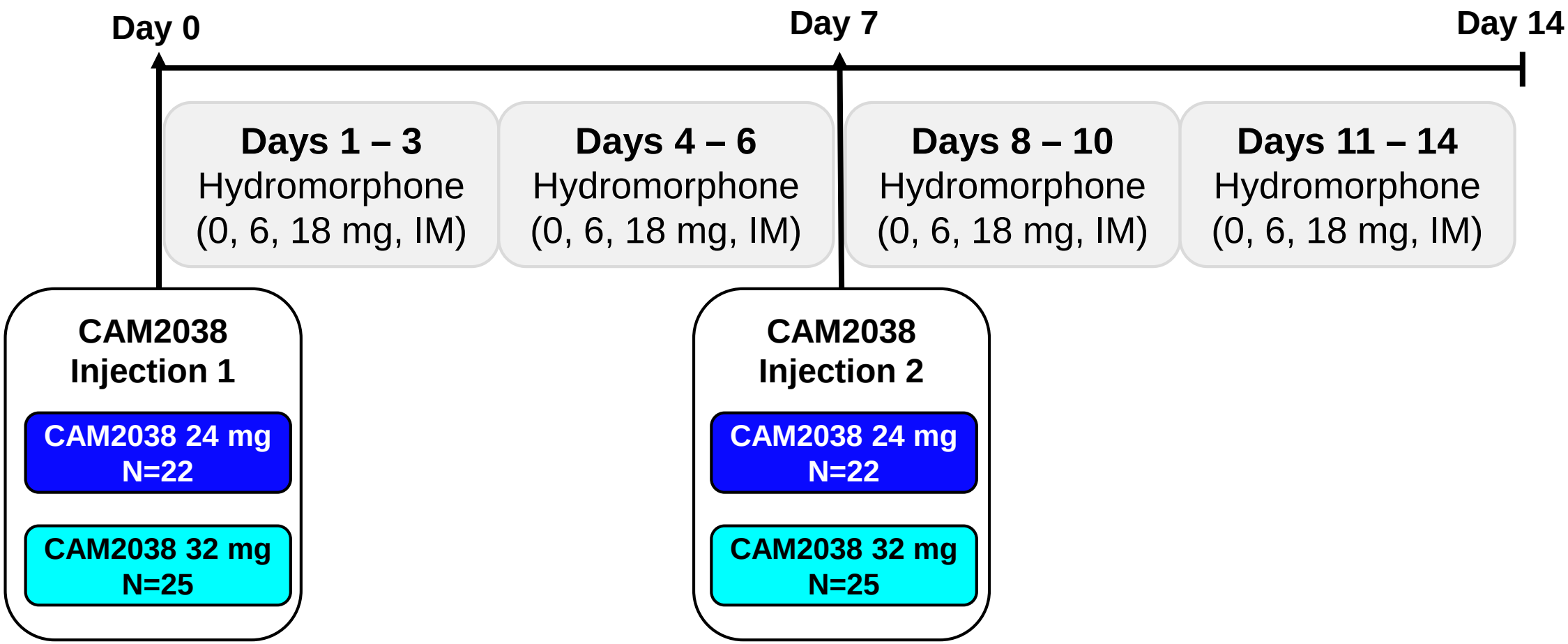
↓

Stabilized on morphine
30 mg, qid, oral
for ≥ 3 days

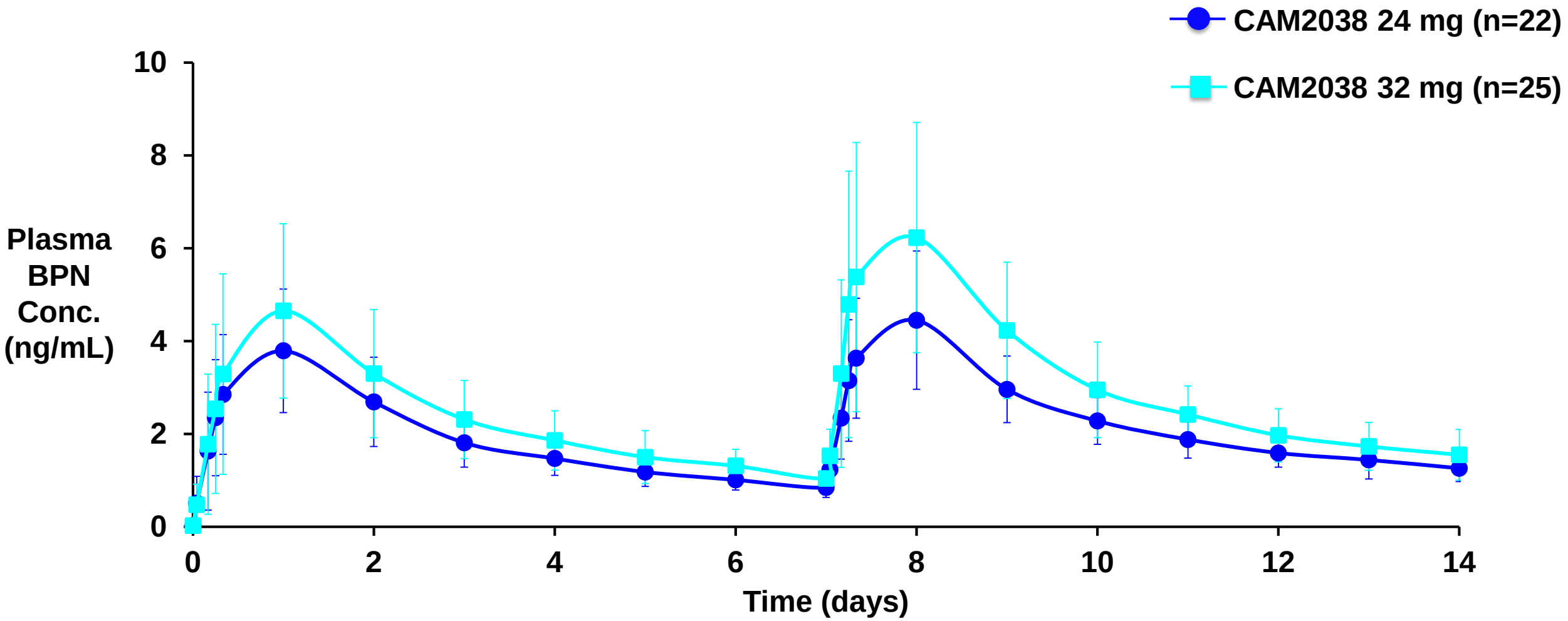
↓

Hydromorphone Challenges
0, 6, 18 mg
Days -1 to -3
randomized order

Study 478 Design: Randomization

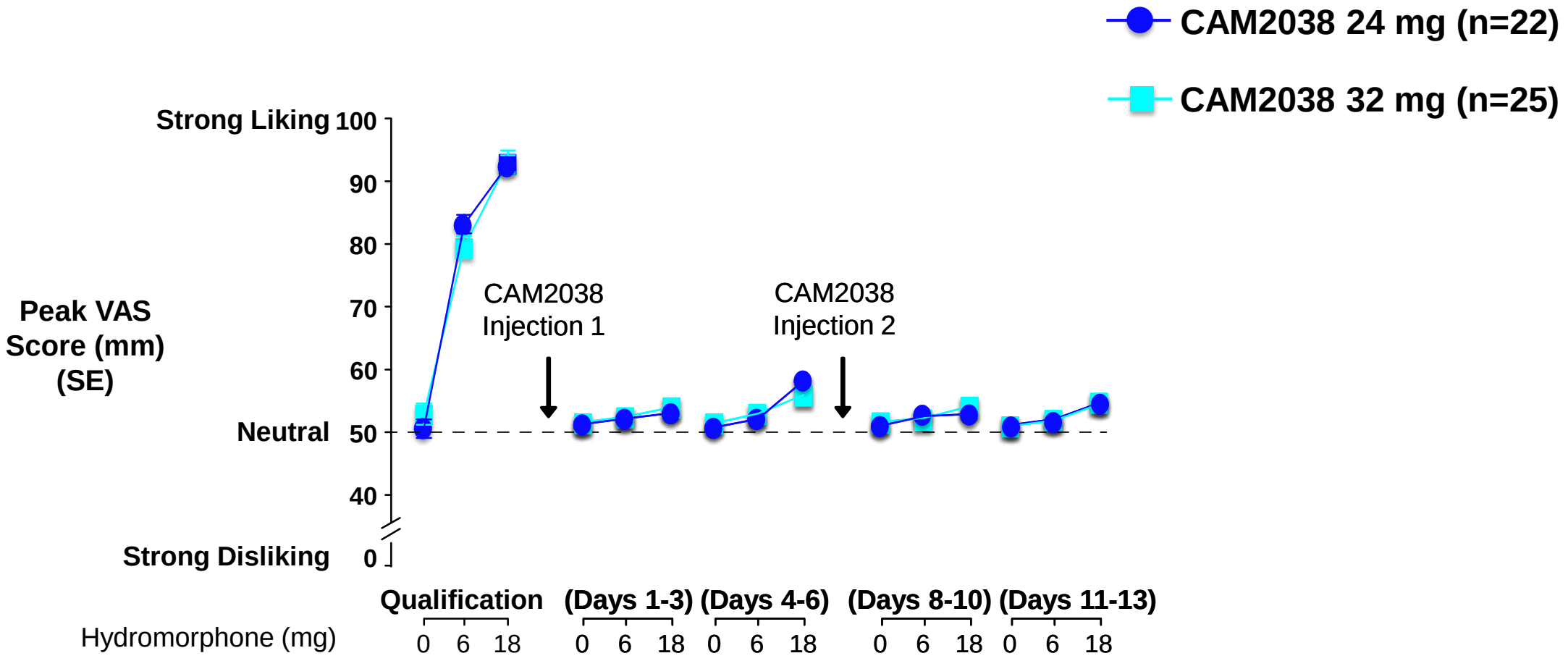


Study 478: Buprenorphine Plasma Concentrations



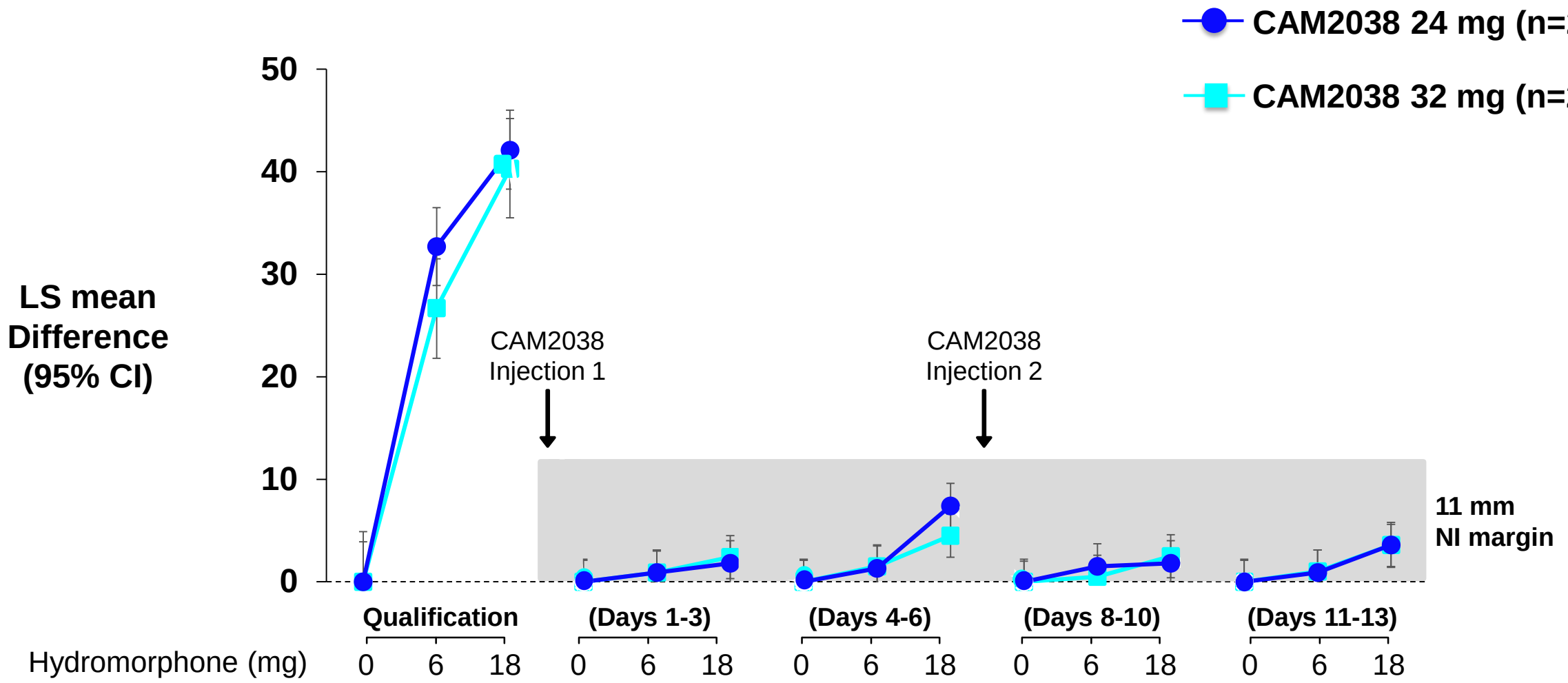
Walsh S., JAMA Psych., 2017

Study 478: CAM2038 Produces Opioid Blockade



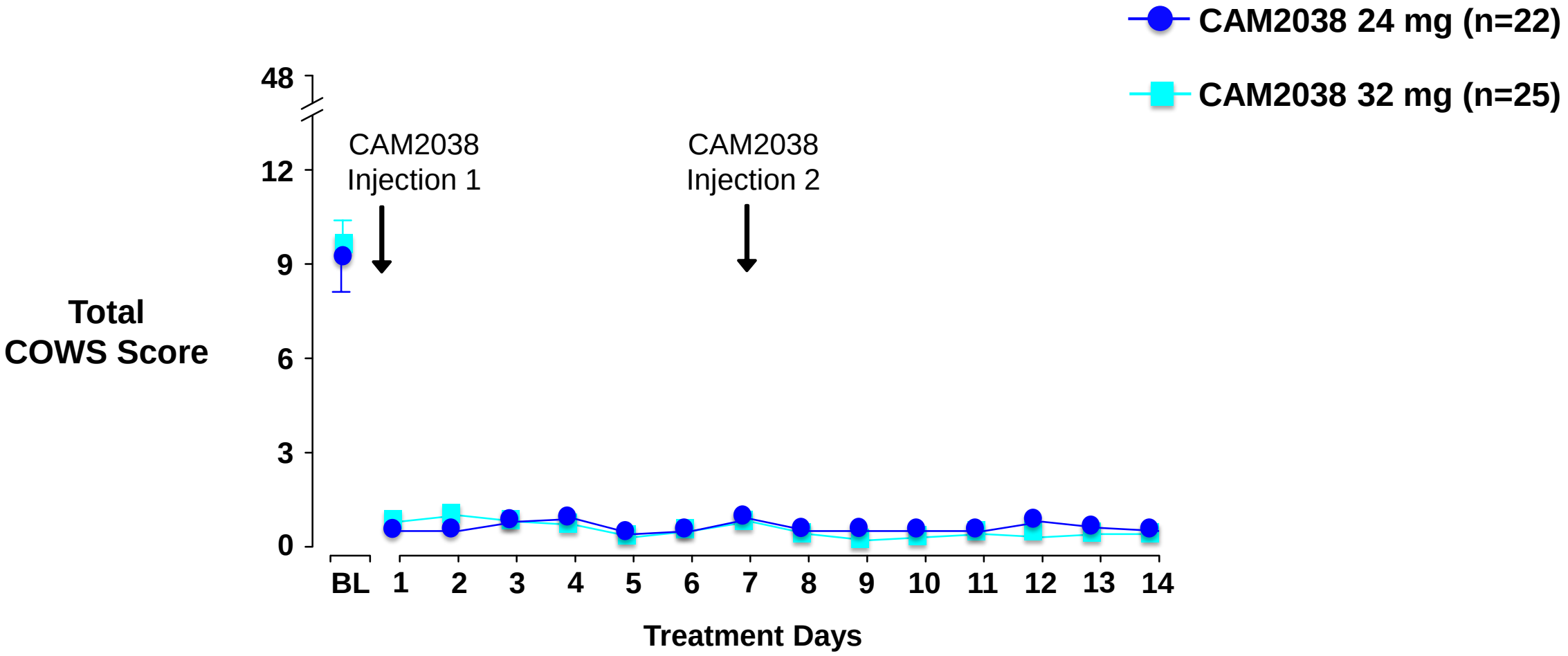
Walsh S., JAMA Psych., 2017

Study 478: Drug Liking Similar Between Placebo and Hydromorphone Following CAM2038 Administration



