Injectable Weekly and Monthly Buprenorphine in the Outpatient Treatment of Fentanyl Users with Opioid Use Disorder

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DISCLOSURES

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Dr. Budilovsky-Kelley is an employee of Braeburn Inc.

The information presented today relates to the scientific data associated with CAM2038, an investigational product for the treatment of moderate to severe Opioid Use Disorder (OUD).

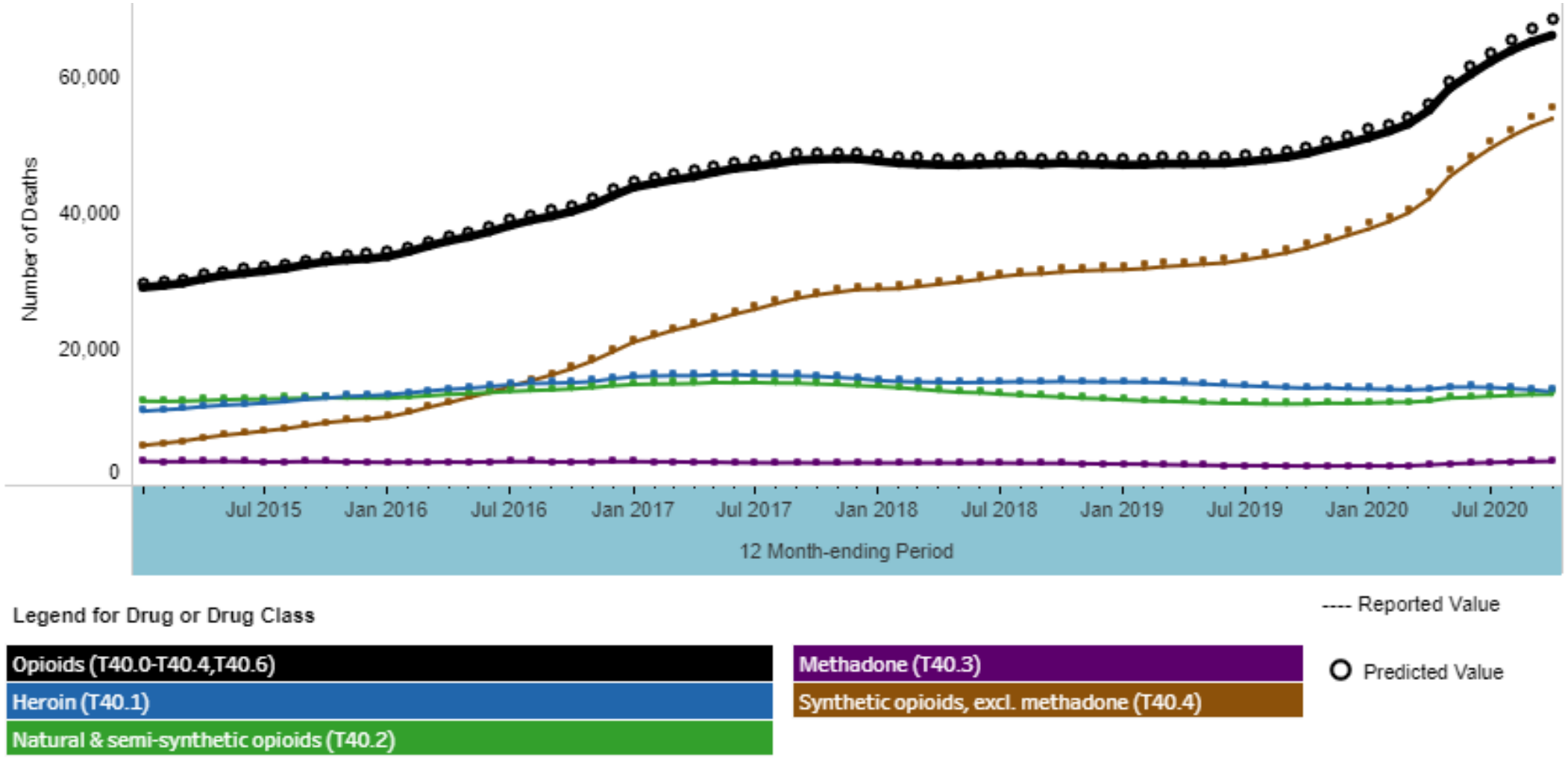
CAM2038 (buprenorphine) INVESTIGATIONAL EXTENDED-RELEASE INJECTION

