

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

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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



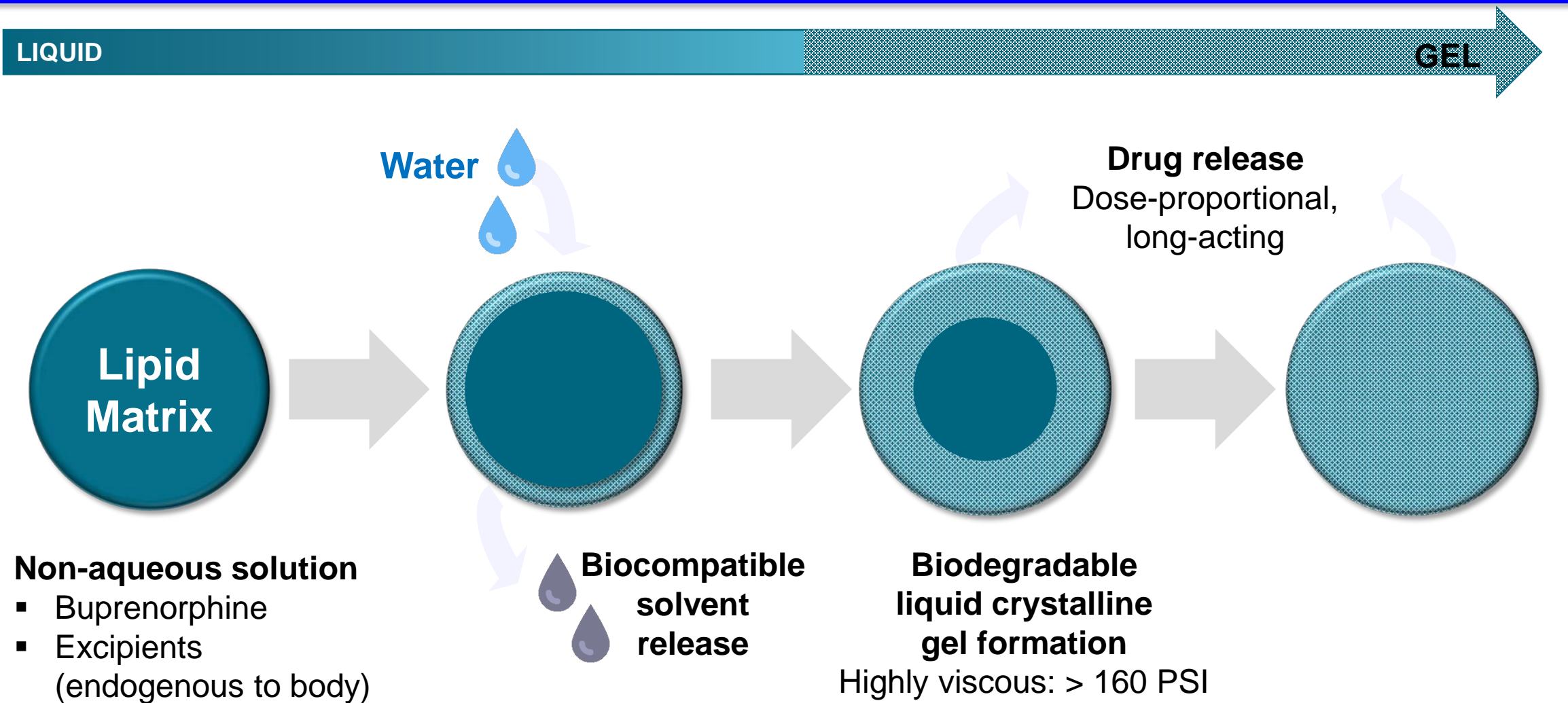
CAM2038 Proposed Indication

- 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



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, 1/2" 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

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

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Psychiatry and Human Behavior
Brown University
- **William Brock, PhD**
Principal
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- **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

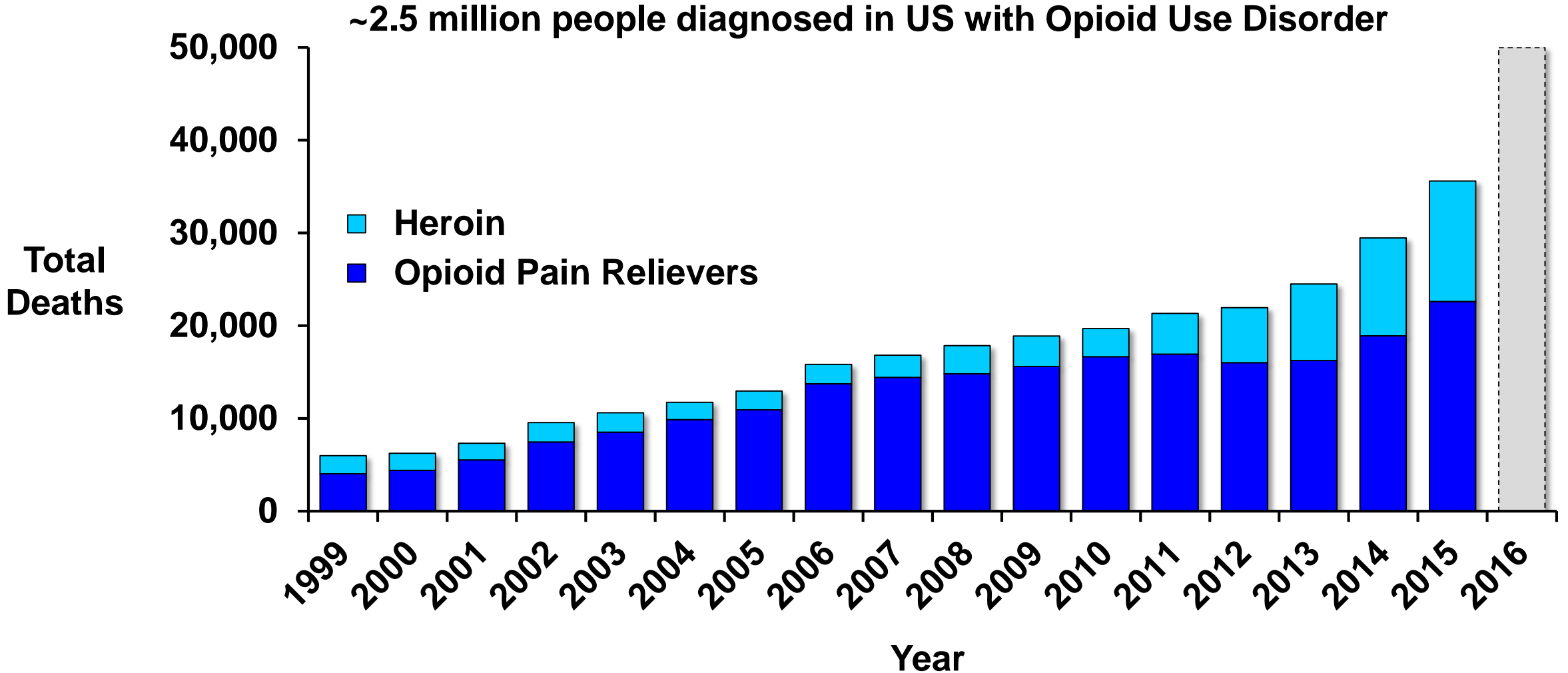
Center on Drug and Alcohol Research

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

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



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

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 2002¹
 - BPN film approved in 2010
 - Sublingual and buccal formulations with increased BPN bioavailability
- Implantable buprenorphine approved in 2015²
 - Clinically stable patients already responsive to transmucosal BPN

Buprenorphine is Well-Established Treatment for Opioid Use Disorder

- Numerous studies show both efficacy and effectiveness¹⁻²
- 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 treatment³⁻⁴

Best Practice Clinical Guidelines Recommend Individualized Therapy

A Treatment
Improvement
Protocol
TIP
40

**Clinical Guidelines for the
Use of Buprenorphine
in the Treatment of
Opioid Addiction**

*“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 ADVISORY
www.samhsa.gov • 1-877-SAMHSA-7 (1-877-726-4727)

Behavioral Health Is Essential To Health • Prevention Works • Treatment Is Effective • People Recover

**SUBLINGUAL AND TRANSMUCOSAL
BUPRENORPHINE FOR OPIOID USE DISORDER:
REVIEW AND UPDATE**

*“**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...”*

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

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 retention¹⁻³
 - Often $\leq 50\%$ after 3 to 6 months
 - Dropout associated with relapse
- Issues of non-adherence⁴⁻⁶
 - 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

Accidental Pediatric Exposure: Death, Hospitalizations and ER Visits

- Pediatric deaths reported due to BPN¹
- 9.5% of emergency visits for drug ingestion among children age ≤ 6 years old were caused by BPN²
- Since 2011, focus to decrease pediatric exposure³⁻⁴
 - Emphasis on safe storage
 - Transition to unit dose packaging
- Some decreases in pediatric exposure but risk remains³⁻⁴