Walsh S., JAMA Psych., 2017

Study 478: CAM2038 Supresses Opioid Withdrawal



Walsh S., JAMA Psych., 2017

COWS = Clinical Opioid Withdrawal Scale

CAM2038 Produced Rapid and Sustained Opioid Blockade and Withdrawal Suppression

- Complete opioid blockade observed after first injection
- Blockade sustained during 1 week inter-dosing interval
- Complete blockade achieved at ≥ 1.2 ng/mL of BPN
- Findings support efficacy of CAM2038 in treatment of OUD

Efficacy of CAM2038: Studies 421

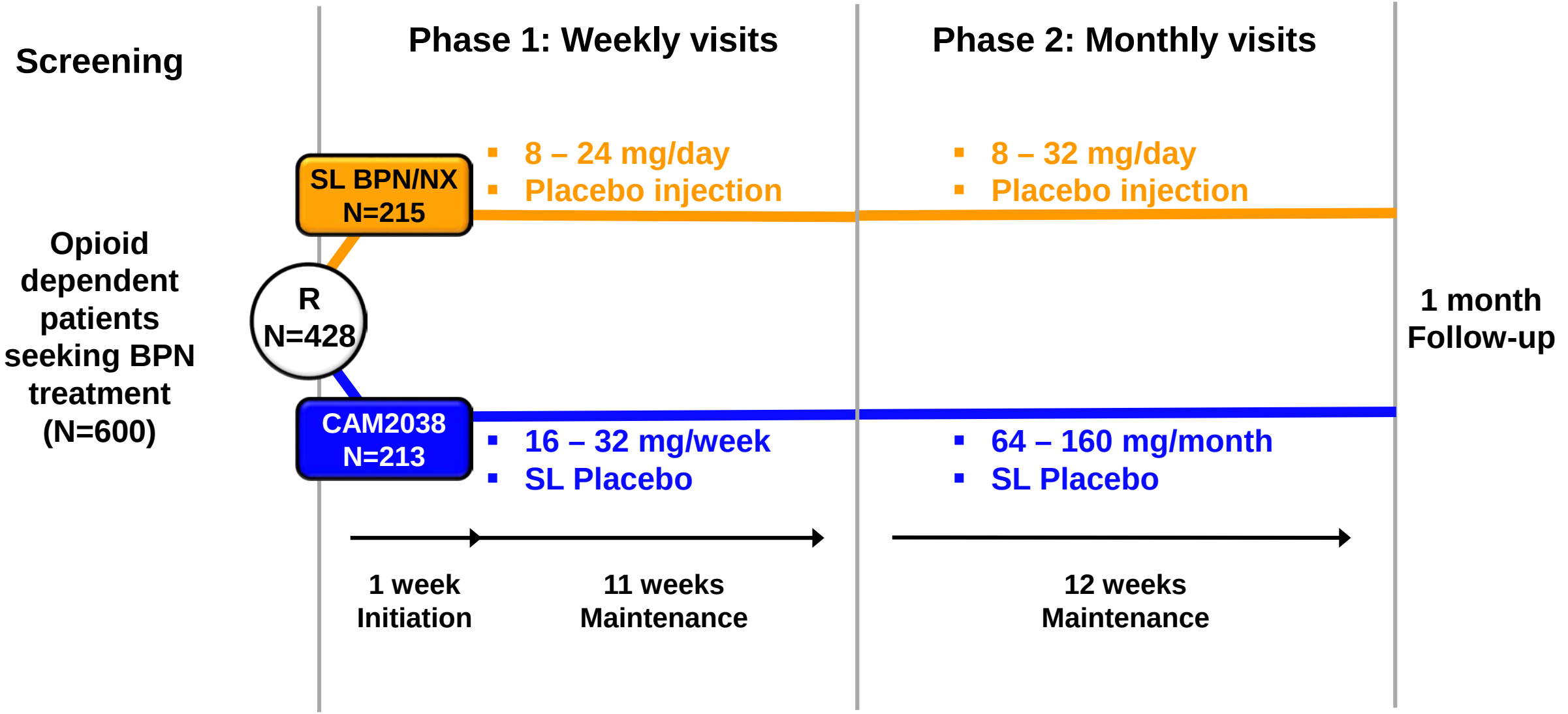
Sonnie Kim, PharmD

Chief Scientific Officer
Braeburn Pharmaceuticals, Inc.