- Intended for healthcare professional administration only
- Weekly or monthly subcutaneous injection
  - Multiple dose strengths
- May allow for individualized dosing based on clinical response and tolerability[1]
  - Aligns with treatment guidelines[2,3]
  - Multiple injection sites
- Low-volume, ready-to-use, pre-filled syringes with 23 gauge needles stored at room temperature



1. Frost, et al., Addiction 2019; 2. SAMHSA 2020; 3. ASAM 2020

Provisional Number of Opioid-Related Overdose Deaths in the United States



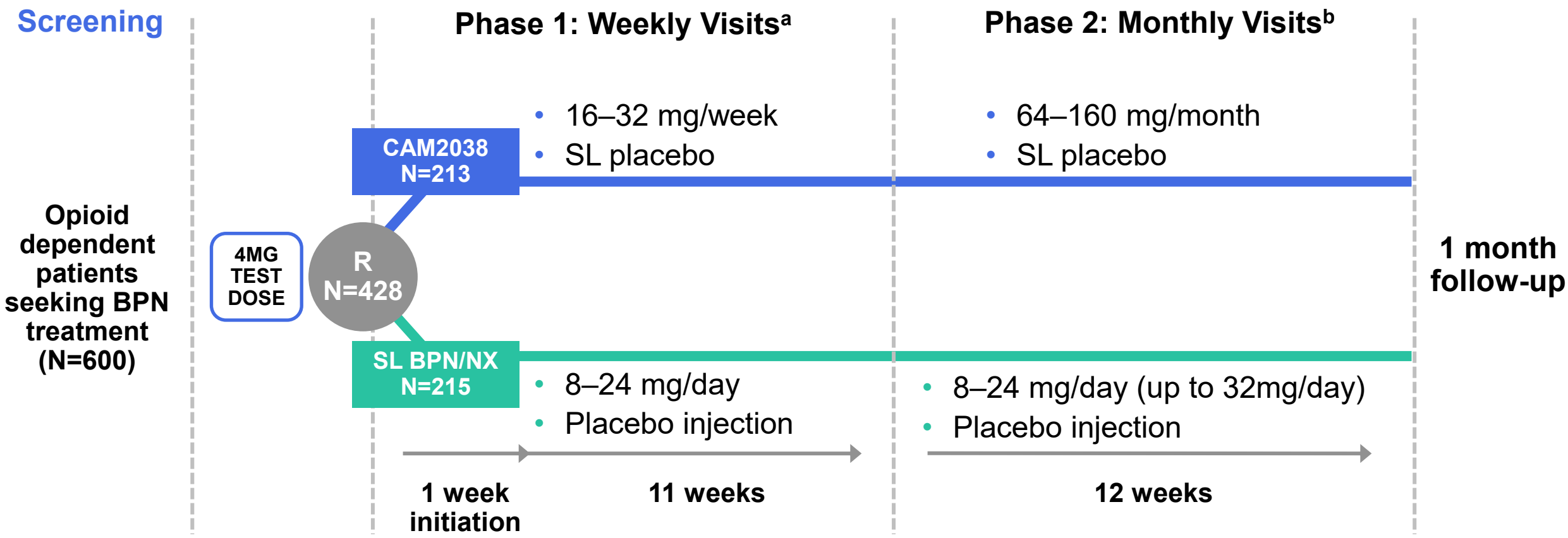
Ahmad FB, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2021.