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

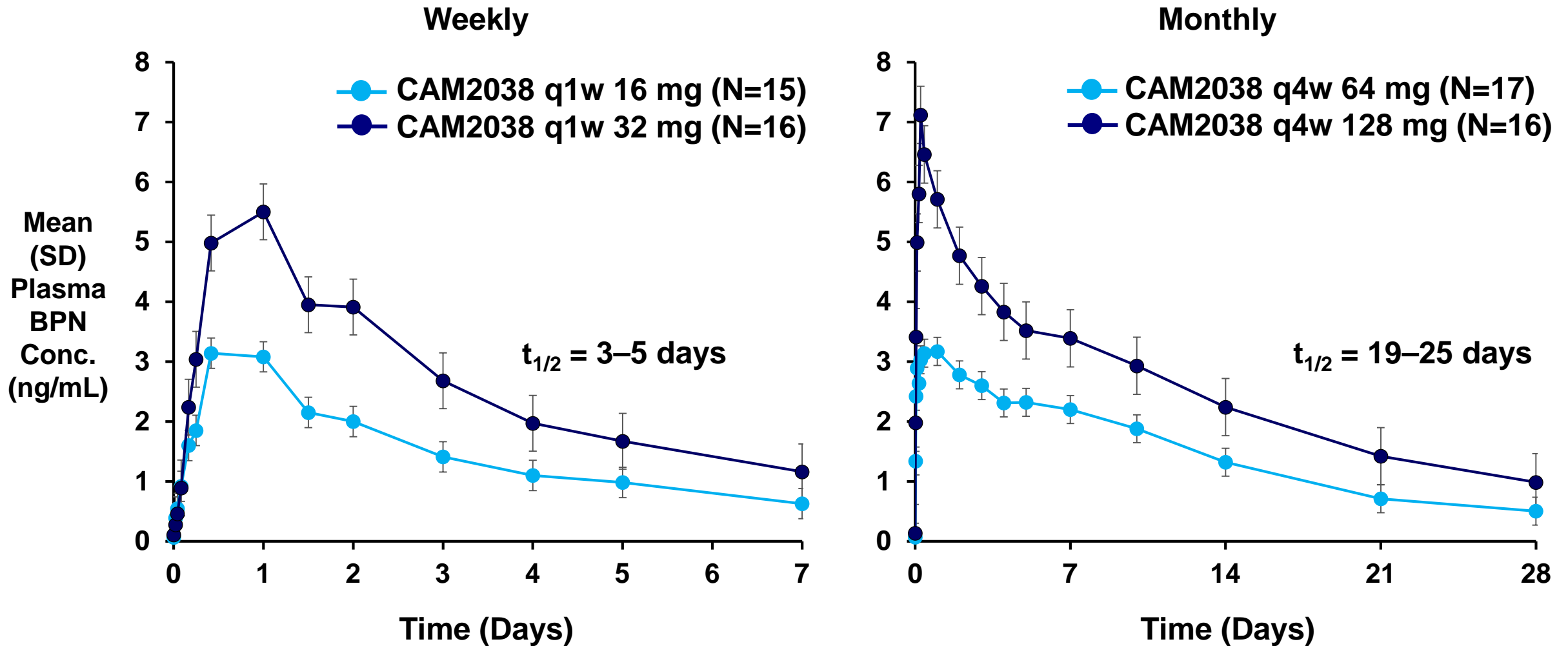
Adjunct Professor of Physical Chemistry

Lund University, Sweden

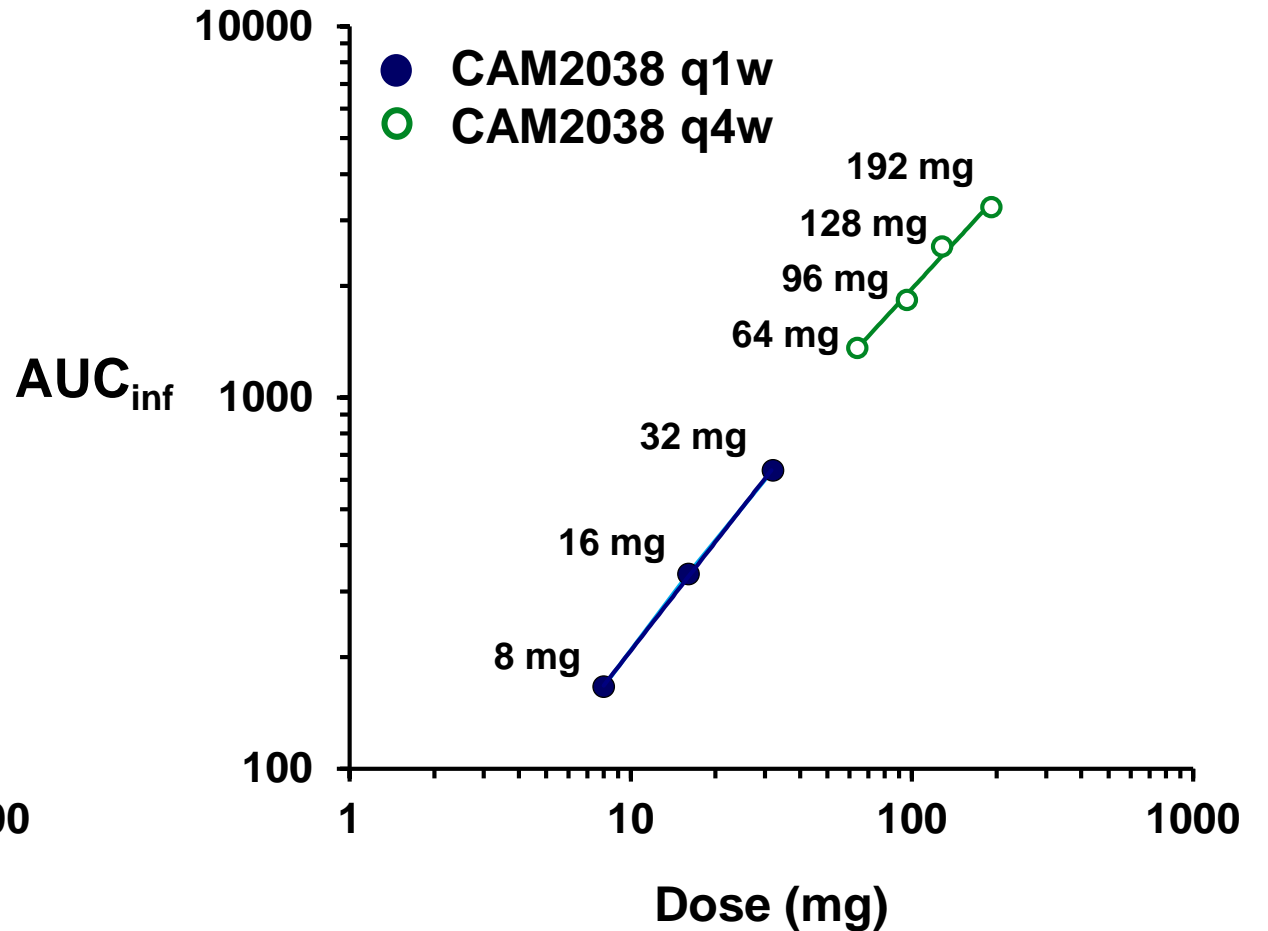
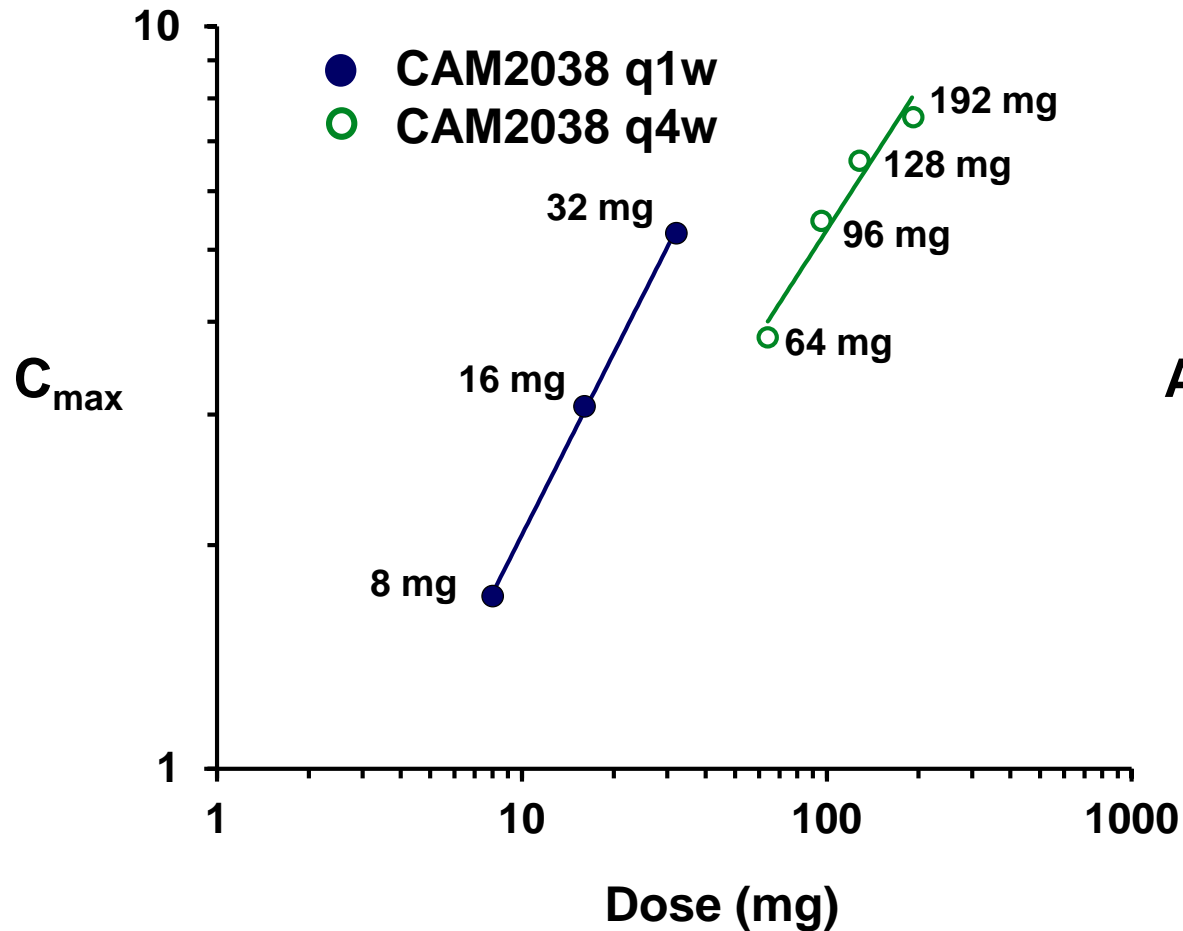
5 Clinical Pharmacokinetic Studies to Support Dosing and Bridging to Sublingual Buprenorphine

- 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

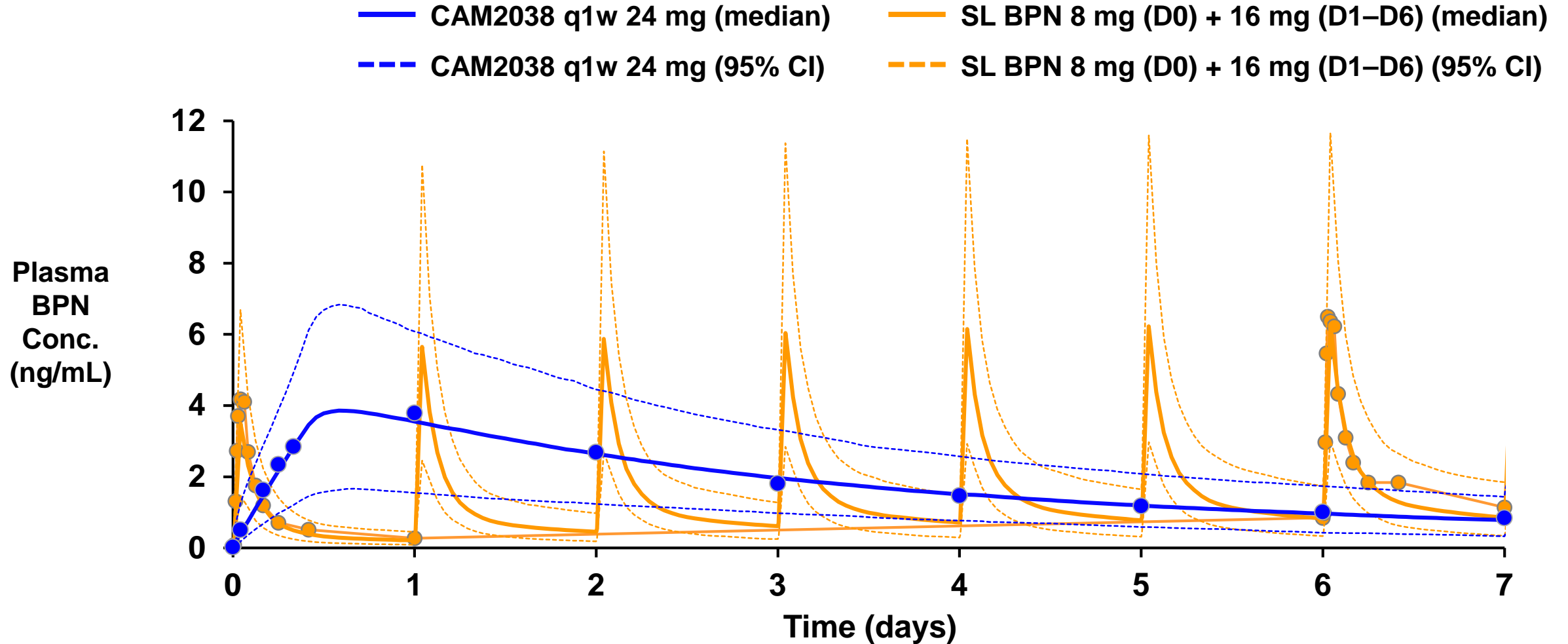
Pharmacokinetic Profiles After Single Dosing of Weekly and Monthly CAM2038 Depots



Dose Proportionality Observed Across CAM2038 Weekly and Monthly Dose-Range

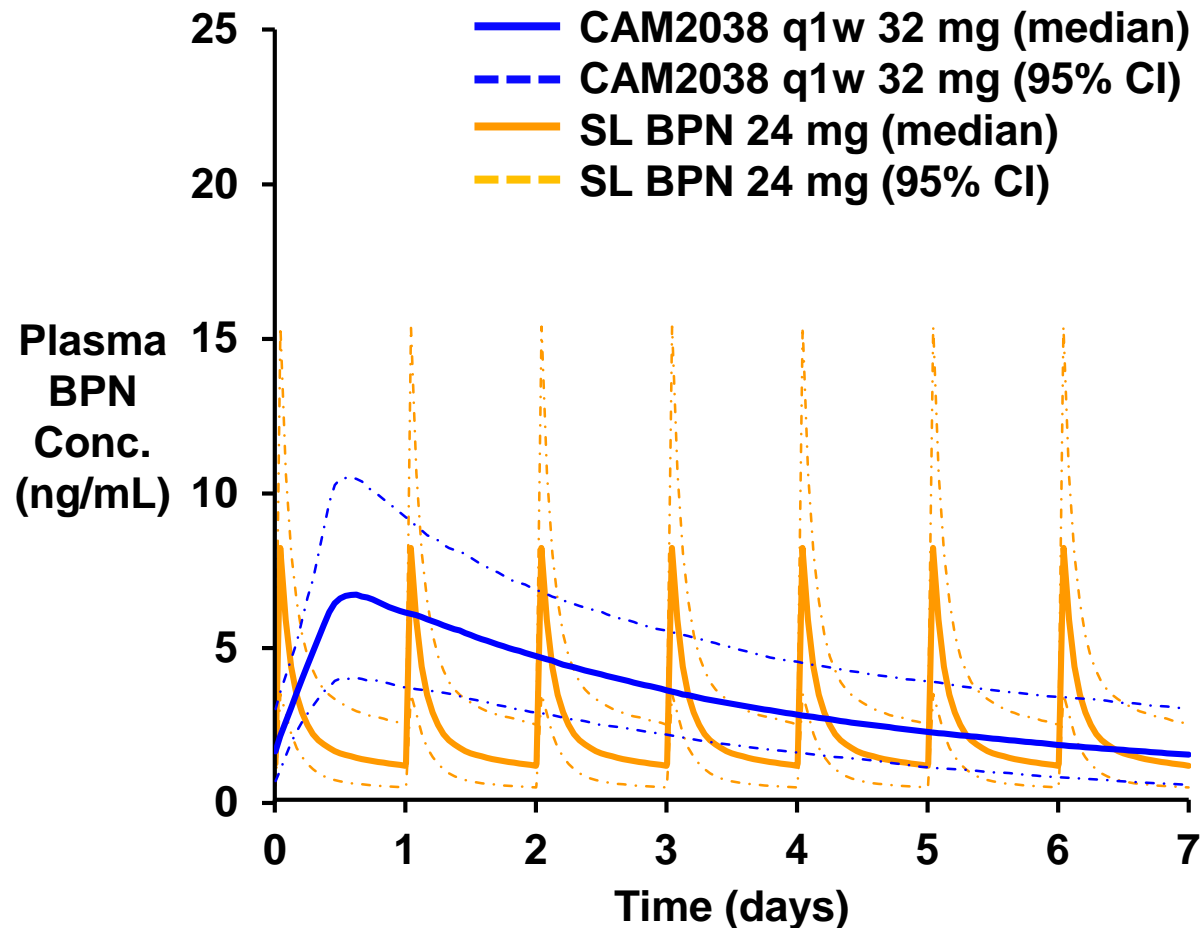


CAM2038 vs. Daily Sublingual Buprenorphine

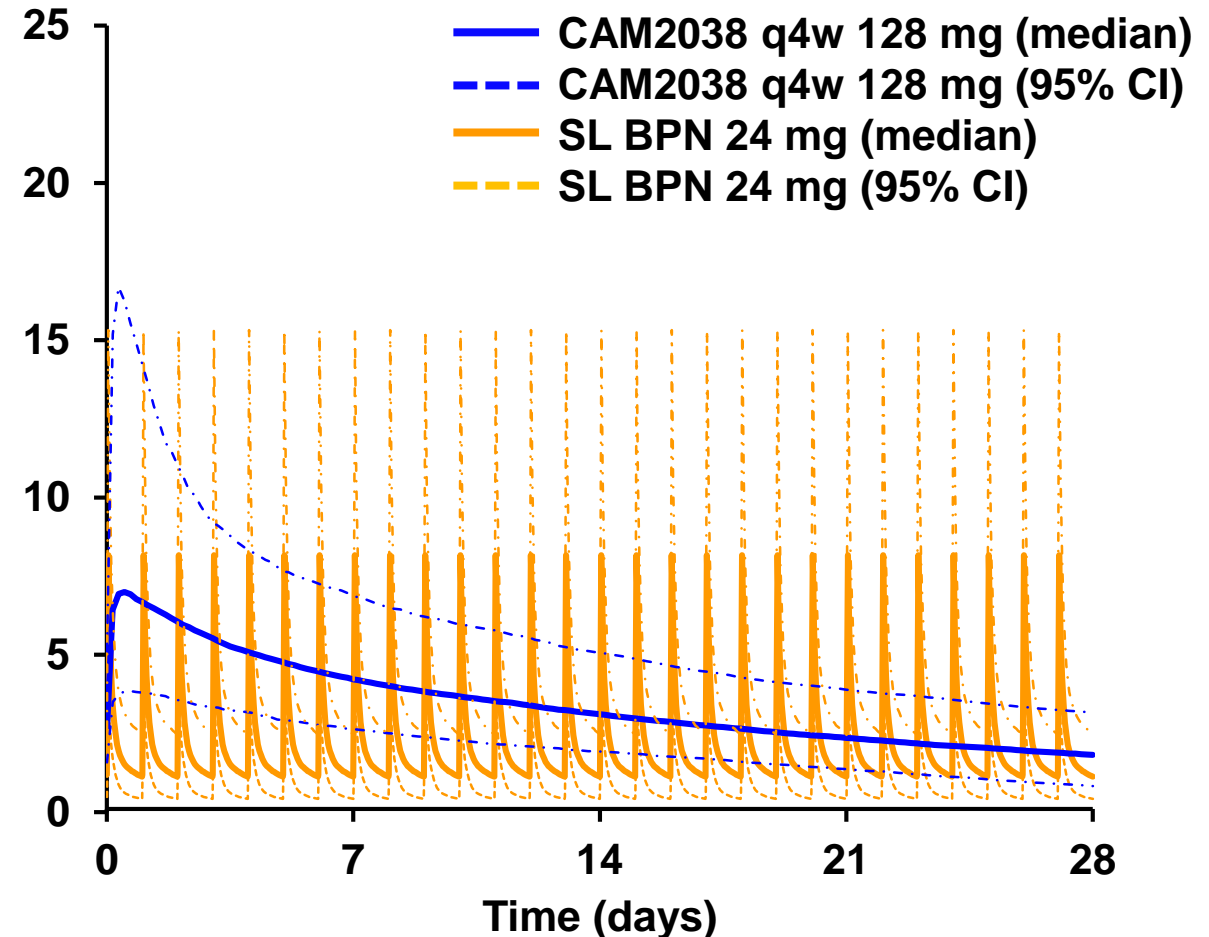


Population PK Steady-State Profiles Show CAM2038 Concentration Within Range of Daily SL BPN