Phase 3 Efficacy and Safety Overview

- Efficacy
  - Study 421: active control study
  - CAM2038 as effective as SL BPN for response rate
  - CAM2038 superior to SL BPN in reducing illicit opioid use
- Safety
  - Study 421: active control study
  - Study 499: long-term safety study

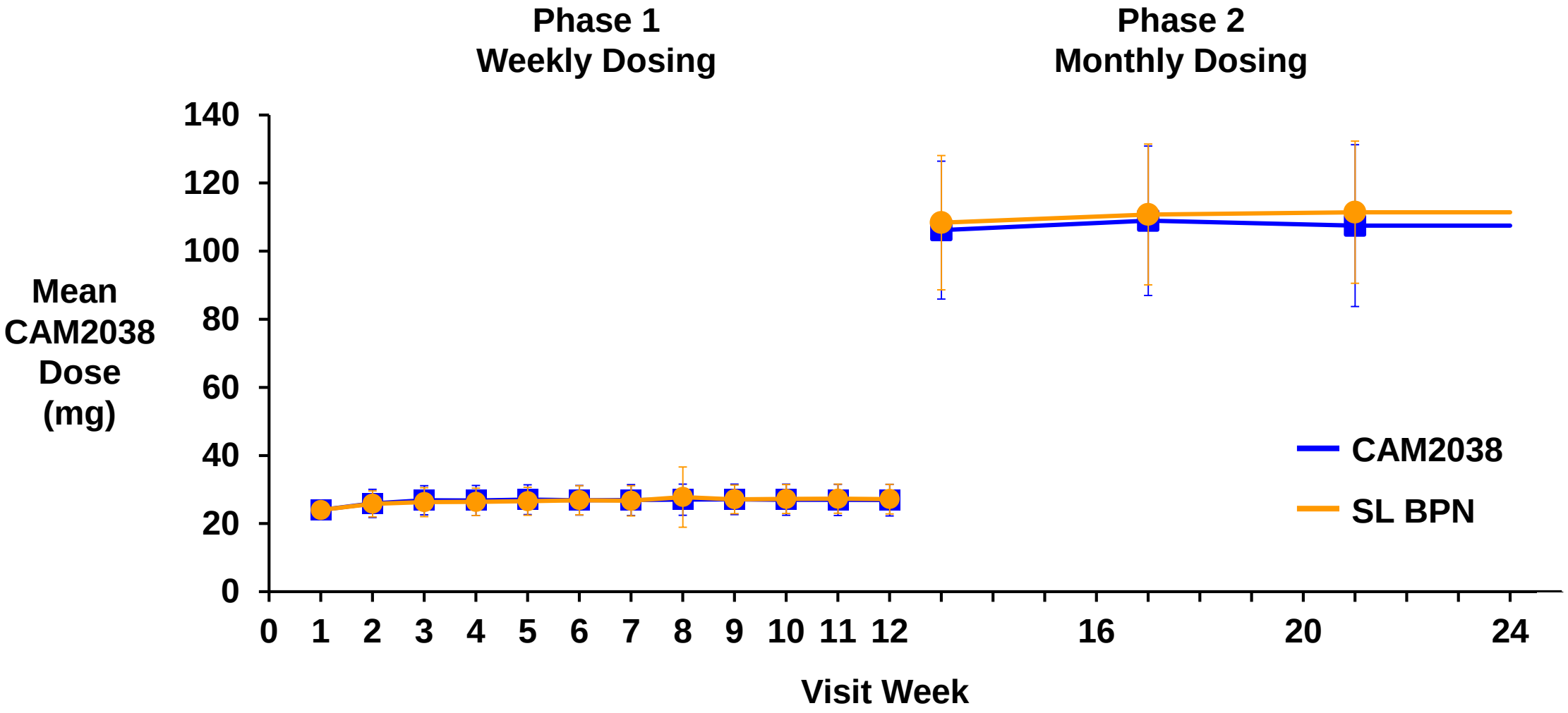
Study 421: Clinical Design



Sublingual Buprenorphine/Naloxone: Active Comparator

- Effective OUD treatments are available
- High risk of failure and predictable poor outcomes for patients on placebo
- Active treatment provides more rigorous comparison

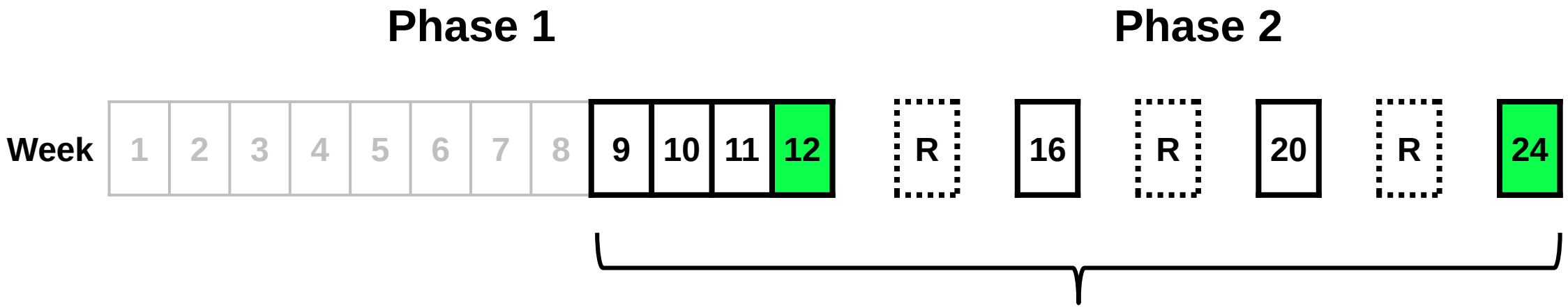
Mean CAM2038 Equivalent Doses by Visits: Doses Similar in SL BPN and CAM2038 Groups



Study 421: Key Inclusion and Exclusion Criteria

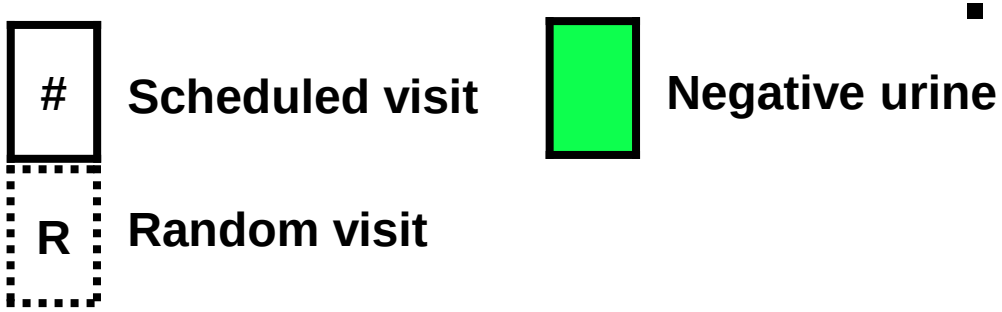
- Inclusion
  - 18 to 65 years of age
  - Moderate or severe OUD
  - Voluntarily sought treatment for disorder
  - Had not received medication-assisted treatment within 60 days prior to randomization
- Exclusion
  - Required opioid treatment for chronic pain

Study 421 Primary Endpoint: Non-Inferiority of Responder Rate



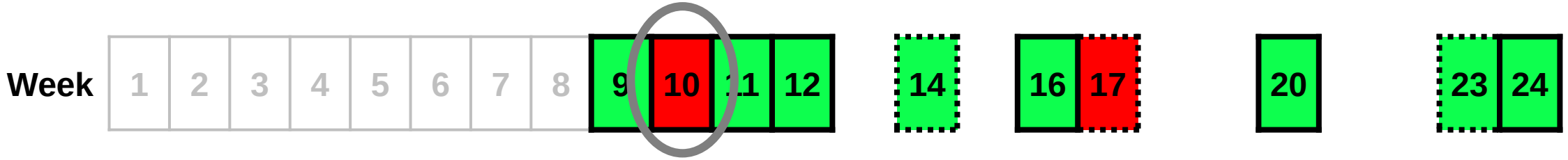
Responder

- 8 of 10 (80%) negative urine samples from Weeks 9 – 24
- Weeks 12 and 24 urine samples must be negative
- Urine samples verified by self-report

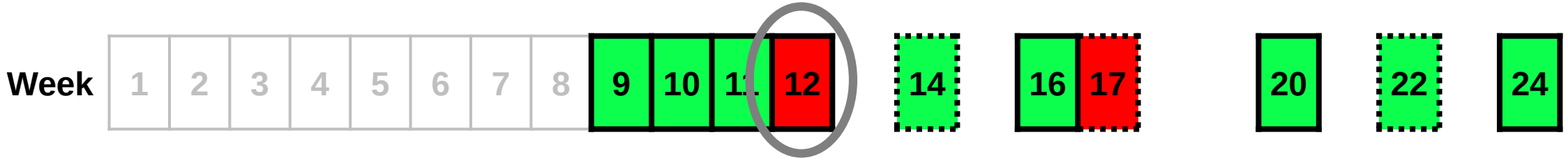


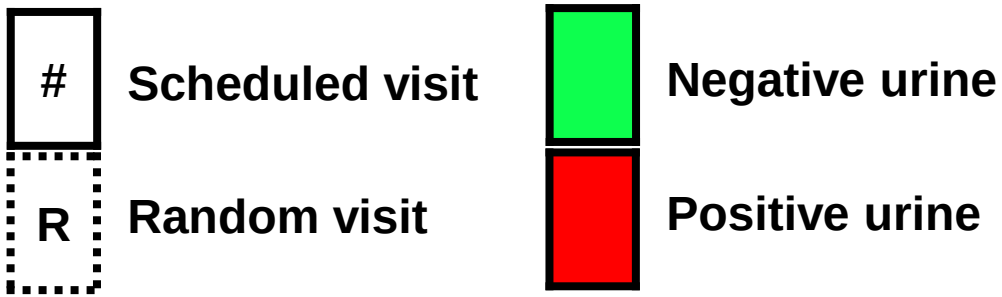
Study 421:
Examples of Responder and Non-Responder