STUDY 421

Weekly and Monthly Subcutaneous Buprenorphine Depot Formulations vs Daily Sublingual Buprenorphine With Naloxone for Treatment of Opioid Use Disorder: A Randomized Clinical Trial

Phase 3, outpatient, double-blind, double-dummy randomized clinical study conducted at 35 sites in the United States.

Study 421: Study design



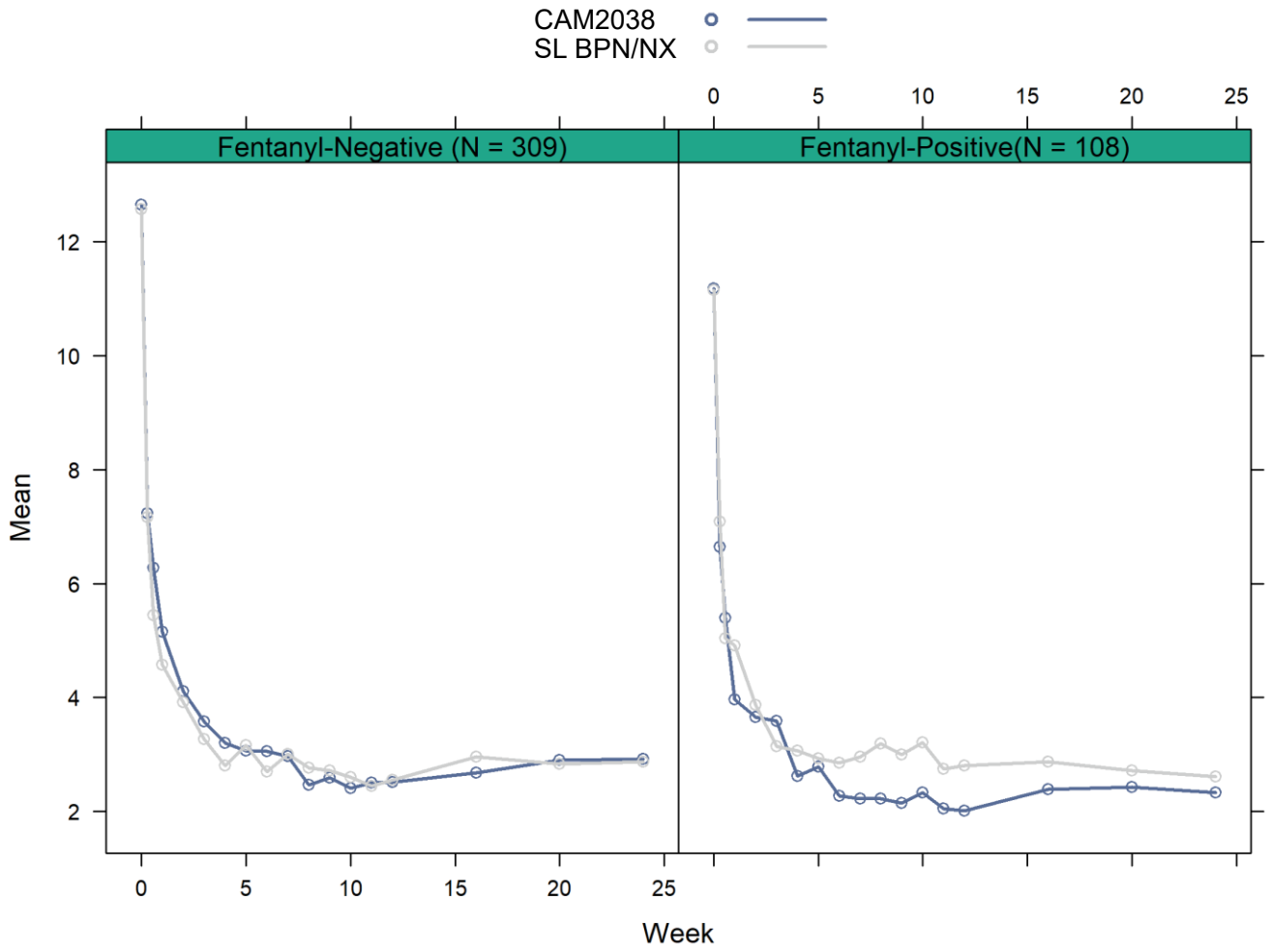
BPN, buprenorphine; SL, sublingual; BPN/NX, buprenorphine/naloxone
[a]Every 7 days ± 2 days; [b]Every 28 days ± 7 days
Lofwall, et. al., 2018 *JAMA Internal Medicine*