Weekly CAM2038 vs. SL BPN

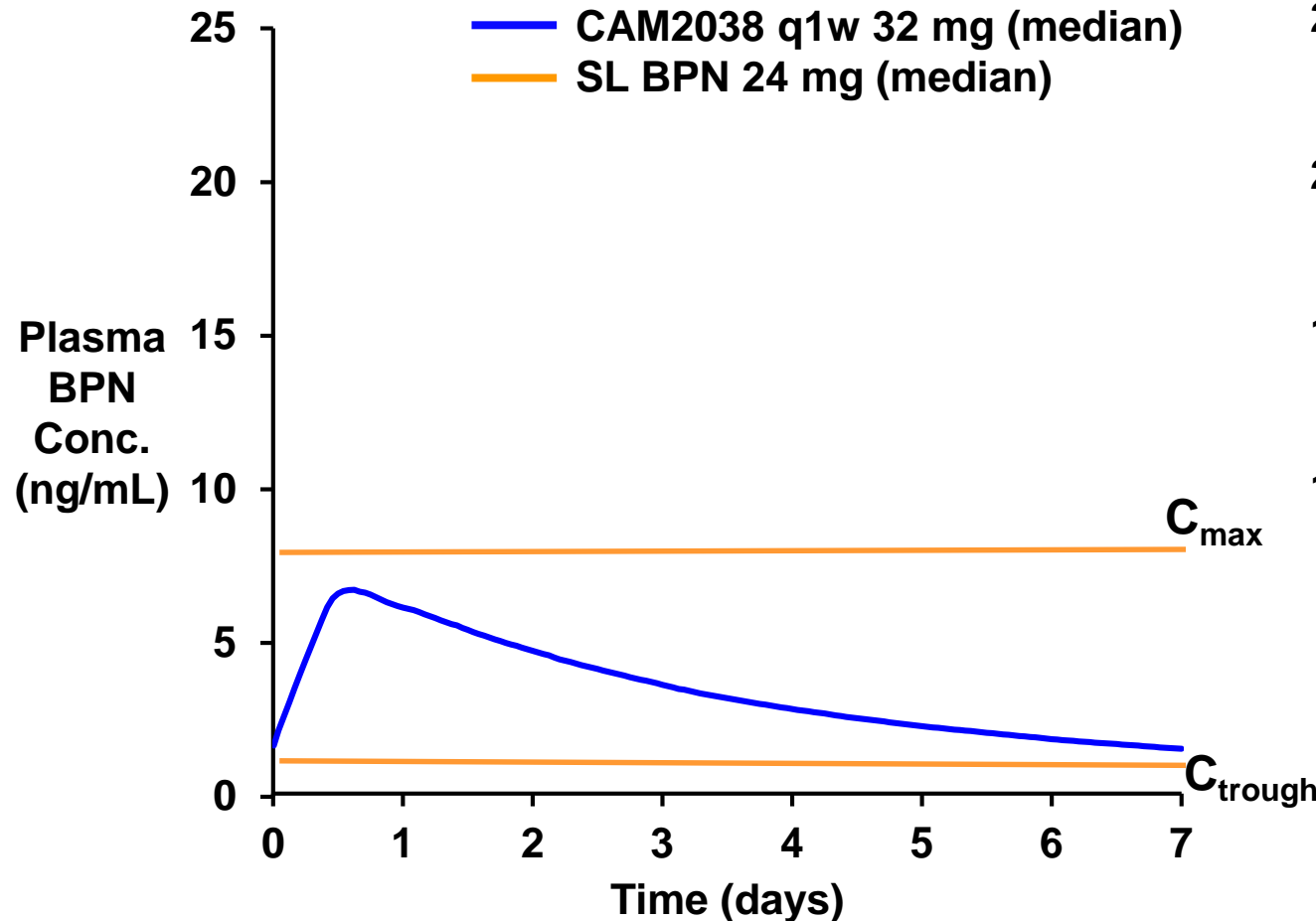


Monthly CAM2038 vs. SL BPN

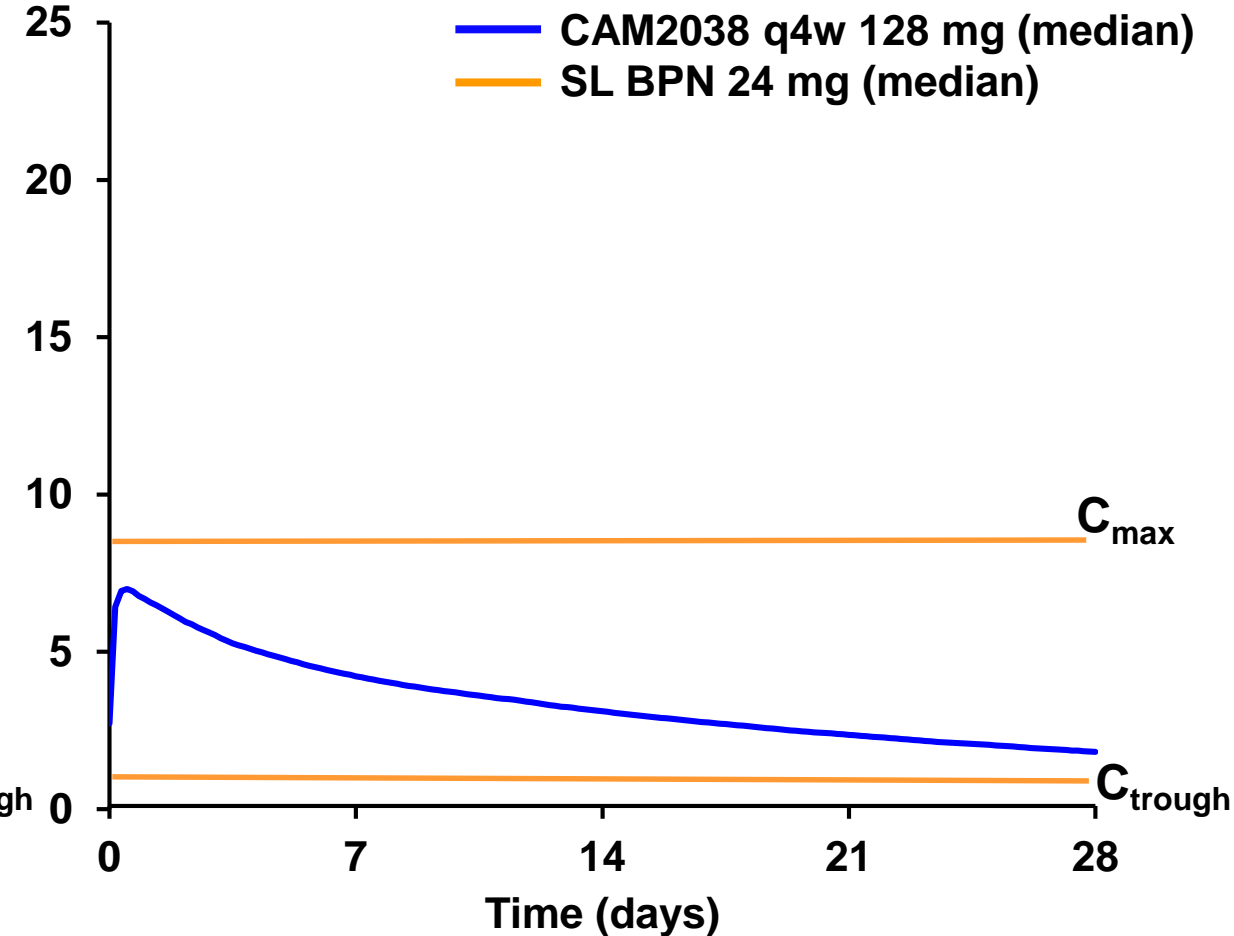


Population PK Steady-State Profiles Show CAM2038 Concentration Within Range of Daily SL BPN

Weekly CAM2038 vs. SL BPN



Monthly CAM2038 vs. SL BPN



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

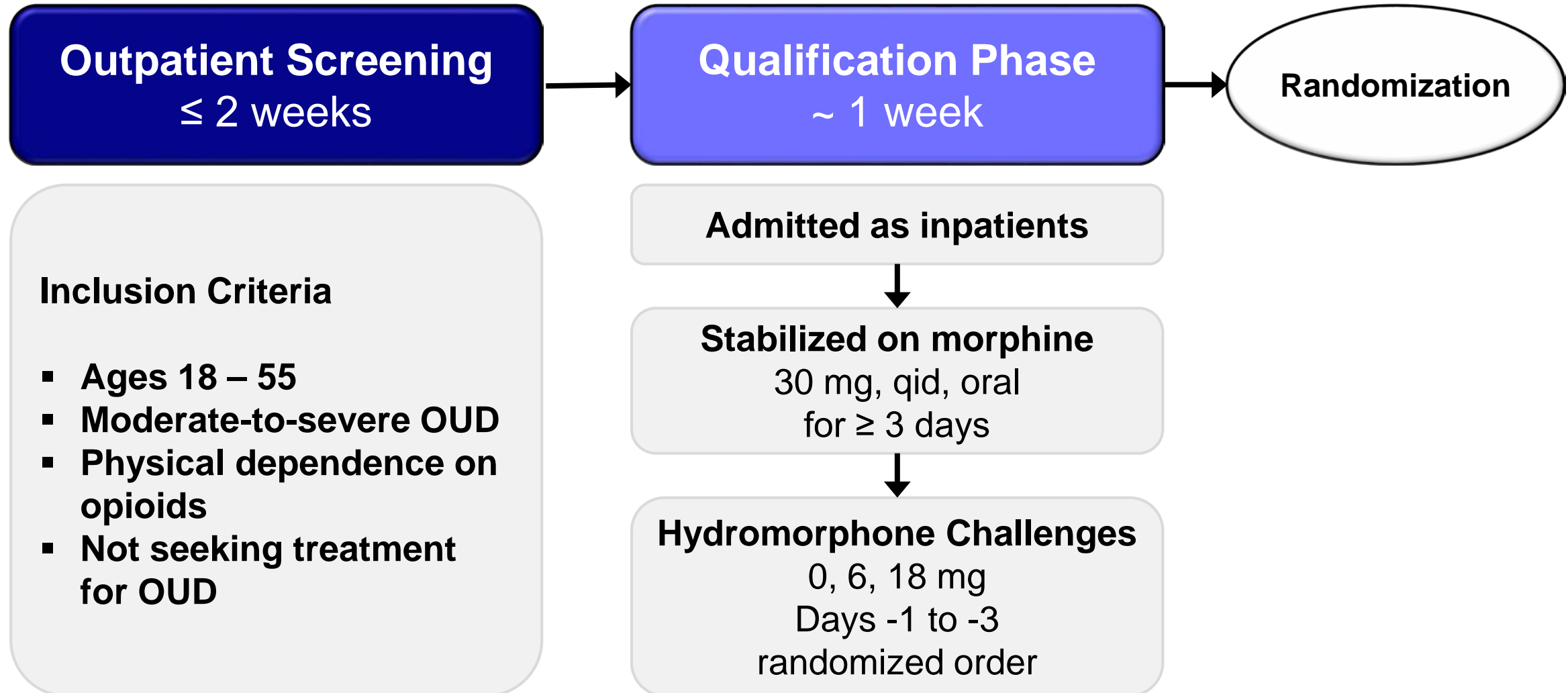
Professor of Behavioral Science, Psychiatry, Pharmacology
and Pharmaceutical Sciences