RESPONDER



NON-RESPONDER





Study 421:
Secondary Endpoints Hierarchically Tested

1. Superiority for cumulative distribution function (CDF) of % negative samples, verified by self-report (Weeks 4 – 24)
2. Superiority for responder rate
3. Superiority for time to sustained abstinence
4. Non-inferiority for retention rate with margin of 15%
5. Superiority for retention rate

Study 421: Additional Outcome Measures

- Percentage mean negative urine confirmed with self-report by
  - Study phase
  - Poly-drug use
  - Dose
- Retention rate over time
- Clinical Opiate Withdrawal Scale (COWS)
- Subjective Opiate Withdrawal Scale (SOWS)
- Need-to-use Visual Analogue Scale (VAS)
- Desire-to-use VAS

Study 421: Demographics Balanced Between Groups

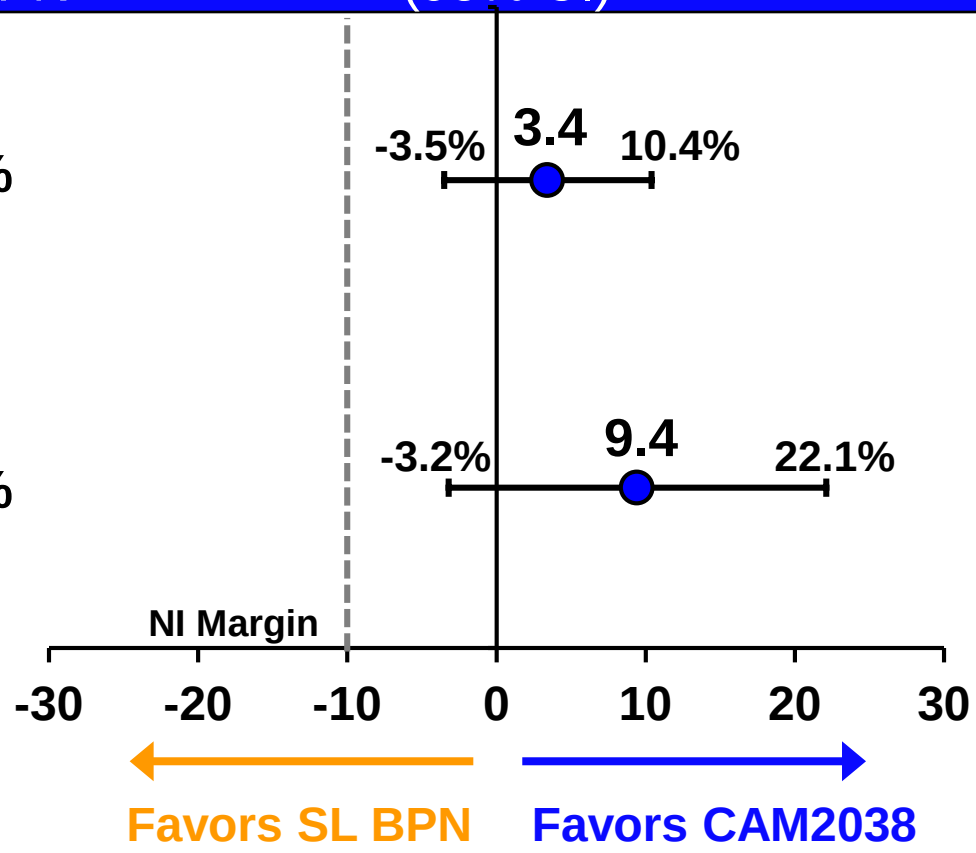
	CAM2038 N=213	SL BPN N=215
Mean age (years)	39	38
Sex (male)	66%	57%
Race		
White	75%	76%
Black or African American	22%	22%
Other	3%	1%
Education		
Did not complete high school	17%	17%
High school diploma	39%	37%
> High school education	46%	45%
Unemployed	54%	56%

Study 421 Included Unstable Patients, Reflecting Real-World OUD Population

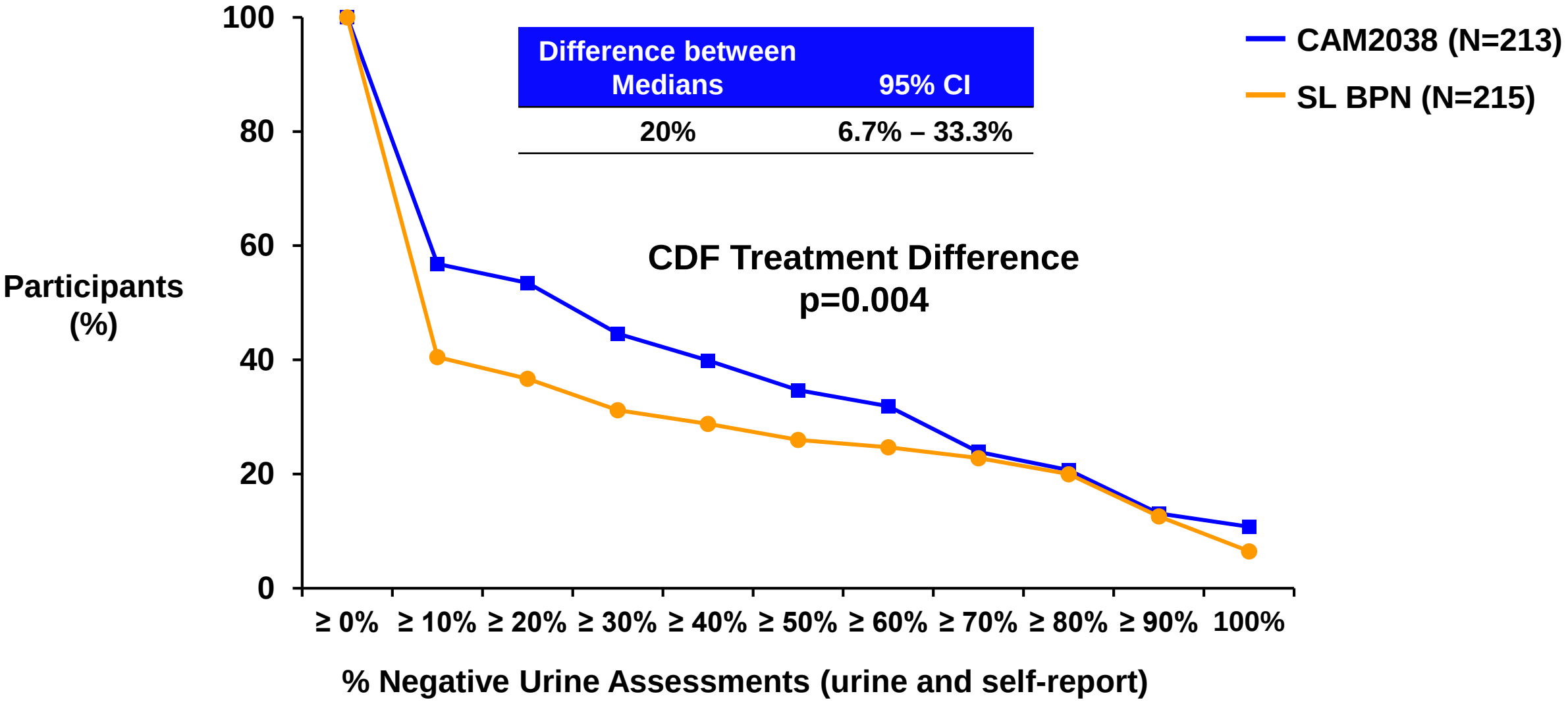
	CAM2038 N=213	SL BPN N=215
Primary opioid of use at initiation		
Heroin	71%	70%
Prescription opioids	29%	30%
Injection opioid use	54%	51%
Fentanyl use	29%	23%
Total non-opioid drug use at screening	73%	69%
Amphetamine	18%	15%
Benzodiazepine	14%	16%
Cocaine	25%	25%
Marijuana	27%	30%
Need-to-use VAS score (0 – 100), mean (SD)	77 (25.4)	76 (24.9)
Desire-to-use VAS score (0 – 100), mean (SD)	77 (26.2)	77 (25.4)
COWS score (0 – 48), mean (SD)	12 (5.4)	12 (6.0)
SOWS score (0 – 64), mean (SD)	32 (15.4)	31 (16.1)

Study 421 Primary Endpoint Met: CAM2038 Non-Inferior to Daily SL BPN for Responder Rate

	Response Rate CAM2038 vs. SL BPN	Treatment Difference (95% CI)	Non-Inferiority p-value
Primary Endpoint: Missing data imputed as positive urine sample for illicit opioids	**17.8% vs. 14.4%**	3.4 (-3.5%, 10.4%)	**< 0.001**
Sensitivity Analysis: No missing data imputed	**35.6% vs. 26.2%**	9.4 (-3.2%, 22.1%)	**< 0.001**



Study 421: CAM2038 Superior to SL BPN for CDF of Percent No Illicit Opioid Use



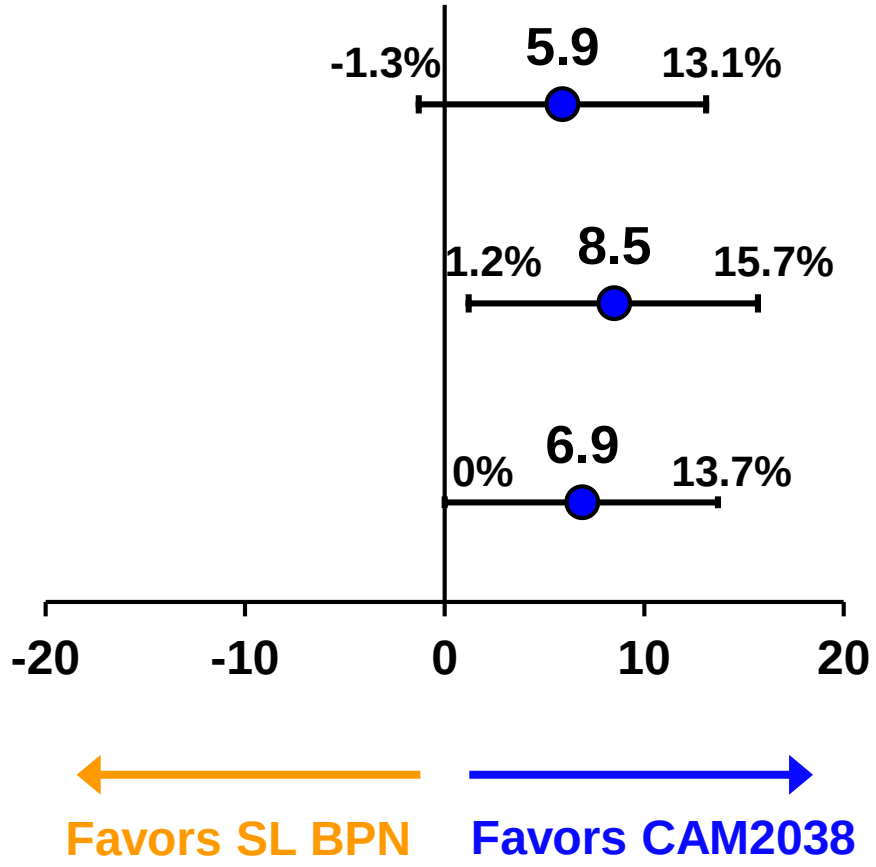
Study 421: Sensitivity Analyses for CDF Demonstrate Superiority with Different Grace Periods

Grace Period	Superiority p-value CDF
0 weeks	0.006
1 week	0.005
3 weeks *(prespecified)*	0.004
4 weeks	0.001
6 weeks	0.001

Efficacy: Study 421 Additional Outcomes

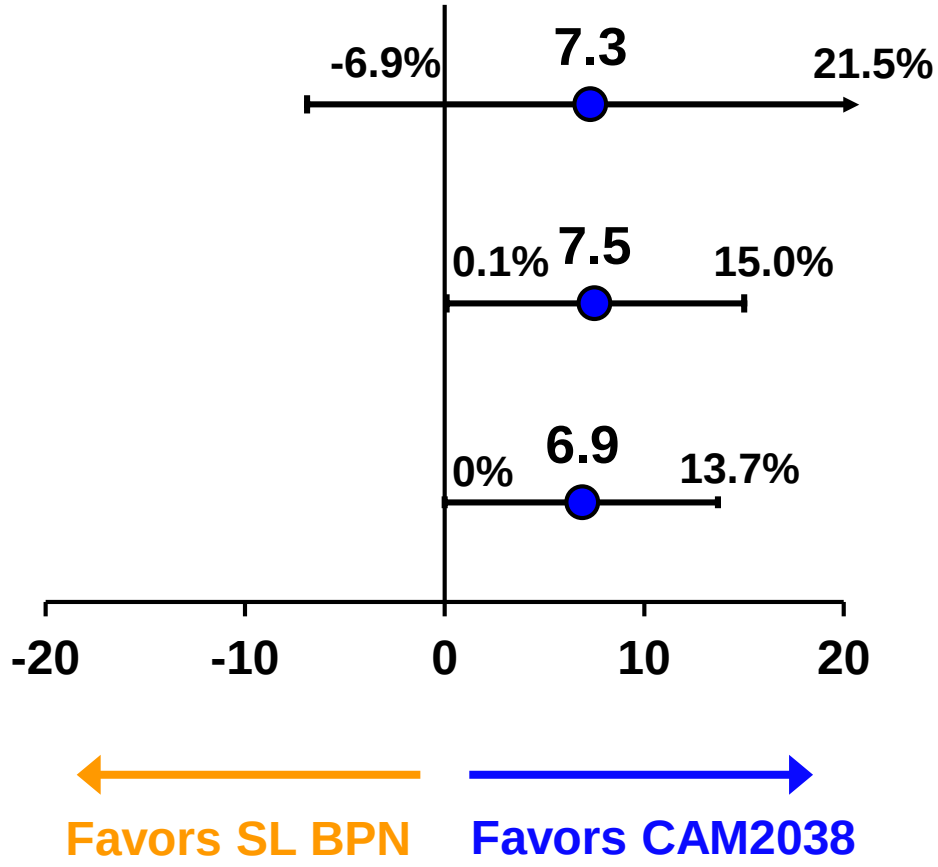
Study 421: Higher Mean % of Negative Urine Samples Verified by Self Report with CAM2038

	% Mean Negative Urine CAM2038 vs. SL BPN	Treatment Difference (95% CI)
Phase 1 (weekly)	35.8% vs. 29.9%	5.9 (-1.3%, 13.1%)
Phase 2 (monthly)	33.9% vs. 25.4%	8.5 (1.2%, 15.7%)
Phase 1 + Phase 2	34.2% vs. 27.4%	6.9 (0%, 13.7%)



Study 421: CAM2038 Effective Across Subpopulations Including Poly-Drug Users

	% Mean Negative Urine CAM2038 vs. SL BPN	Treatment Difference (95% CI)
No poly-drug use	46.9% vs. 39.6%	7.3 (-6.9%, 21.5%)
Poly-drug use*	29.5% vs. 22.0%	7.5 (0.1%, 15.0%)
Total Population	34.2% vs. 27.4%	6.9 (0%, 13.7%)



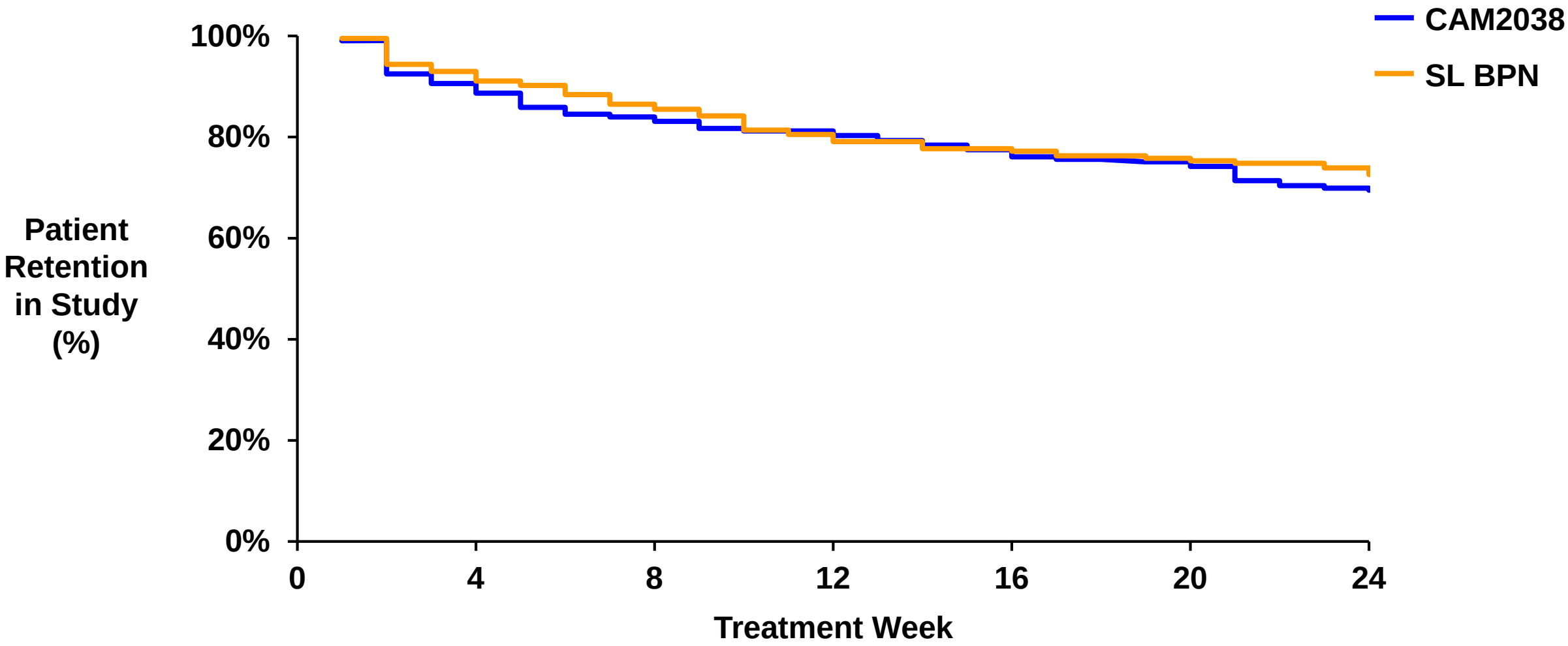
*Cocaine, benzodiazepines, marijuana, methamphetamines, barbiturates, phencyclidine

Study 421:
Percentage of Negative Urine Samples by Dose

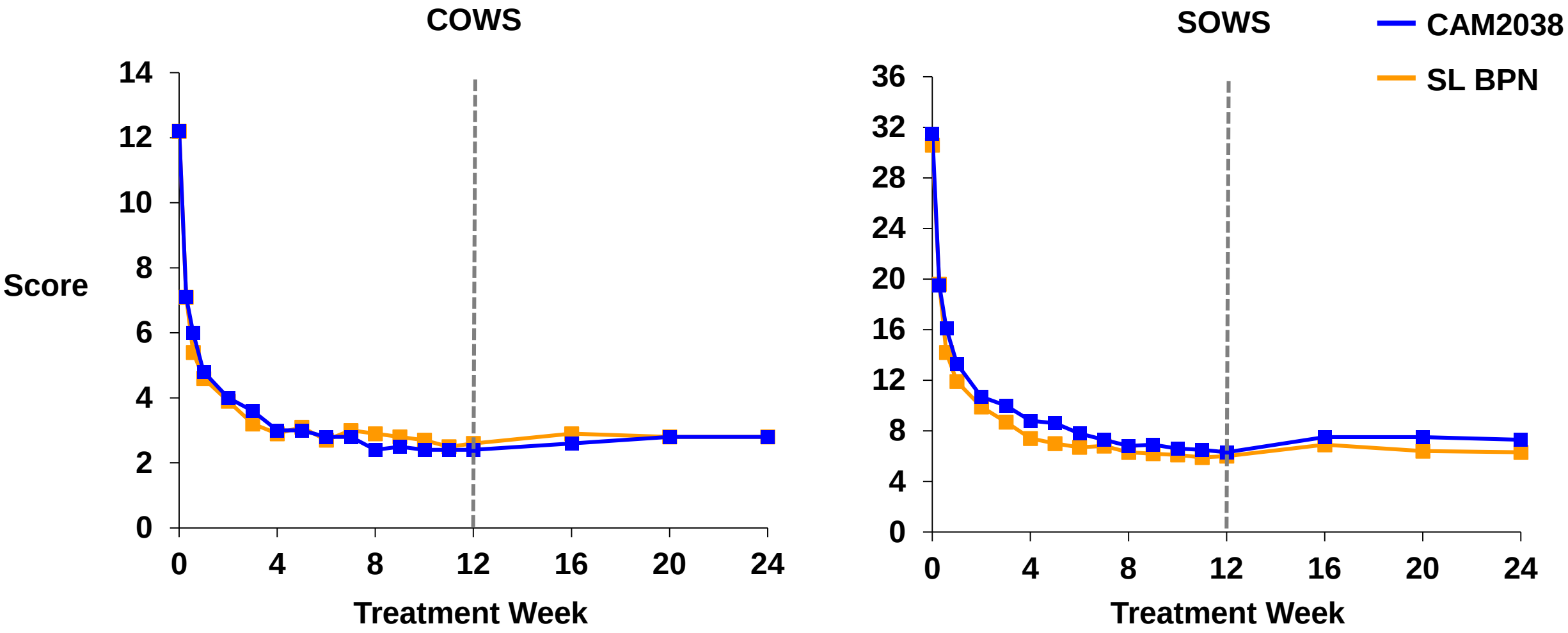
CAM2038	CAM2038 Dose	# Urine Assessments	% Negative Urine
Phase 1 q1w	16 mg	67	56.7
	24 mg	1006	42.7
	32 mg	687	53.9
Phase 2 q4w	64 mg	50	66.0
	96 mg	413	54.2
	128 mg	266	54.1
	160 mg	26	50.0