University of Kentucky

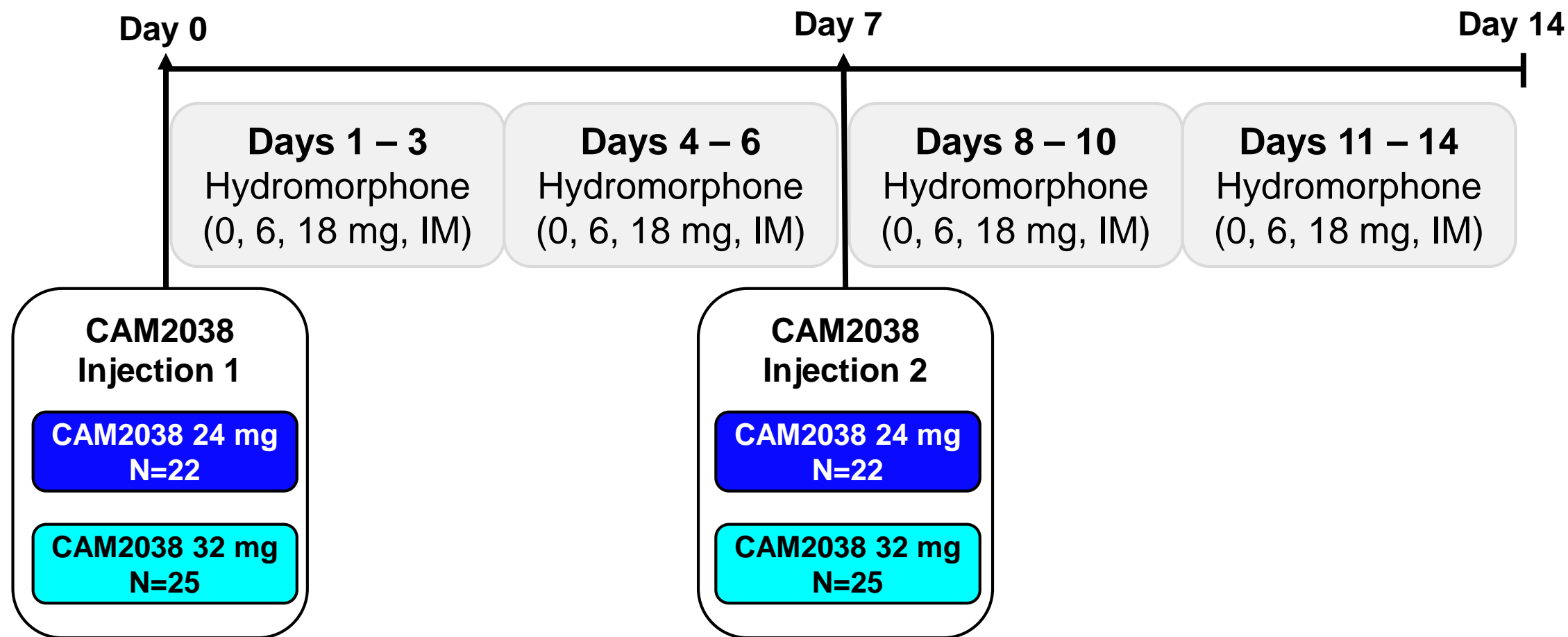
Study 478: Double-Blind, Randomized, Within-Subject, Inpatient Laboratory Study

- 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 $\leq 11 \text{ mm}^1$
- Secondary measures
 - VAS ratings of high, good effect, any effect, alertness and drowsiness, withdrawal and craving

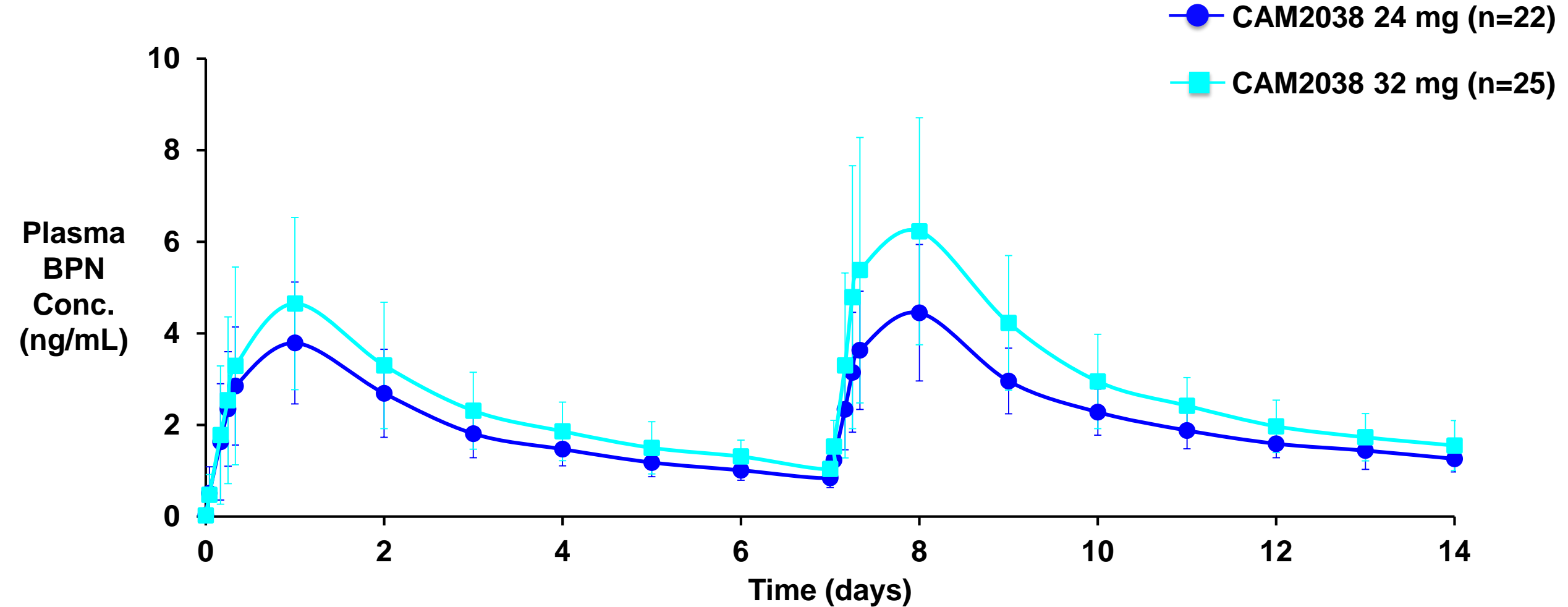
Study 478 Design: Screening and Qualification



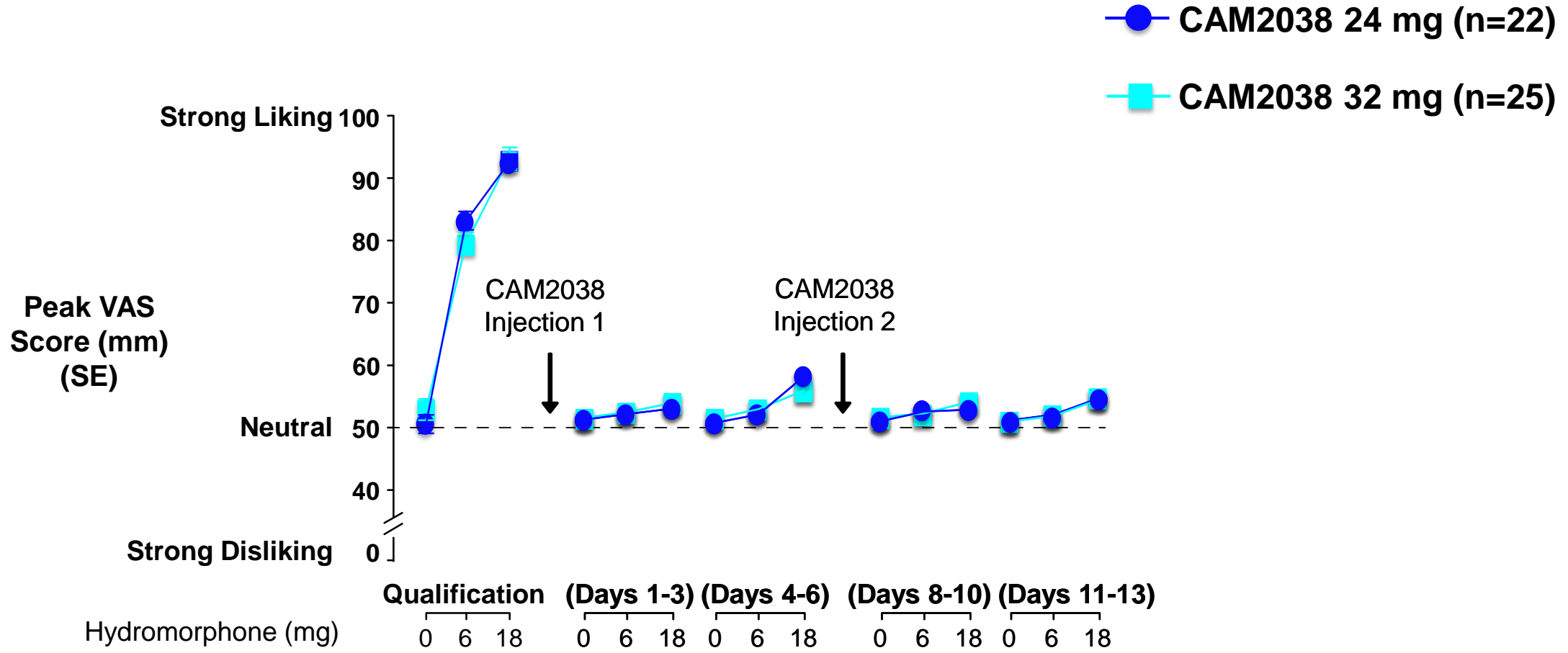
Study 478 Design: Randomization



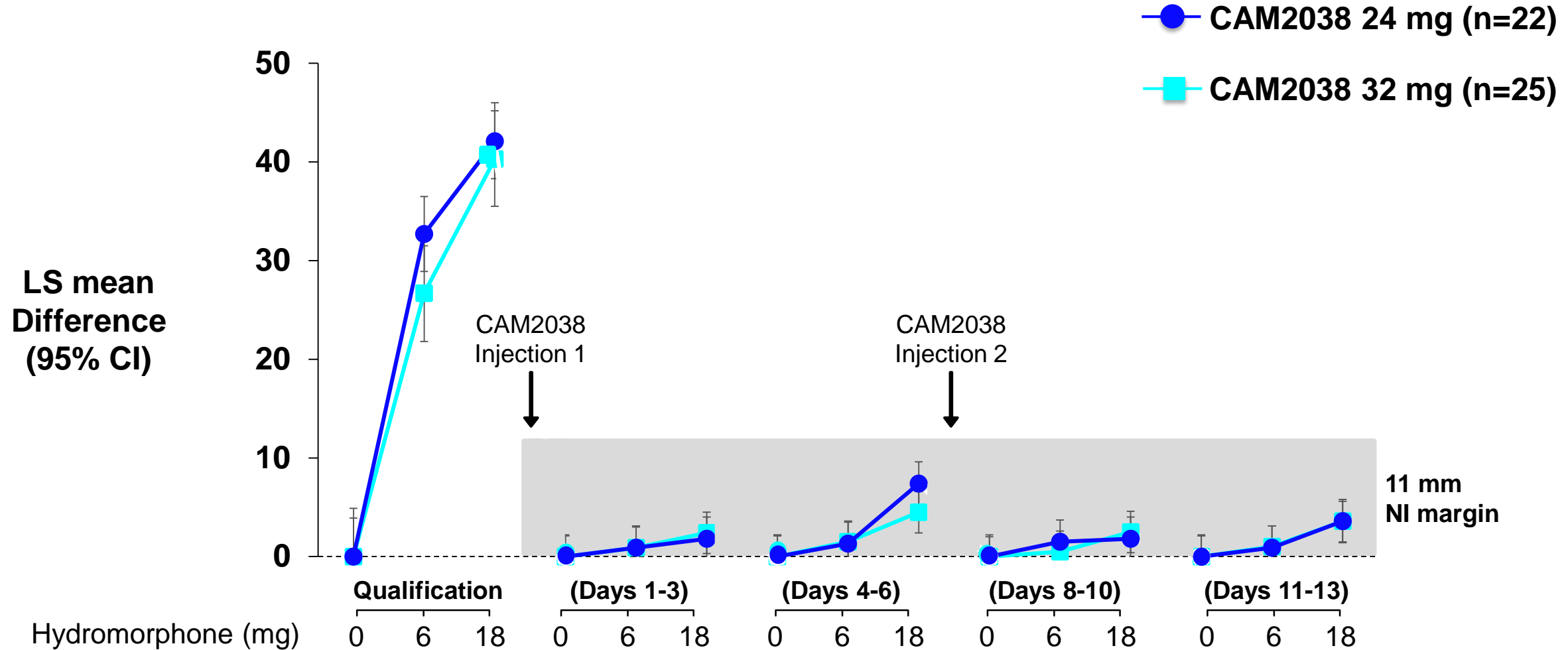
Study 478: Buprenorphine Plasma Concentrations



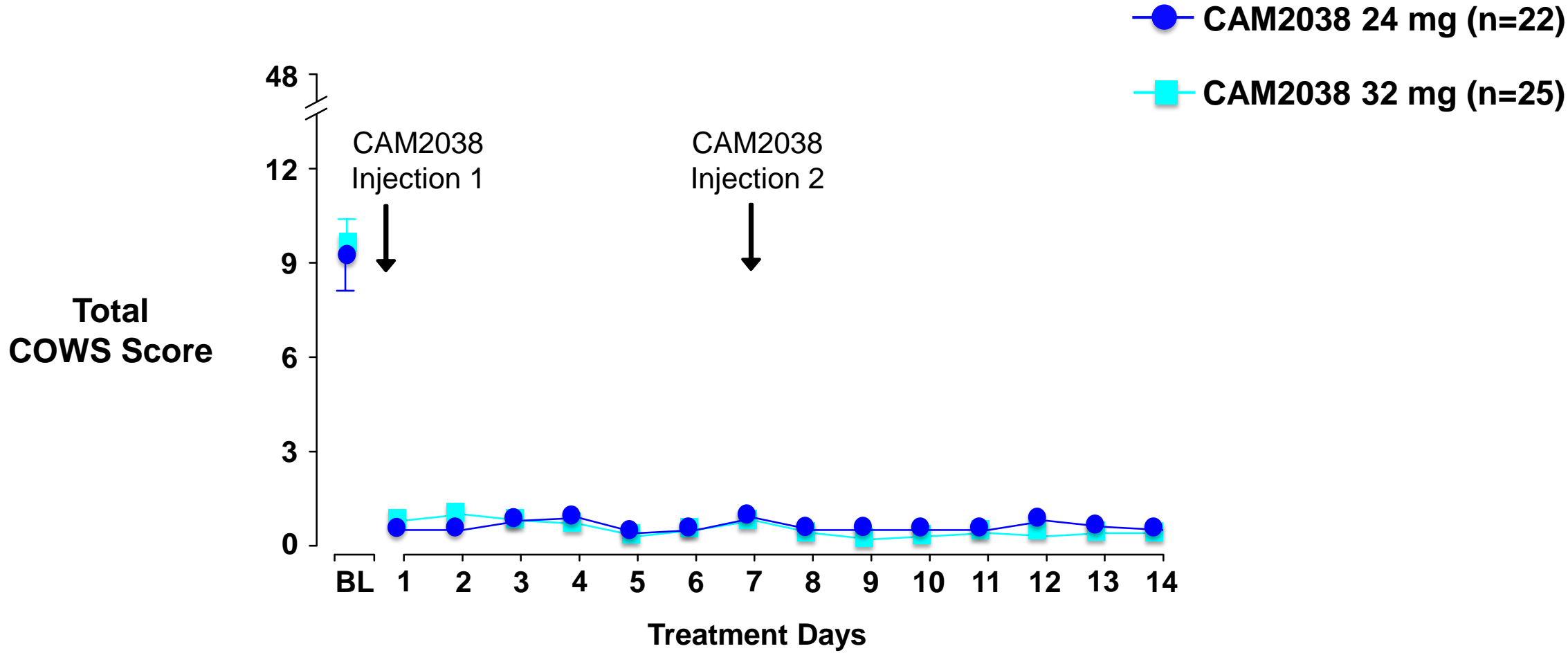
Study 478: CAM2038 Produces Opioid Blockade