Urine assessments = urine samples verified by self-reports
Safety Population

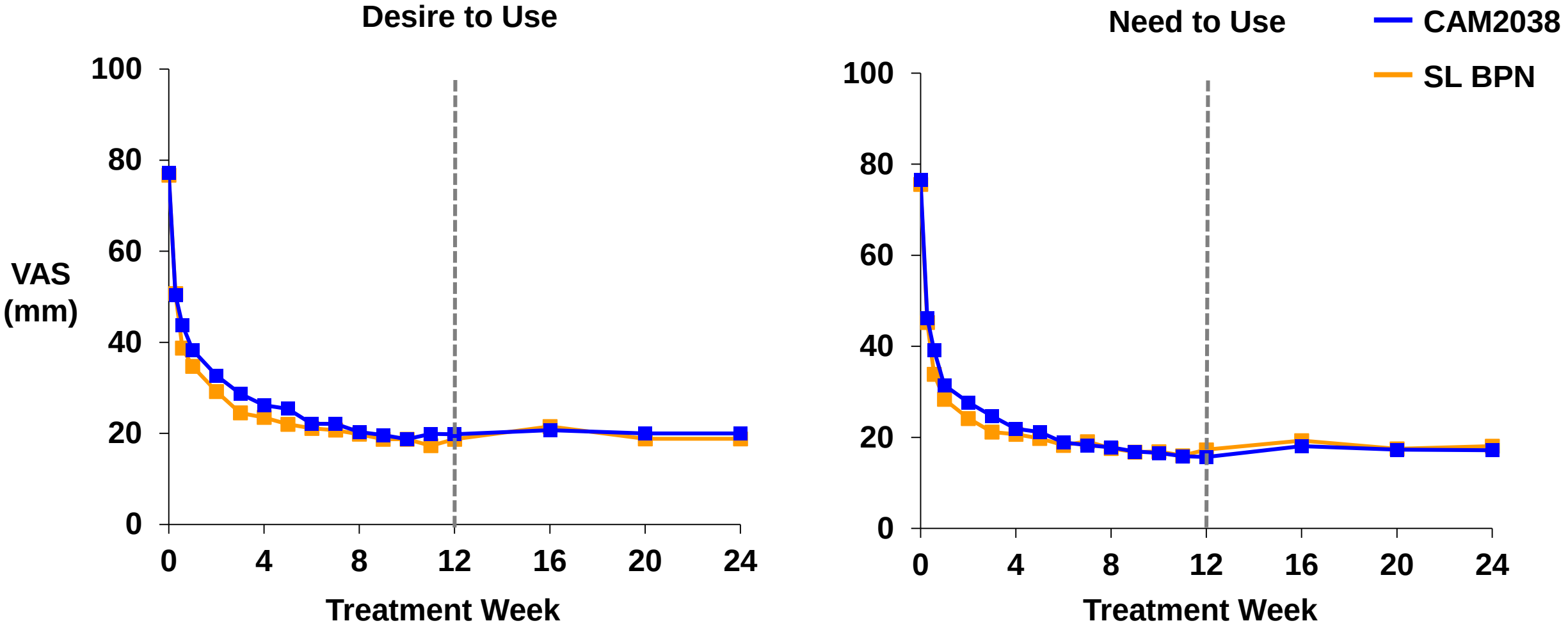
Study 421:
71% Treatment Retention at 24 Weeks



Study 421: Suppression of Withdrawal Signs and Symptoms as Measured by COWS and SOWS



Study 421: Opioid Cravings Suppressed for Duration of Study as Measured by Visual Analogue Scale (VAS)



CAM2038 is a Beneficial Treatment for OUD

- Demonstrated opioid blocking effect ≥ 1.2 ng/mL (Study 478)
- Non-inferior to SL BPN for responder rate across Phase 1 (weekly) and Phase 2 (monthly)
- Superior to SL BPN for CDF of opioid negative urines

Safety

Study 421: Summary of Adverse Events (AEs)

Category	CAM2038 N=213	SL BPN N=215
Patients with at least 1 AE	60%	55%
Severity		
Mild	48%	45%
Moderate	28%	31%
Severe	3%	7%
Patients with at least 1 SAE	2%	6%
Patients with at least 1 AE leading to discontinuation	3%	1%
Deaths	0.5%*	0%

*1 patient, pedestrian hit by car

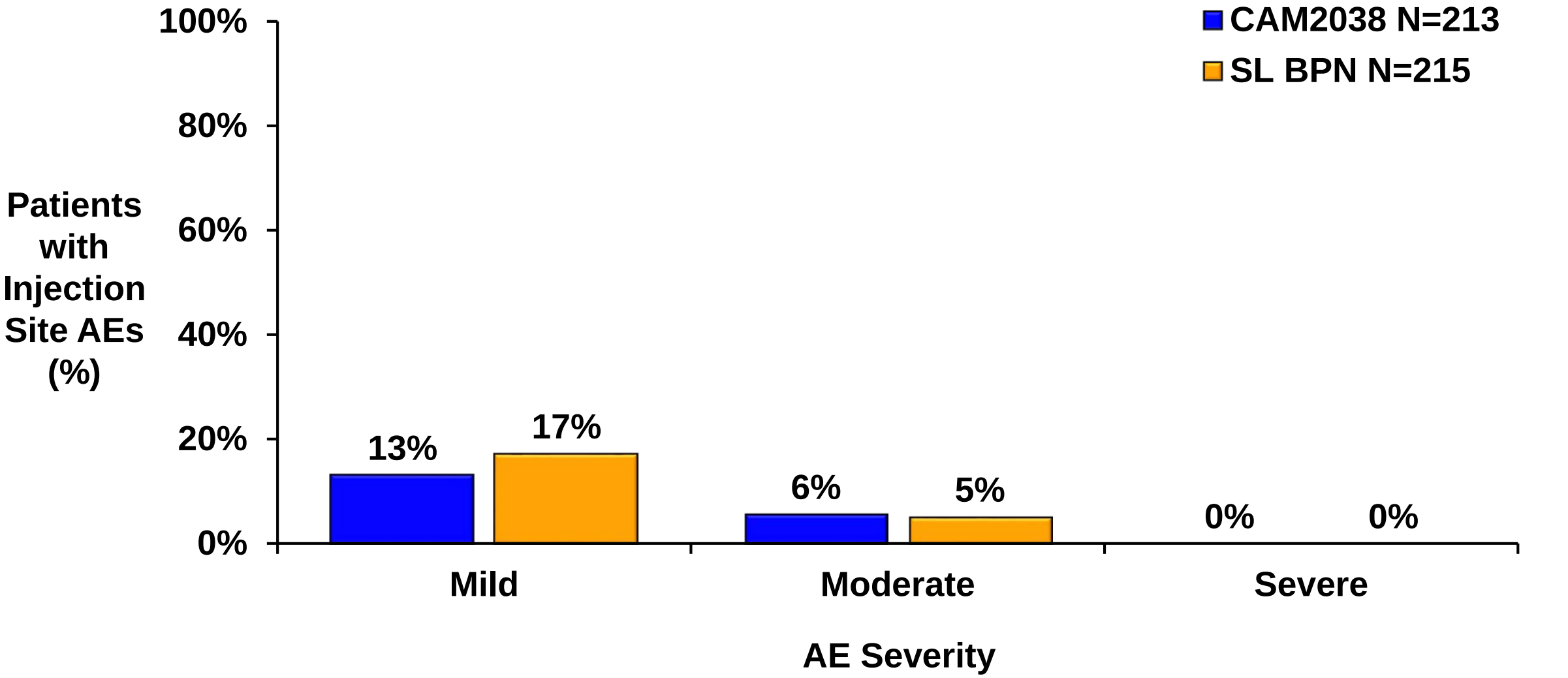
Study 421: Common Non-Injection Site AEs ≥ 3% in Either Treatment Group

Preferred Term	CAM2038 N=213	SL BPN N=215
Headache	7.5%	7.9%
Constipation	7.5%	7.4%
Nausea	7.0%	7.9%
Insomnia	5.6%	2.8%
Urinary tract infection	5.2%	4.7%
Upper respiratory tract infections	4.2%	4.2%
Vomiting	4.2%	3.7%
Anxiety	2.8%	3.3%
Diarrhea	2.8%	3.3%
Toothache	1.4%	3.7%
Arthralgia	1.4%	3.3%
Cellulitis	0.5%	3.3%

Study 421: Injection Site AEs > 2%

Preferred Term	CAM2038 N=213	SL BPN N=215
Patients with at least 1 injection site reaction	19%	22%
Pain	9%	8%
Pruritus	6%	6%
Erythema	6%	6%
Reaction	4%	3%
Swelling	4%	3%
Induration	2%	3%
Inflammation	1%	4%

Study 421: CAM2038 Well-Tolerated with Low Frequency of Injection Site Adverse Events



Study 421: Serious Adverse Events (SAEs)

Preferred Term	CAM2038 N=213	SL BPN N=215
Overall SAE	2.3%	6.0%
Road traffic accident	0.5%	0
Suicidal ideation	0.5%	0.5%
Vomiting	0.5%	0
Non-cardiac chest pain	0.5%	0
Accidental overdose	0	1.4%
Intentional overdose	0	0.5%
Acute hepatitis C	0	0.5%
Pneumonia	0	0.5%
Bipolar disorder	0	0.5%
Substance-induced mood disorders	0	0.5%
Hemophilia	0	0.5%
Seizure	0	0.5%
Abscess limb	0	0.5%
Cellulitis	0	0.5%
Localized infection	0	0.5%
Osteomyelitis	0	0.5%
Sepsis	0	0.5%
Subcutaneous abscess	0	0.5%

Study 421 Safety Consistent with SL BPN

- Safety profile consistent with known profile of SL BPN and CAM2038 route of administration
- No unexpected safety findings

Study 499: Long-Term Study

Open-label, 48-week safety study

Study 499: Long-Term Safety Data

	CAM2038 N=227	
	n	%
Patients with at least 1 AE	143	63%
Patients with at least 1 related AE	60	26%
Patients with at least 1 SAE	12	5%
Patients with at least 1 AE leading to discontinuation	3	2%
Deaths	0	0%
Injection site AEs	46	20%

Study 499: AEs Occurring ≥ 5% of Patients

Preferred Term	CAM2038 N=227	
	n	%
Patients with at least 1 AE	143	63%
Injection site pain	35	15%
Injection site swelling	27	12%
Injection site erythema	21	9%
Headache	18	8%
Nasopharyngitis	18	8%
Nausea	16	7%
Urinary tract infection	12	5%
Vomiting	12	5%

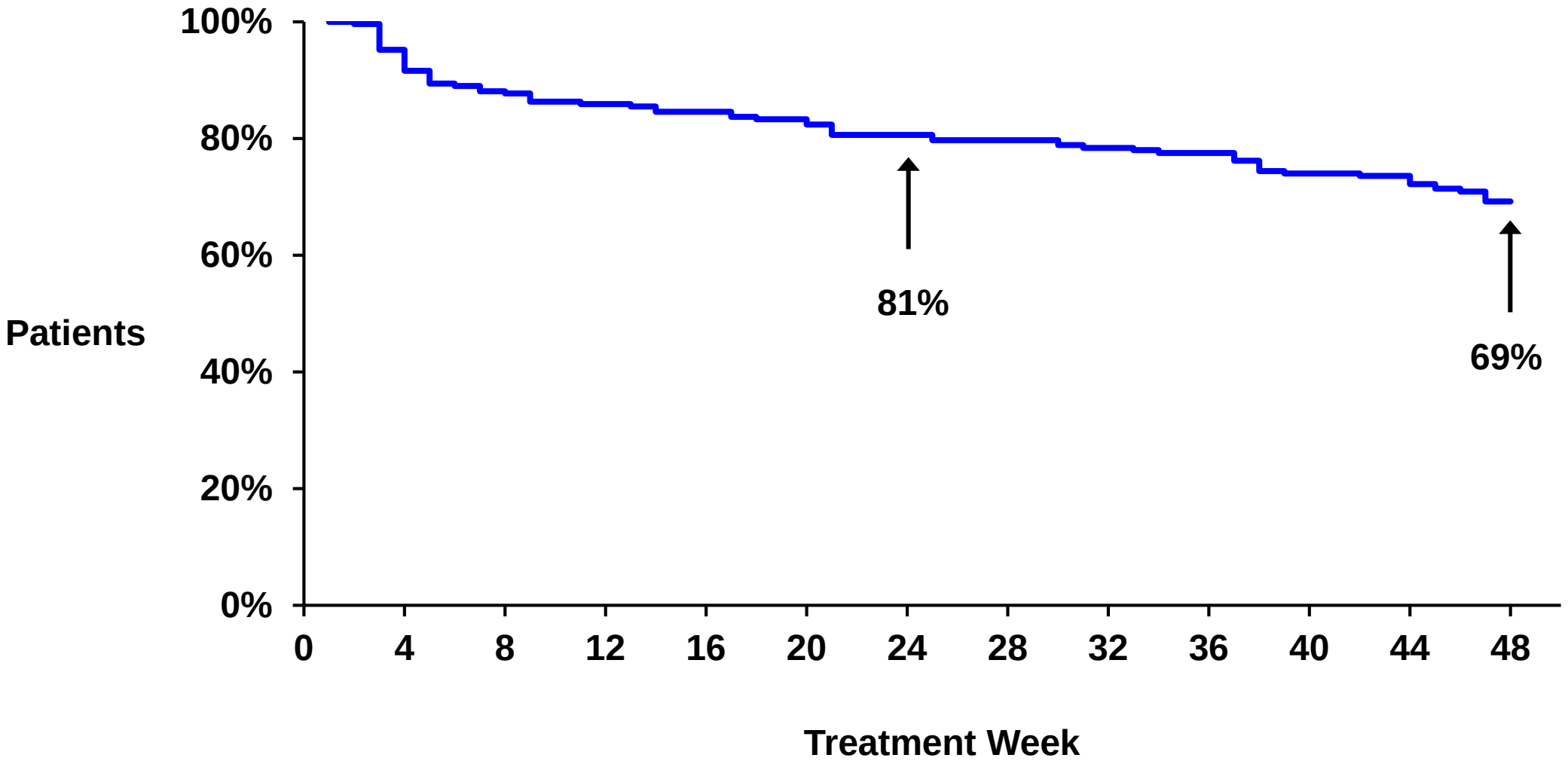
Safety Population

Pooled Analysis of Exposures from Studies ≥ 12 Weeks for CAM2038 vs. SL BPN

	CAM2038				SL BPN	
	32 mg (q1w) N=175		160 mg (q4w) N=48		24 mg (daily) N=89	
Number of patients with at least one	n	%	n	%	n	%
AEs	98	56%	25	52%	52	58%
Non-Injection Site AEs	85	49%	23	48%	46	52%
Injection Site AEs	33	19%	4	8%	18	20%

Safety Population
Studies 421, 499, 549

Study 499:
High Treatment Retention at 24 and 48 Weeks



N=227

Minimizing Risk of Accidental or Intentional IV Administration

Proposed REMS

Goals

- Mitigate risk of accidental or intentional IV administration
- Ensure CAM2038 only dispensed and administered in healthcare settings by HCP

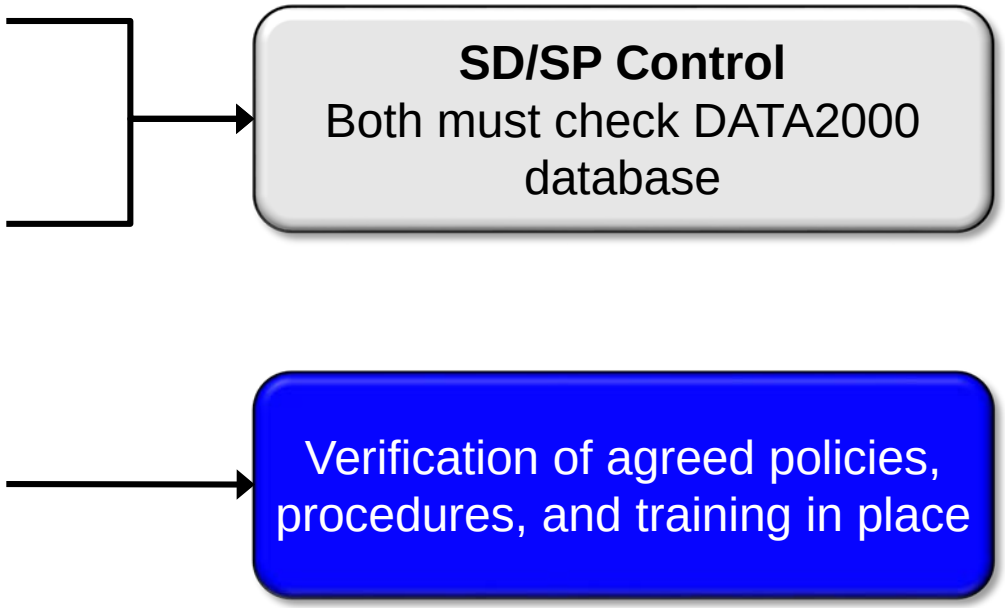
Elements to Assure Safe Use

- Educate prescribers, pharmacists and patients regarding risks
- Controlled distribution system

Ensure Patient Access

Controlled Distribution and Access

- Controlled shipment of CAM2038 to qualified healthcare settings
  - **HCP office (DATA 2000 waived only)**
    - Specialty Distributor delivery to HCP office: Buy and Bill
    - Specialty Pharmacy delivery to HCP office for named patient
  - **Hospitals/Healthcare Facilities**
    - For HCP administration only



Summary

- Comparable safety profile to well-established BPN
- Mild to moderate injection site reactions
- Restricting administration to healthcare professionals
  - Controlled distribution system
- CAM2038 provides an effective treatment from day 1 and similar safety profile to SL BPN