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



Study 478: CAM2038 Supresses Opioid Withdrawal



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

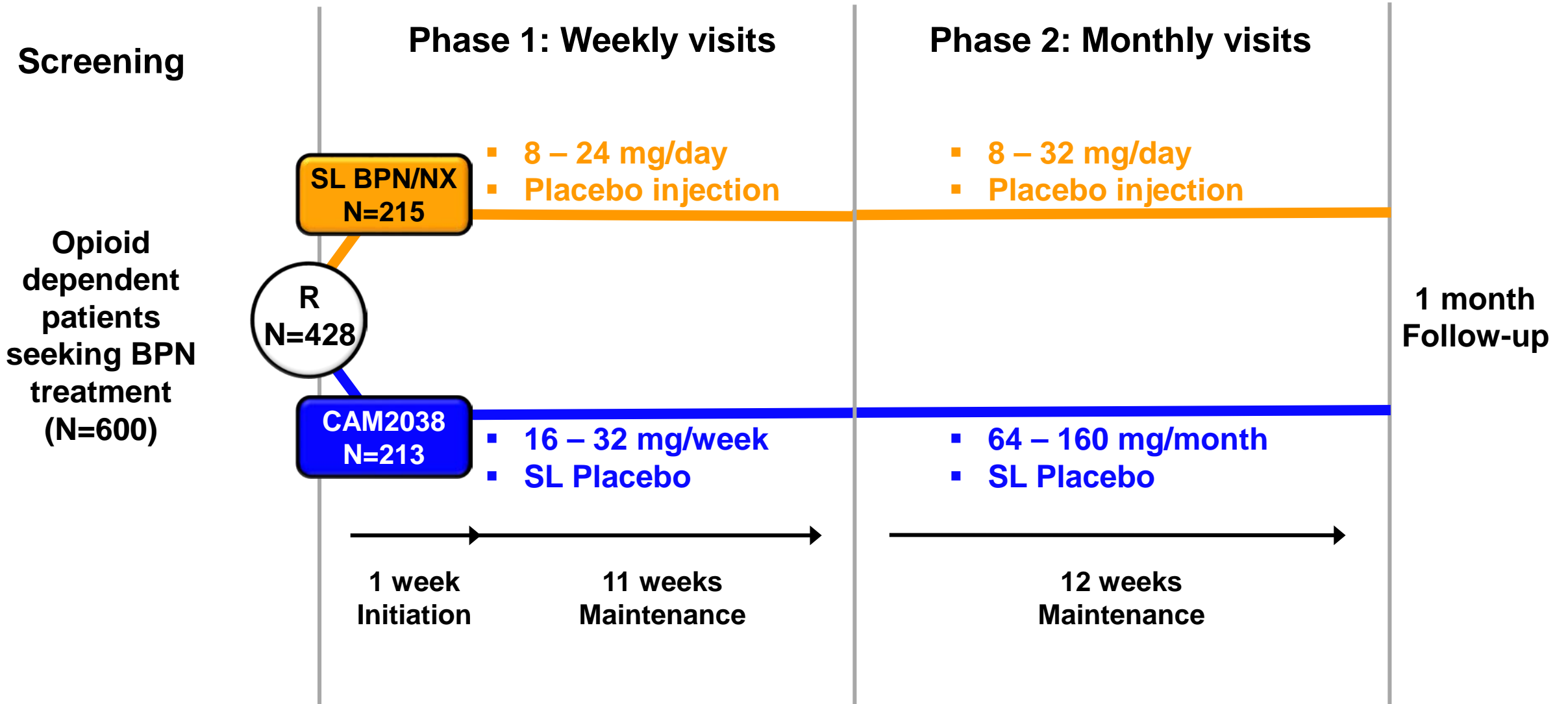
Chief Scientific Officer

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

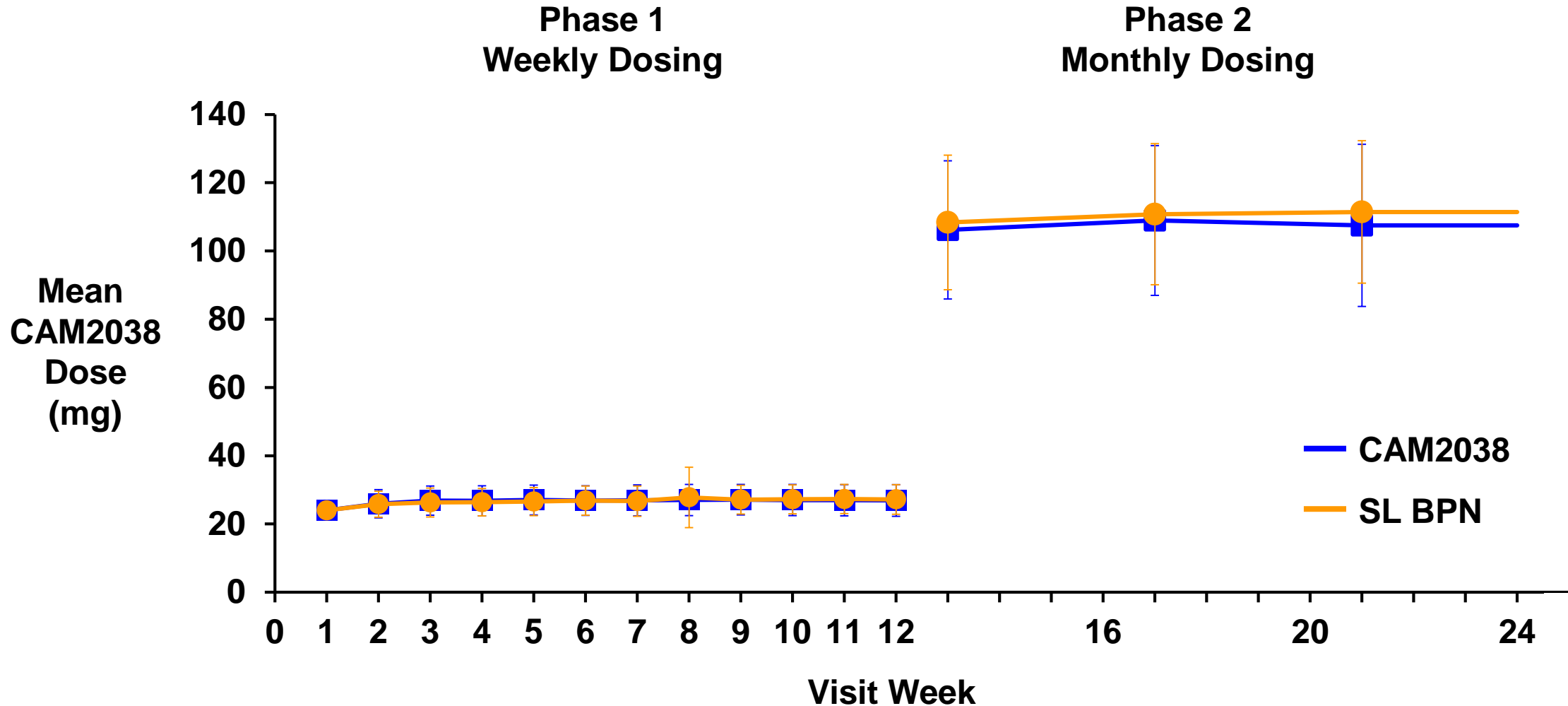
Study 421: Clinical Design



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

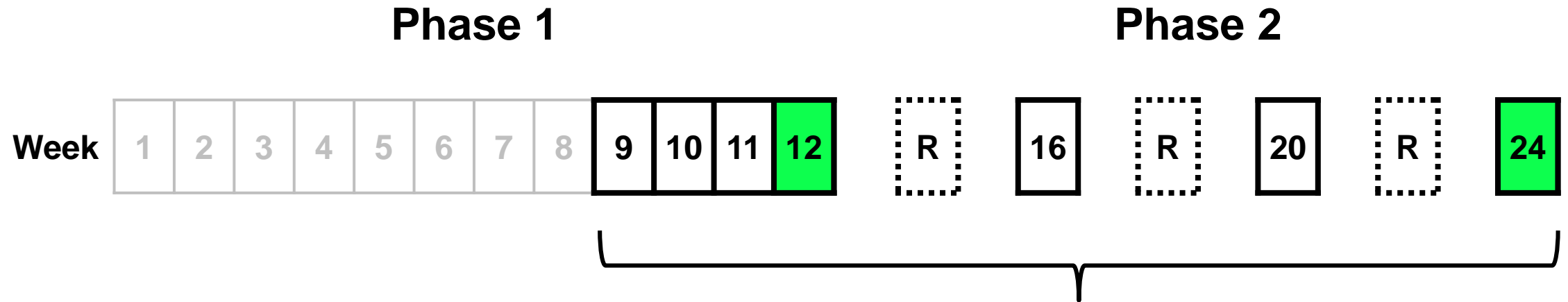
Mean CAM2038 Equivalent Doses by Visits: Doses Similar in SL BPN and CAM2038 Groups



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

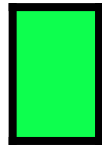


Responder

- 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



Scheduled visit



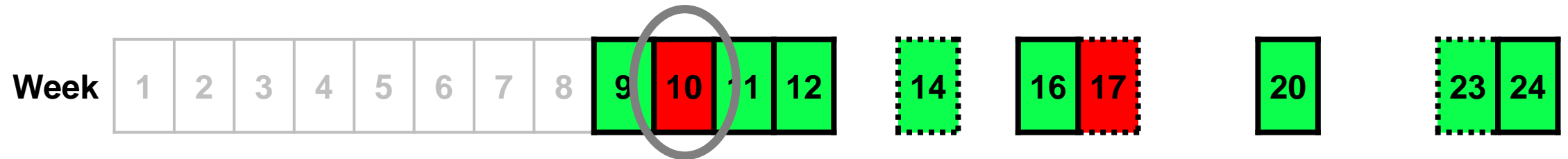
Negative urine



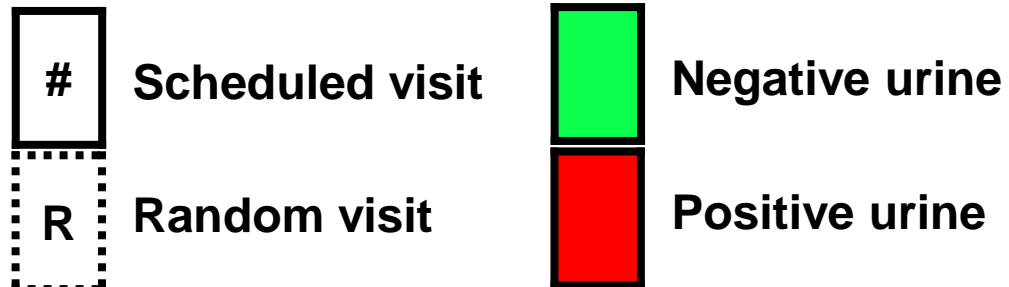
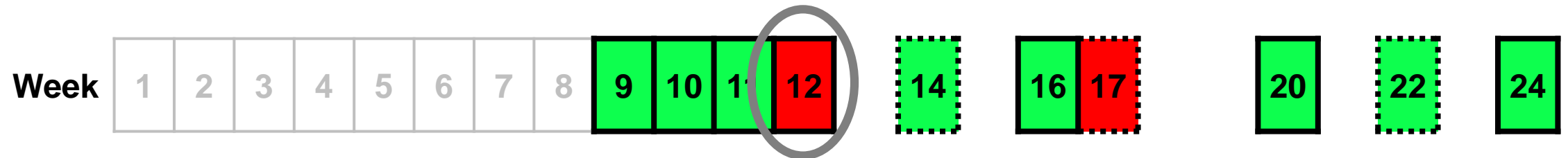
Random visit

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

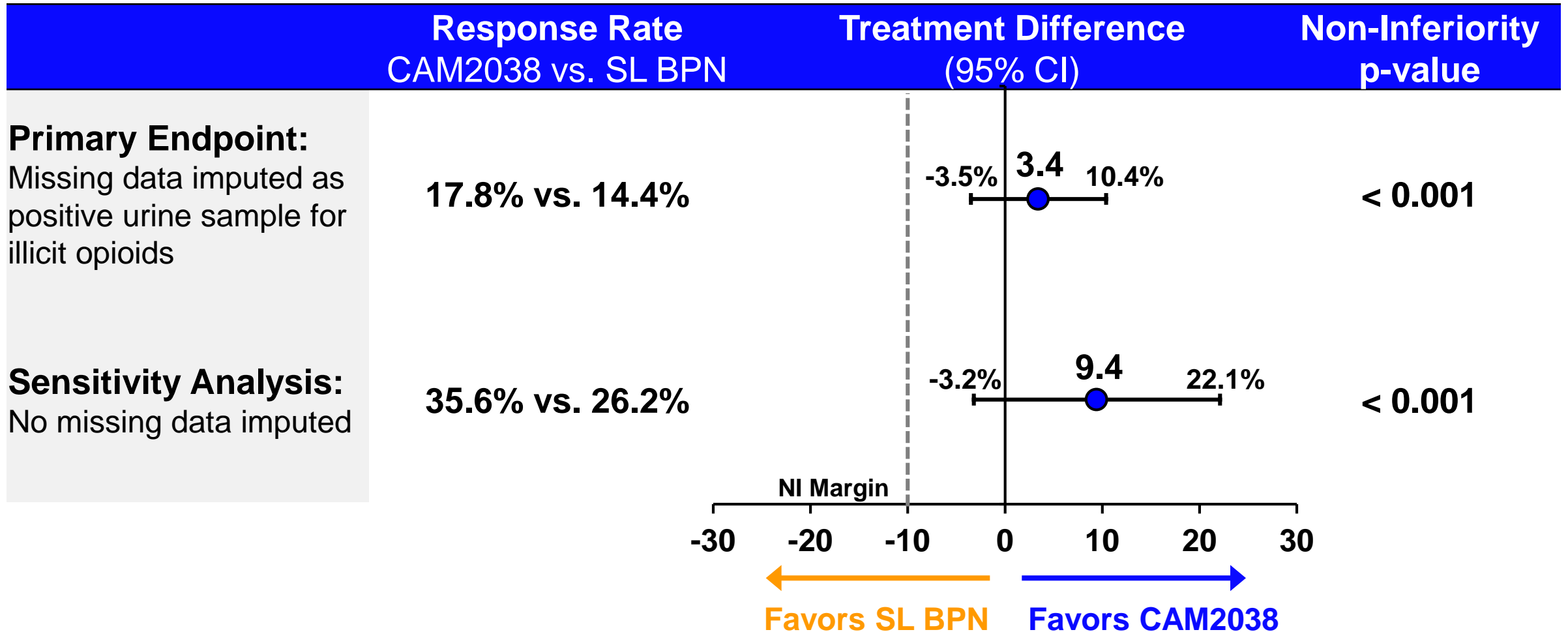
Study 421: Demographics Balanced Between Groups

	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%

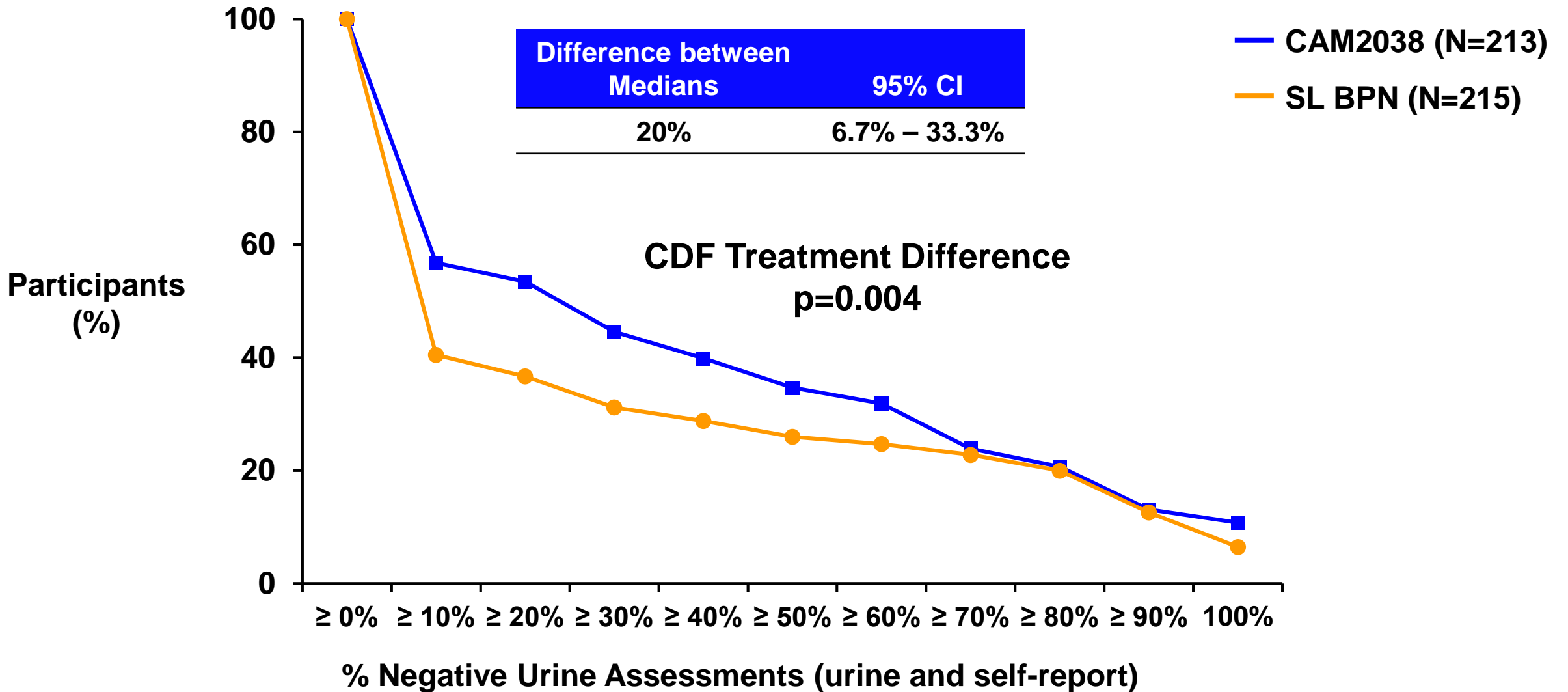
Study 421 Included Unstable Patients, Reflecting Real-World OUD Population

	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



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

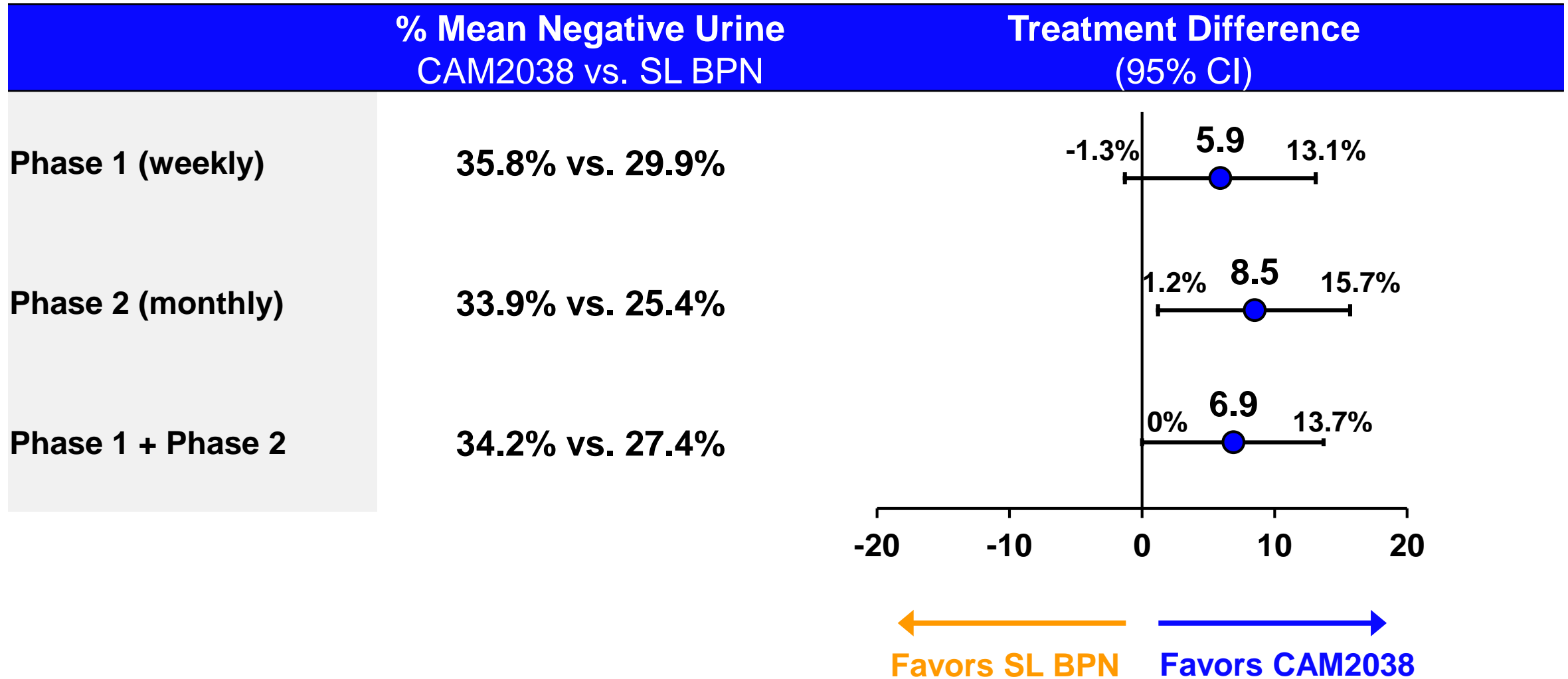


Study 421: Sensitivity Analyses for CDF Demonstrate Superiority with Different Grace Periods

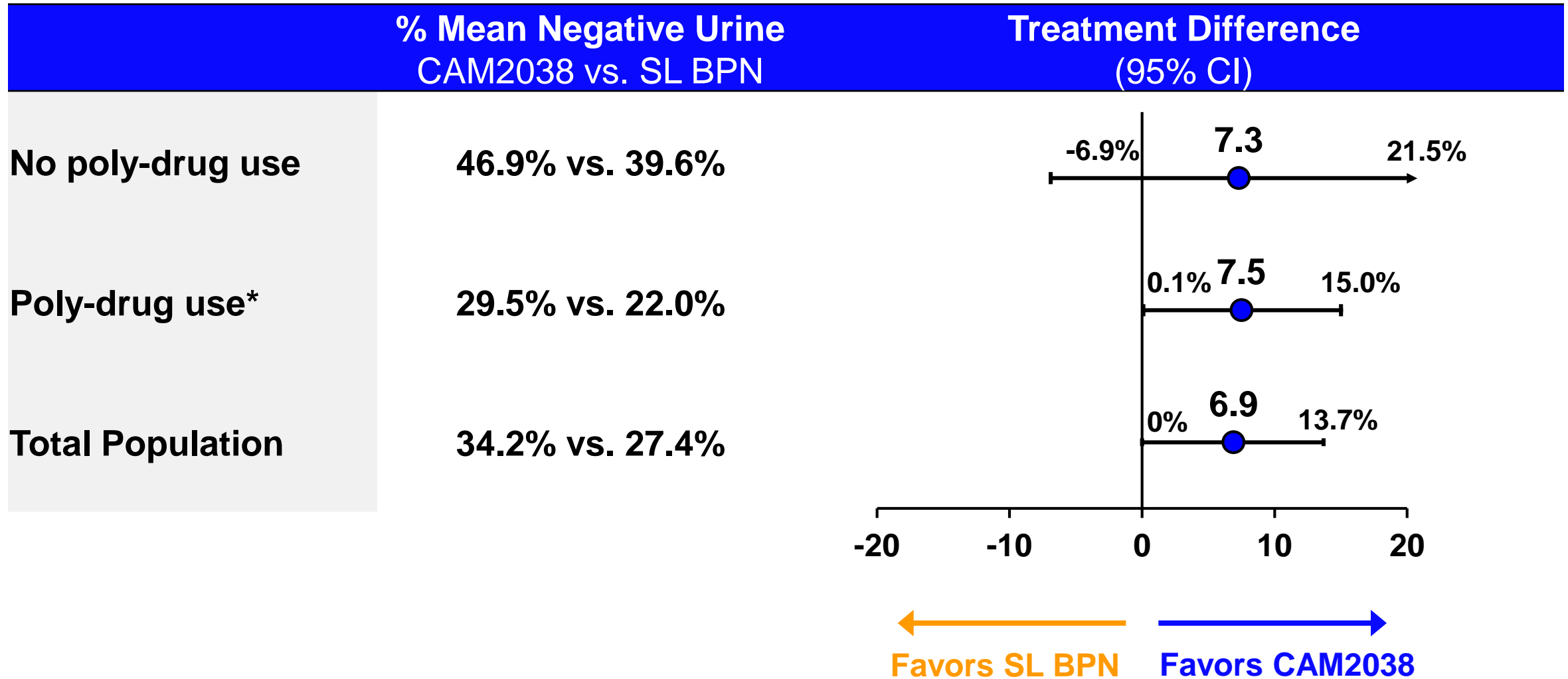
Grace Period	Superiority p-value CDF
0 weeks	0.006
1 week	0.005
3 weeks (<i>prespecified</i>)	0.004
4 weeks	0.001
6 weeks	0.001

Efficacy: Study 421 Additional Outcomes

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



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



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

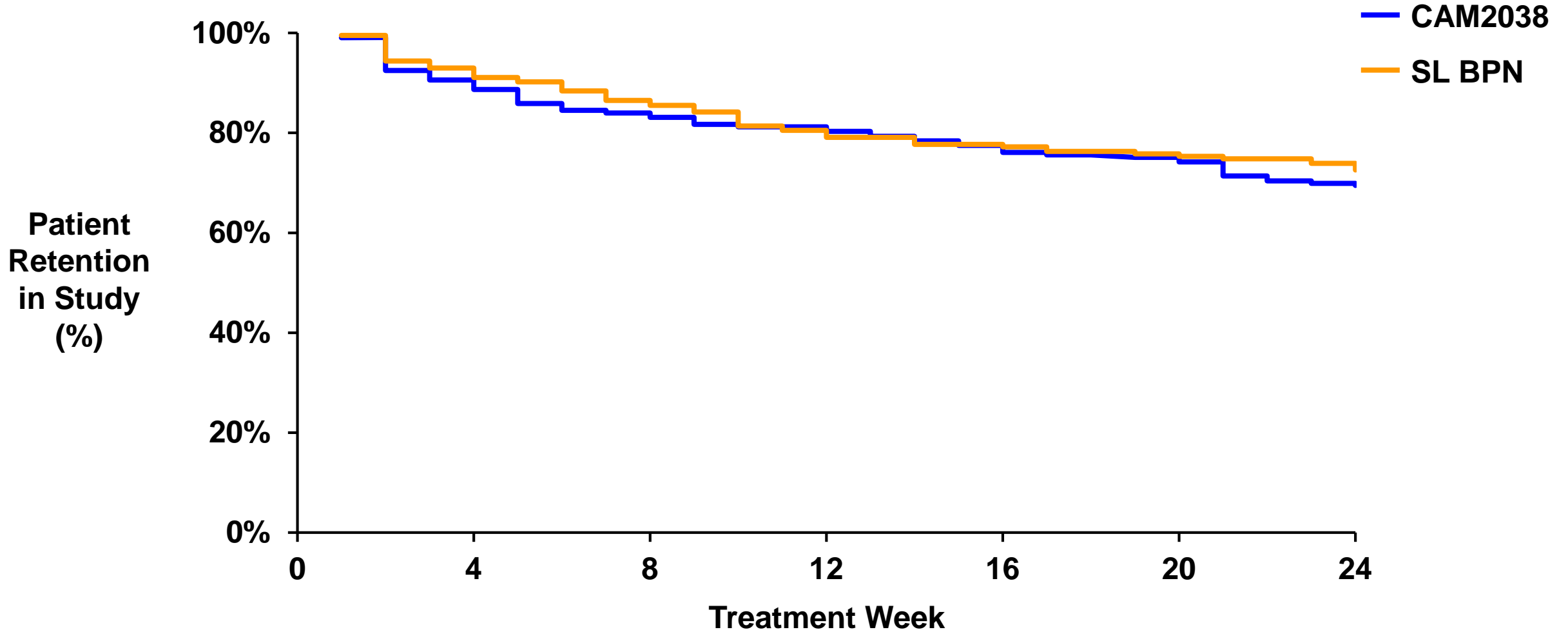
Study 421: Percentage of Negative Urine Samples by Dose