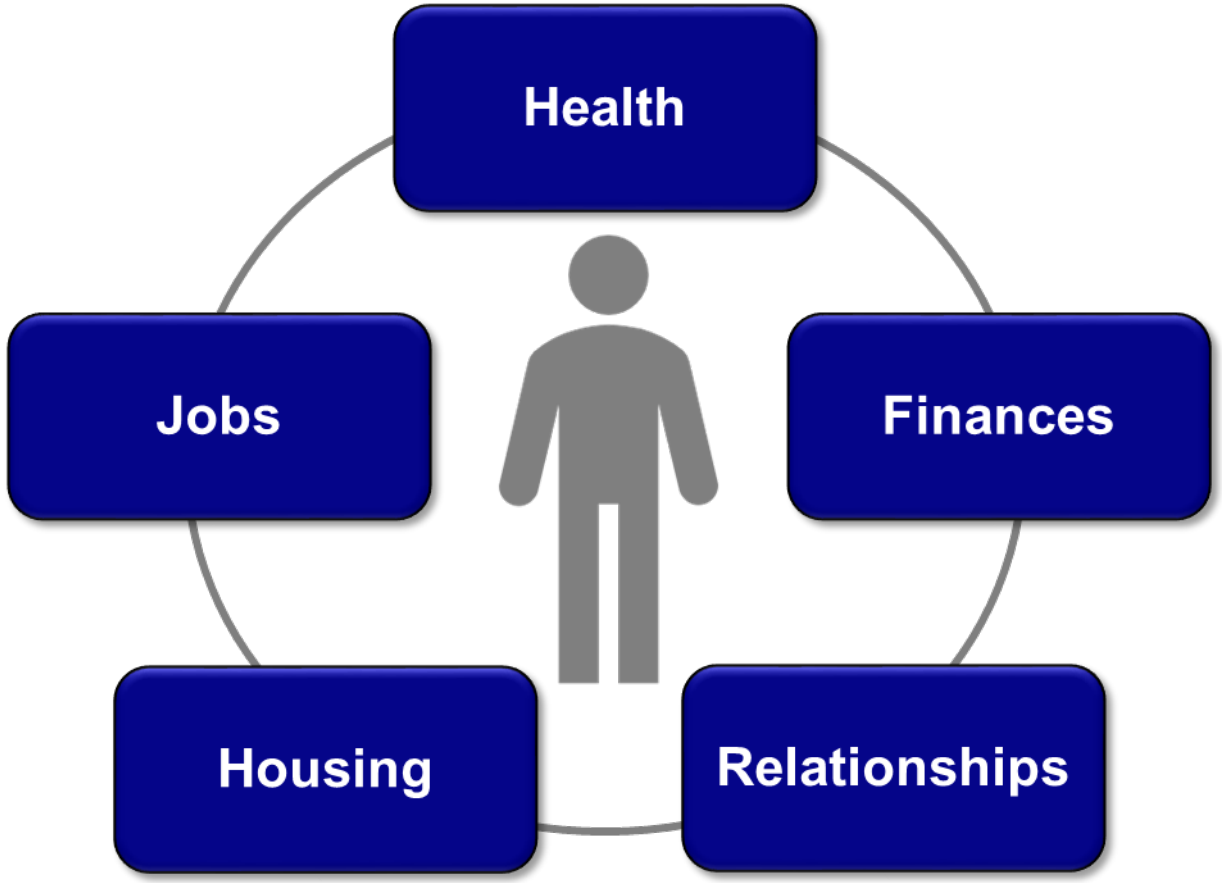
Clinical Perspective

Michael Frost, MD, FACP, FASAM, CMRO

President/Medical Director
Frost Medical Group, LLC

Assistant Professor, Psychiatry
Drexel University, College of Medicine

Opioid Use Disorder: Complex, Chronic and, Potentially Fatal Brain Disease



Treatment Success May Differ From Patient to Patient

- Success takes into account more than urine toxicology
  - Example: patient enters treatment using illicit opioids every day, now only uses 1/week = clinical improvement
- Effective treatments allow patients to improve in other aspects of their illness
  - Medication adherence
  - Building of therapeutic relationships
  - Stabilization of psychosocial factors

Relatively Few Treatment Options for Patients with OUD

- Buprenorphine is one of best OUD treatments
- Changed clinical landscape
  - Effective and safe treatment to an office-based setting
- Used in clinical practice for past 15 years
- Patients often remaining on treatment indefinitely
- Addiction medicine specialists familiar with buprenorphine's benefit-risk profile

Buprenorphine Beneficial Compound but Current Sublingual Formulations have Limitations

- Treatment adherence with sublingual buprenorphine problematic[1-3]
  - Easy to forget or to decide not to take
  - Can lead to relapse
- Risk of overdose/abuse when a patient self-administers medication
- Unused tablets or films sold, stolen or shared
- Can be accidentally ingested by children[4-5]
- Barriers to use
  - Challenge of sublingual formulation
  - Discrimination and stigma around use of daily dosed buprenorphine encountered by both patients and providers

1. Lofwall, 2014; 2. CDC, 2013; 3. Toce, 2017; 4. CDC, 2010-2011; 5. MMWR Morb Mortal Wkly Rep., 2013

CAM2038: Novel Formulation of Buprenorphine With Benefits for Providers

HCP Administered

- Intended dose
- Adherence
- Limits risk of misuse
- Limits risk of diversion

Multiple Weekly and Monthly Doses

- Titrate up/down
- Lowest effective dose
- Maintain schedule

Maintains Common Treatment Strategies

- Similar initiation strategy
- 24 mg CAM2038 or 8 mg + 16 mg SL BPN

CAM2038 Benefits for Patients

Convenience

- Don’t need to remember to take medication daily
- Travel without packing medication

Reassurance

- Cannot run out early
- Cannot be misplaced or stolen
- Limit pediatric exposure

Psychological Benefit

- Reduce daily reminder of OUD
- Removed from active addiction

CAM2038 Favorable Benefit-Risk Profile

- Compared to sublingual buprenorphine, CAM2038
  - Non-inferior in response rate
  - Superior in reducing overall use of illicit opioids
- Well-tolerated safety profile
- Study 499 confirms long-term safety of CAM2038

CAM2038 for Treatment of Opioid Use Disorder

November 1, 2017

Braeburn Pharmaceuticals, Inc.

Joint Meeting of the Psychopharmacologic Drugs and Drug Safety and Risk Management Advisory Committees

Backup Slides Shown

Table 5: Proposed Transfer from Daily Doses of SL BPN to Initial Weekly or Monthly Doses of CAM2038 Q1w or CAM2038 Q4w

Dose of daily SL BPN	Dose of CAM2038 q1w
2-6 mg	8 mg
8-10 mg	16 mg
12-16 mg	24 mg
18-24 mg	32 mg
Dose of daily SL BPN	**Dose of CAM2038 q4w**
8-10 mg	64 mg
12-16 mg	96 mg
18-24 mg	128 mg
26-32 mg	160 mg

Abbreviation: SL BPN, sublingual buprenorphine

Source: Extracted from Summary of clinical pharmacology, Table 28

Study 421: Doses Achieved in Phase 1 & Phase 2

	CAM2038 N=213			SL BPN N=215		
Phase	Dose	n	%	Dose	n	%
Phase 1	16 mg	21	9.9%	8 mg	16	7.4%
	24 mg	108	50.7%	16 mg	110	51.2%
	32 mg	84	39.4%	24 mg	89	41.4%
Phase 2	64 mg	7	4.4%	8 mg	3	1.9%
	96 mg	83	52.5%	16 mg	82	51.6%
	128 mg	59	37.3%	24 mg	65	40.9%
	160 mg	9	5.7%	32 mg	9	5.7%

No Unexpected Accumulation Observed Following CAM2038 q1w and q4w

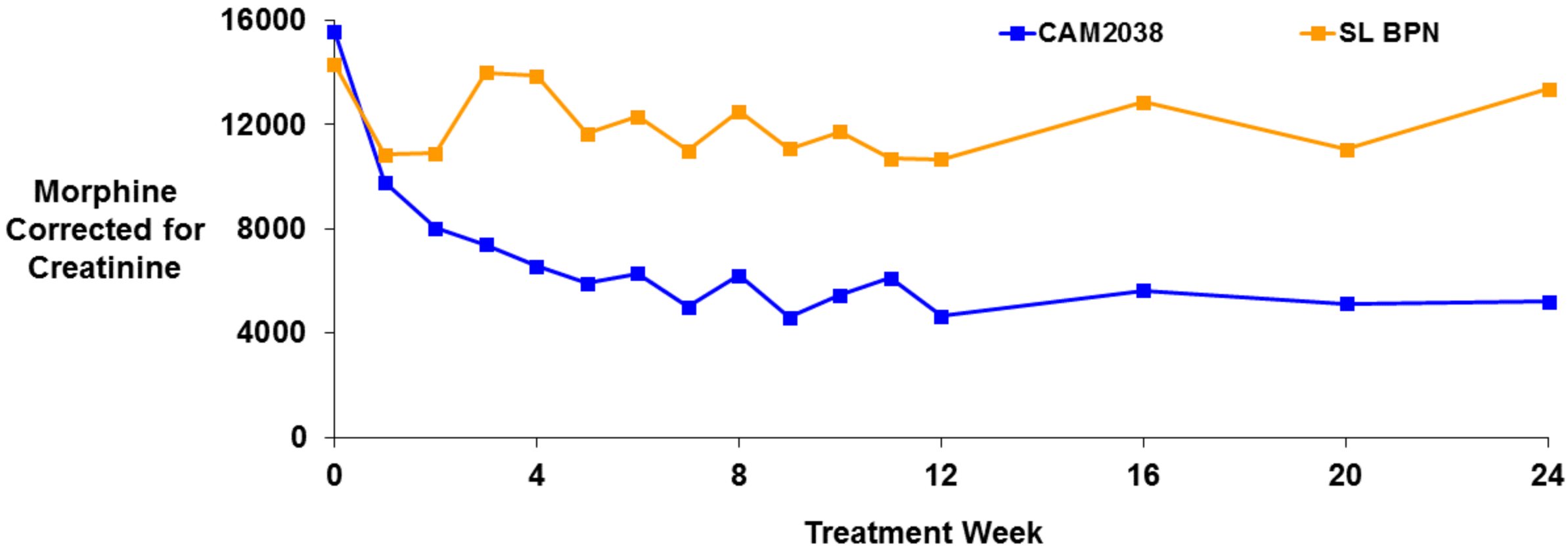
- Moderate accumulation with steady state exposures in the range of 1.4-1.6-times the initial exposure (after first dose)

- Accumulation expected based on the products half-lives and treatment durations
  - $t_{1/2}$=3-5 days for weekly CAM2038 q1w
  - $t_{1/2}$=19-25 days for monthly CAM2038 q4w

Study 421: CAM2038 Effective Across Subpopulations Including Injection Users

	% Mean Negative Urine CAM2038 vs. SL BPN
Injection use	**29.7% vs. 15.9%**
Non injection	**39.5% vs. 39.5%**
Total Population	**34.2% vs. 27.4%**

Study 421: Morphine Corrected for Creatinine



Week	0	1	2	3	4	5	6	7	8	9	10	11	12	16	20	24
CAM2038 (n)	206	191	183	178	168	166	163	164	163	155	157	158	160	147	138	120
SL BPN (n)	211	196	191	191	187	178	174	166	164	159	156	156	153	152	145	133