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

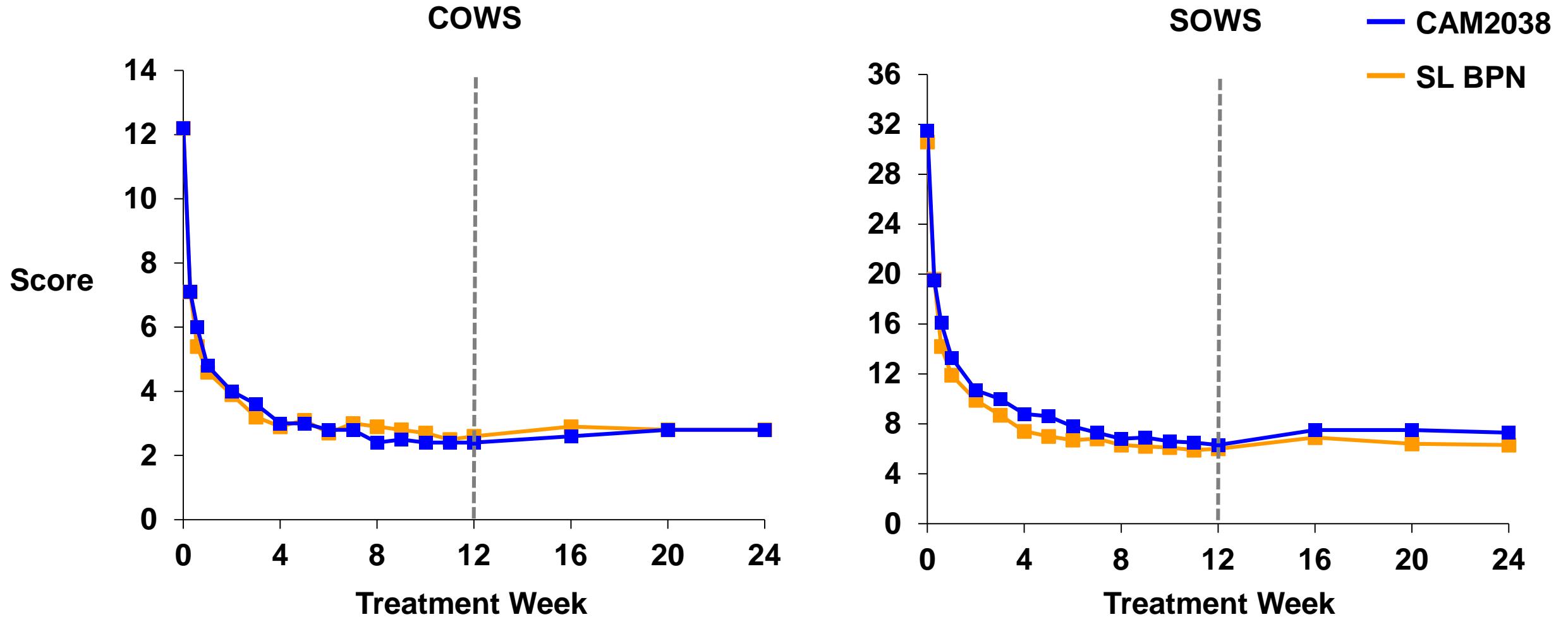
Urine assessments = urine samples verified by self-reports

Safety Population

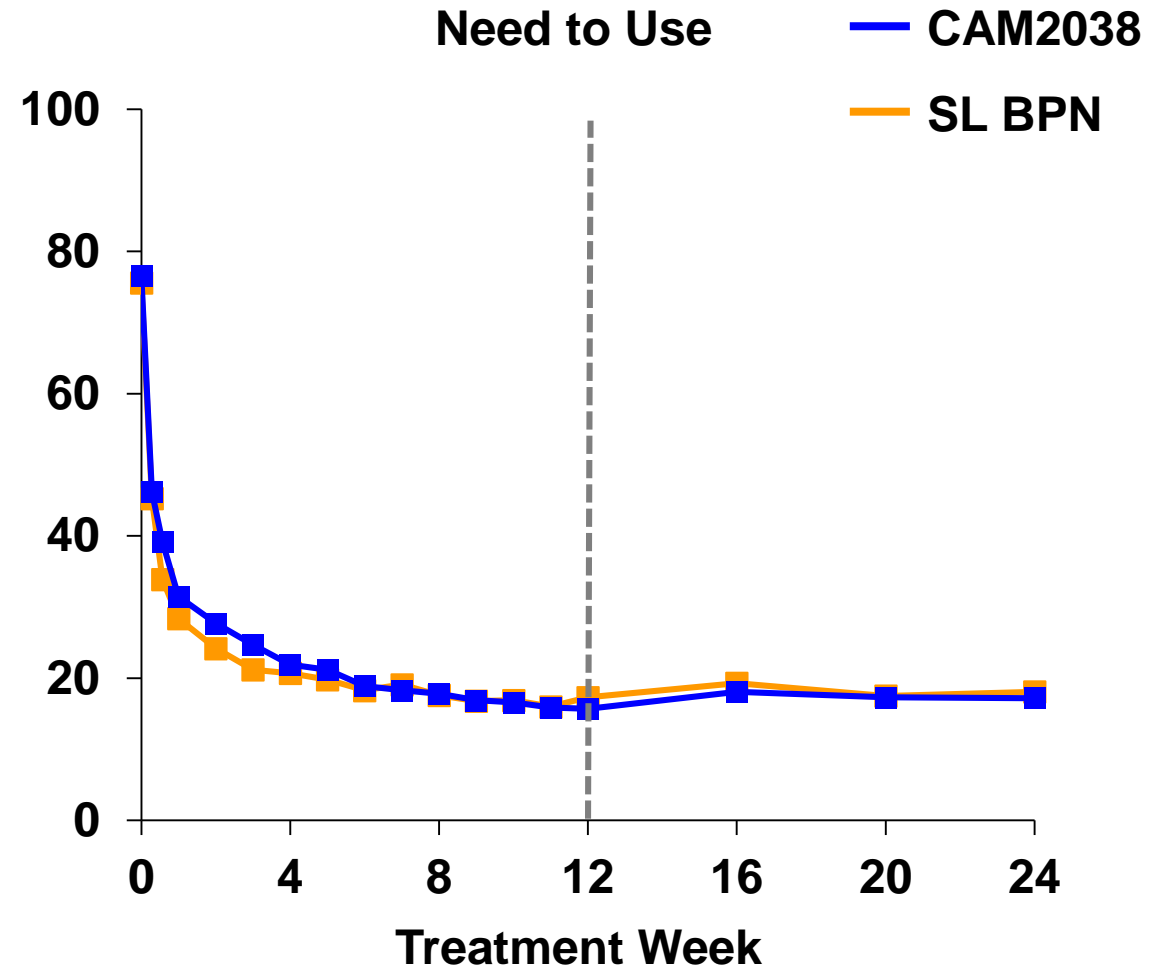
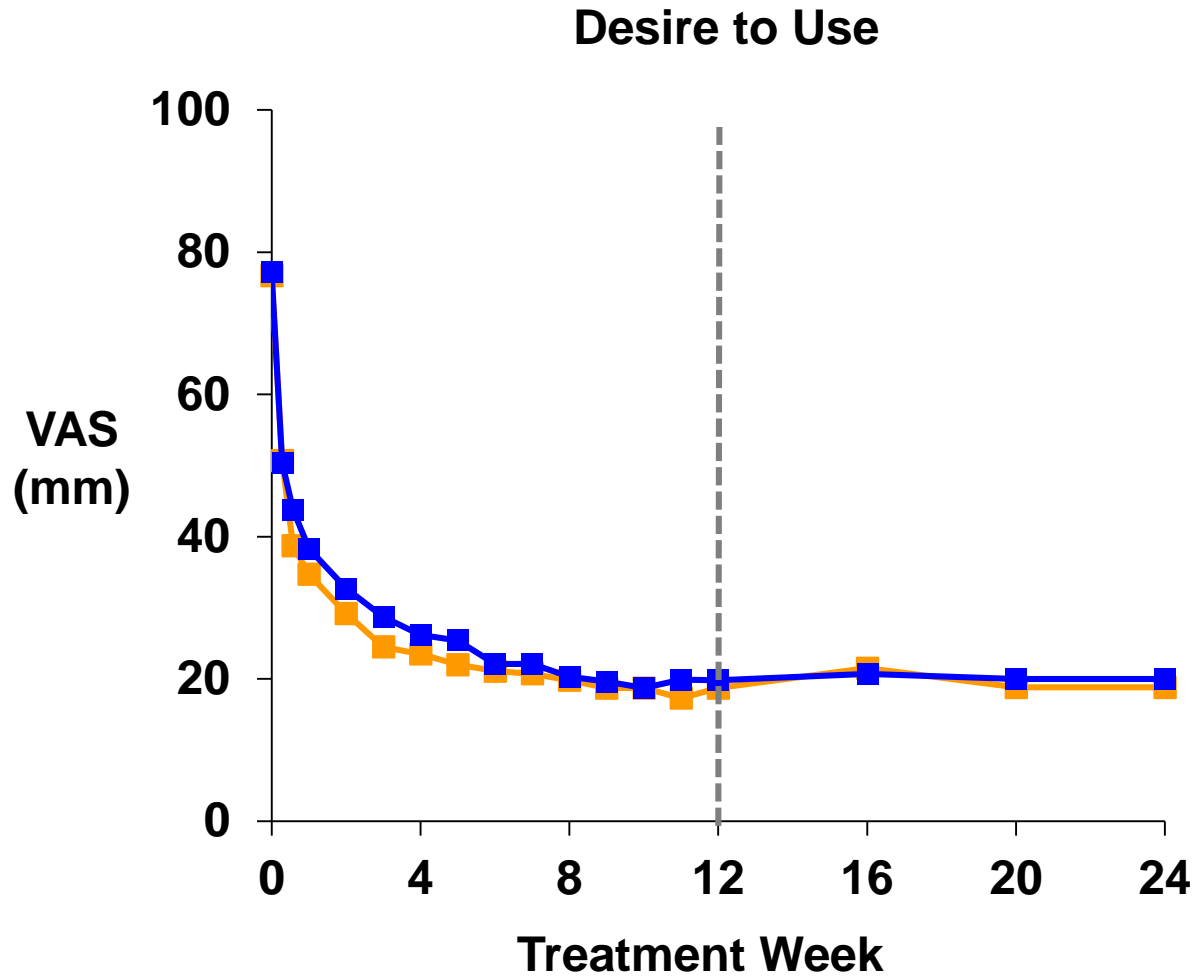
Study 421: 71% Treatment Retention at 24 Weeks



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

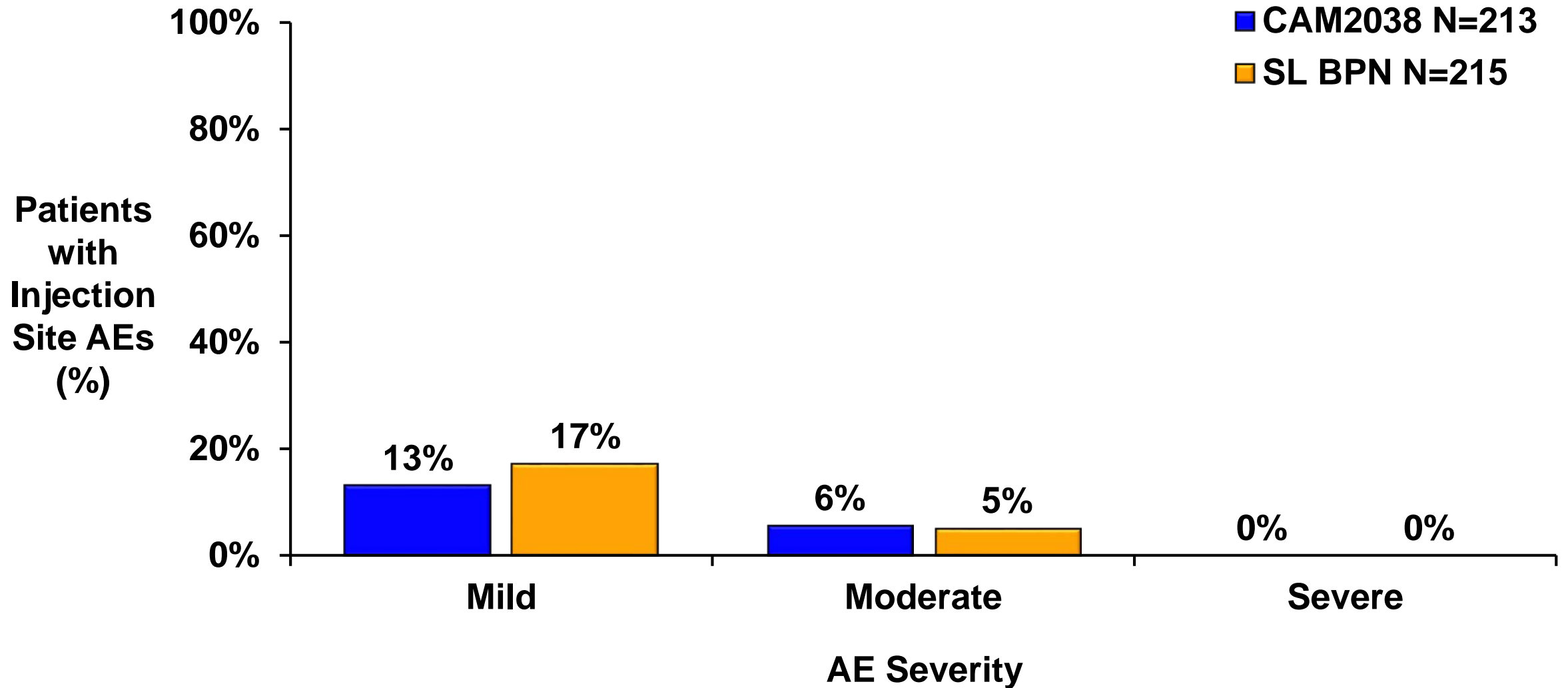
Study 421: Common Non-Injection Site AEs ≥ 3% in Either Treatment Group

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%

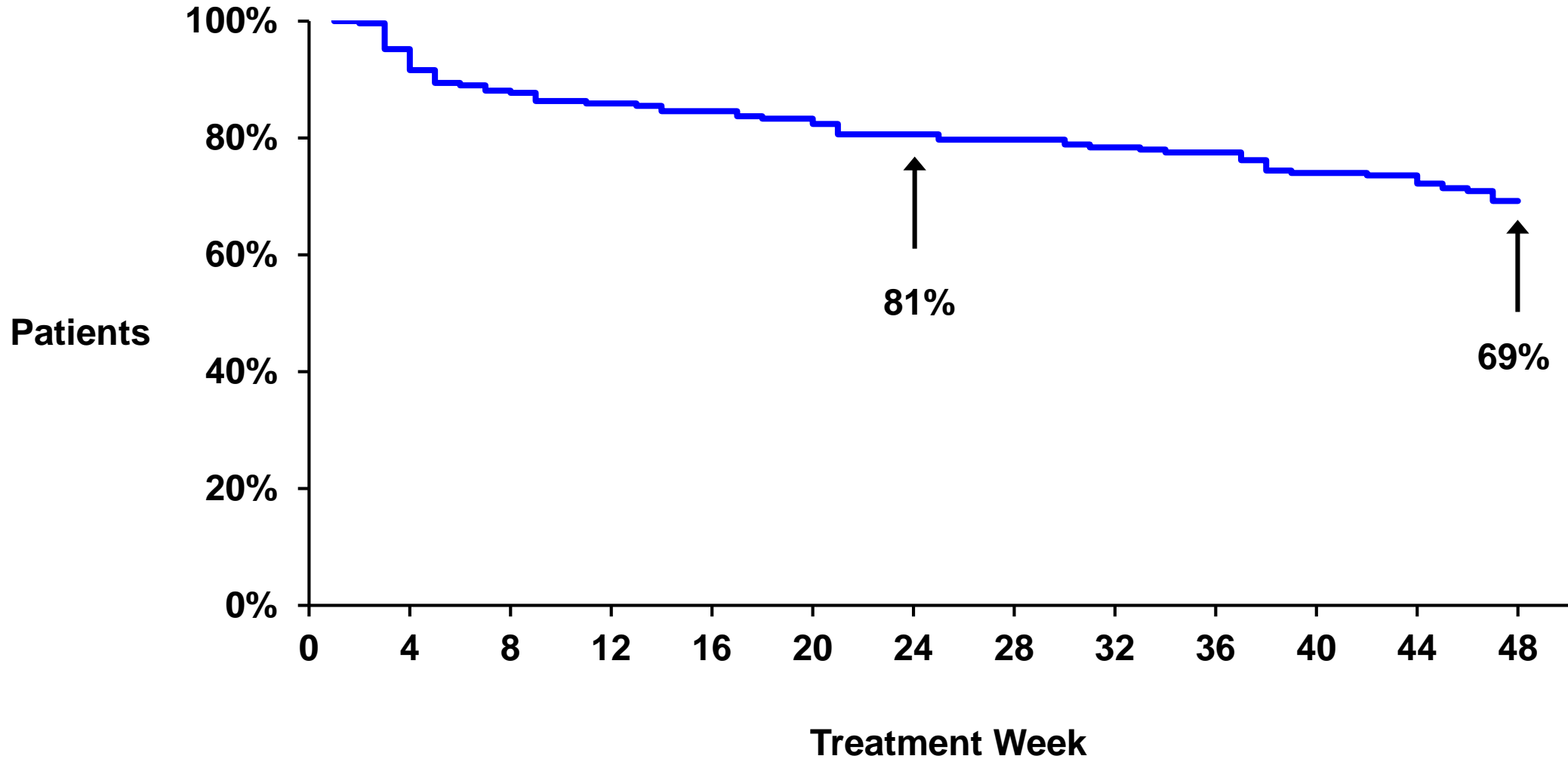
Study 499: AEs Occurring \geq 5% of Patients

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%

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

Number of patients with at least one	CAM2038				SL BPN	
	32 mg (q1w) N=175		160 mg (q4w) N=48		24 mg (daily) N=89	
	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%

Study 499: High Treatment Retention at 24 and 48 Weeks



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

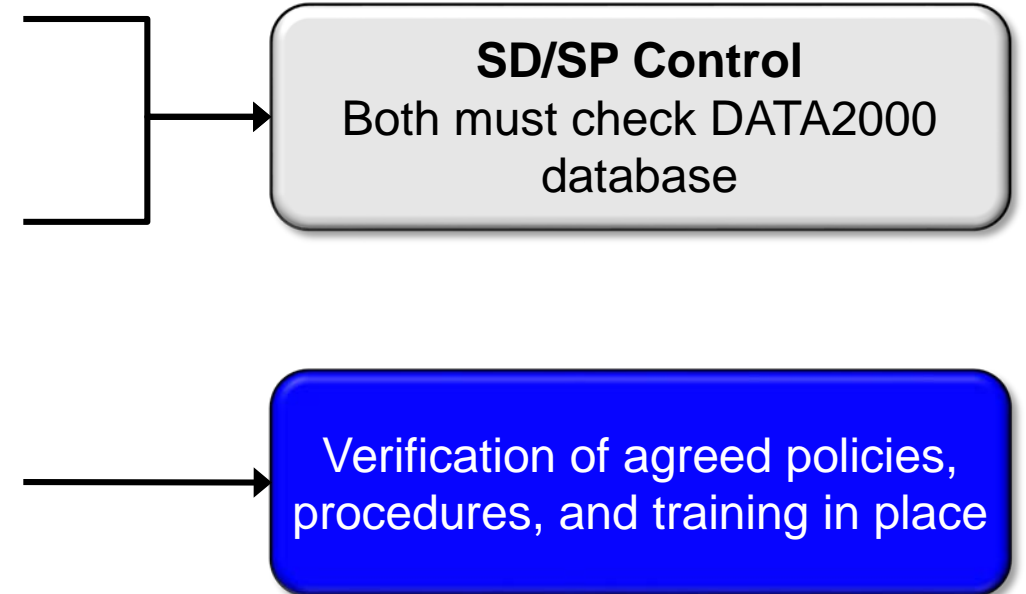
- Educate prescribers, pharmacists and patients regarding risks
- Controlled distribution system

Ensure Patient Access

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graph TD; Goals[Goals] --- Junction; Elements[Elements to Assure Safe Use] --- Junction; Junction --> Access[Ensure Patient Access];
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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

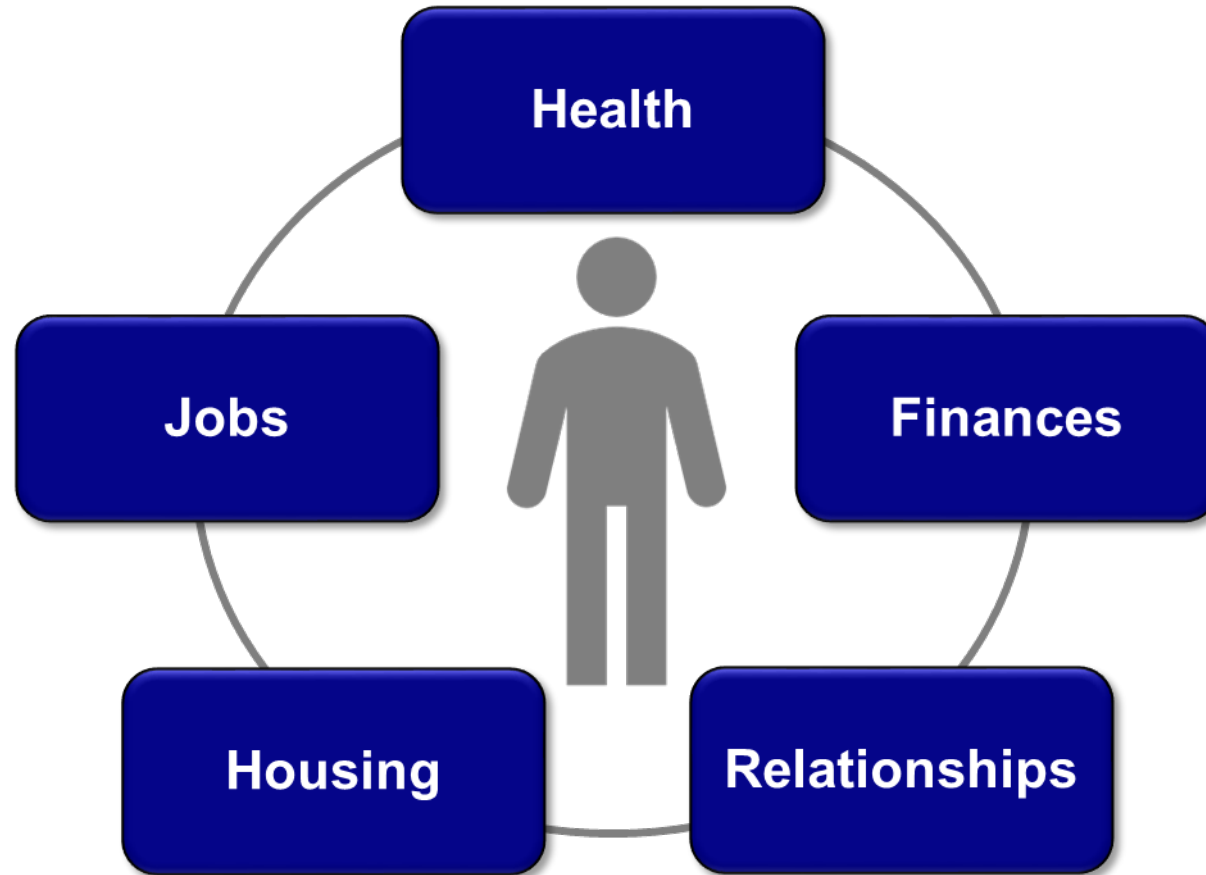
Clinical Perspective

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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 problematic¹⁻³
 - 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 children⁴⁻⁵
- Barriers to use
 - Challenge of sublingual formulation
 - Discrimination and stigma around use of daily dosed buprenorphine encountered by both patients and providers

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

Phase	CAM2038 N=213			SL BPN N=215		
	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%

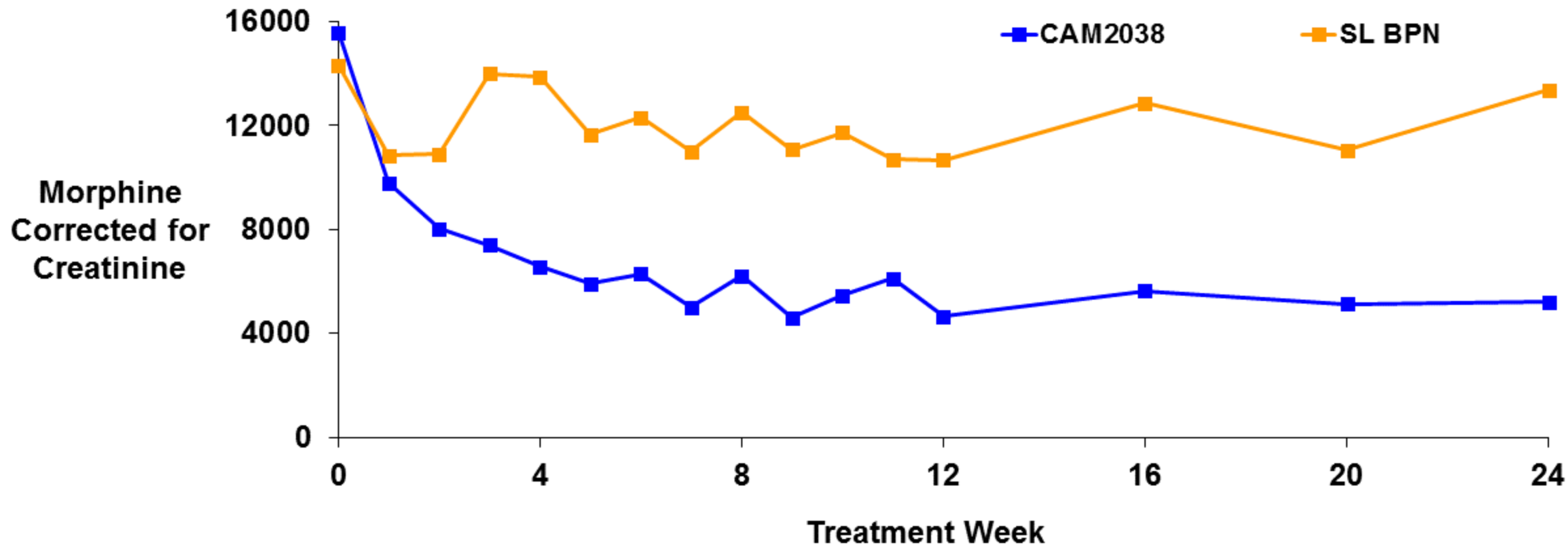
No Unexpected Accumulation Observed Following CAM2038 q1w and q4w

- 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