Demographics and baseline clinical characteristics by treatment and fentanyl use at baseline

Demographics and characteristics	Fentanyl positive			Fentanyl negative		
	CAM2038 N = 62	SL BPN/NX N = 49	Total N=111	CAM2038 N = 151	SL BPN/NX N = 166	Total N=317
Age, mean (SD), y	39.9 (11.1)	38.0 (10.7)	39.1 (10.9)	38.3 (11.2)	38.0 (11)	38.1 (11.1)
Male, No. (%)	32 (51.6)	33 (67.3)	65 (58.6)	89 (58.9)	109 (65.7)	198 (62.5)
White, No. (%)	47 (75.8)	34 (69.4)	81 (73.0)	112 (74.2)	130 (78.3)	242 (76.3)
Employed full or part time, No. (%)	19 (30.6)	15 (30.6)	34 (30.6)	57 (37.7)	57 (34.3)	114 (36.0)
Positive history of any arrest, No. (%)	36 (58.1)	25 (51.0)	61 (55.0)	94 (62.3)	119 (71.7)	213 (67.2)
Duration since OUD diagnosis, mean (SD), y	10.6 (14.6)	3.4 (6.8)	7.5 (12.1)	2.9 (4.8)	4.9 (6.0)	3.7 (5.4)
Injection route of illicit opioid use, No. (%)	36 (58.1)	24 (49.0)	60 (54.1)	78 (51.7)	86 (51.8)	164 (51.7)
Heroin primary opioid of use, No. (%)	54 (87.1)	39 (79.6)	93 (83.8)	98 (64.9)	112 (67.5)	210 (66.2/3)
Nonopioid drug use at screening, No (%):	55 (88.7)	47 (95.9)	102 (91.9)	123 (81.4)	137 (82.5)	260 (82.0)
Methamphetamine	7 (11.3)	3 (6.1)	10 (9.0)	31 (20.5)	29 (17.5)	60 (18.9)
Benzodiazepine	13 (21.0)	11 (22.4)	24 (21.6)	17 (11.3)	24 (14.5)	41 (12.9)
Marijuana	12 (19.4)	14 (28.6)	26 (23.4)	45 (29.8)	50 (30.1)	95 (30.0)
Cocaine	23 (37.1)	19 (38.8)	42 (37.8)	30 (19.9)	34 (20.5)	64 (20.2)
Hep. C antibody positive at screening, No. (%)	33 (53.2)	18 (36.7)	51 (45.9)	53 (35.1)	63 (38.0)	116 (36.6)
COWS score, mean (SD)	11.2 (4.0)	11.1 (5.0)	11.2 (4.4)	12.6 (5.9)	12.6 (6.3)	12.6 (6.1)
SOWS score, mean (SD)	33.9 (14.6)	32.5 (15.8)	33.3 (15.1)	30.5 (15.7)	30.0 (16.1)	30.2 (15.9)
Opioid craving: desire-to-use VAS (SD)	78.9 (22.1)	73.7 (24.9)	76.7 (23.4)	76.5 (27.8)	77.6 (25.5)	77.0 (26.6)
Opioid craving: need-to-use VAS (SD)	77.4 (26.0)	75.8 (25.0)	76.7 (25.8)	76.2 (25.2)	75.5 (24.7)	75.9 (24.9)

Data presented as n (%) unless otherwise noted. Clinical opioid withdrawal scale (COWS);Standard deviation (SD); Sublingual buprenorphine/naloxone (SL BPN/NX); Subjective opioid withdrawal scale (SOWS); Visual analog scale (VAS)

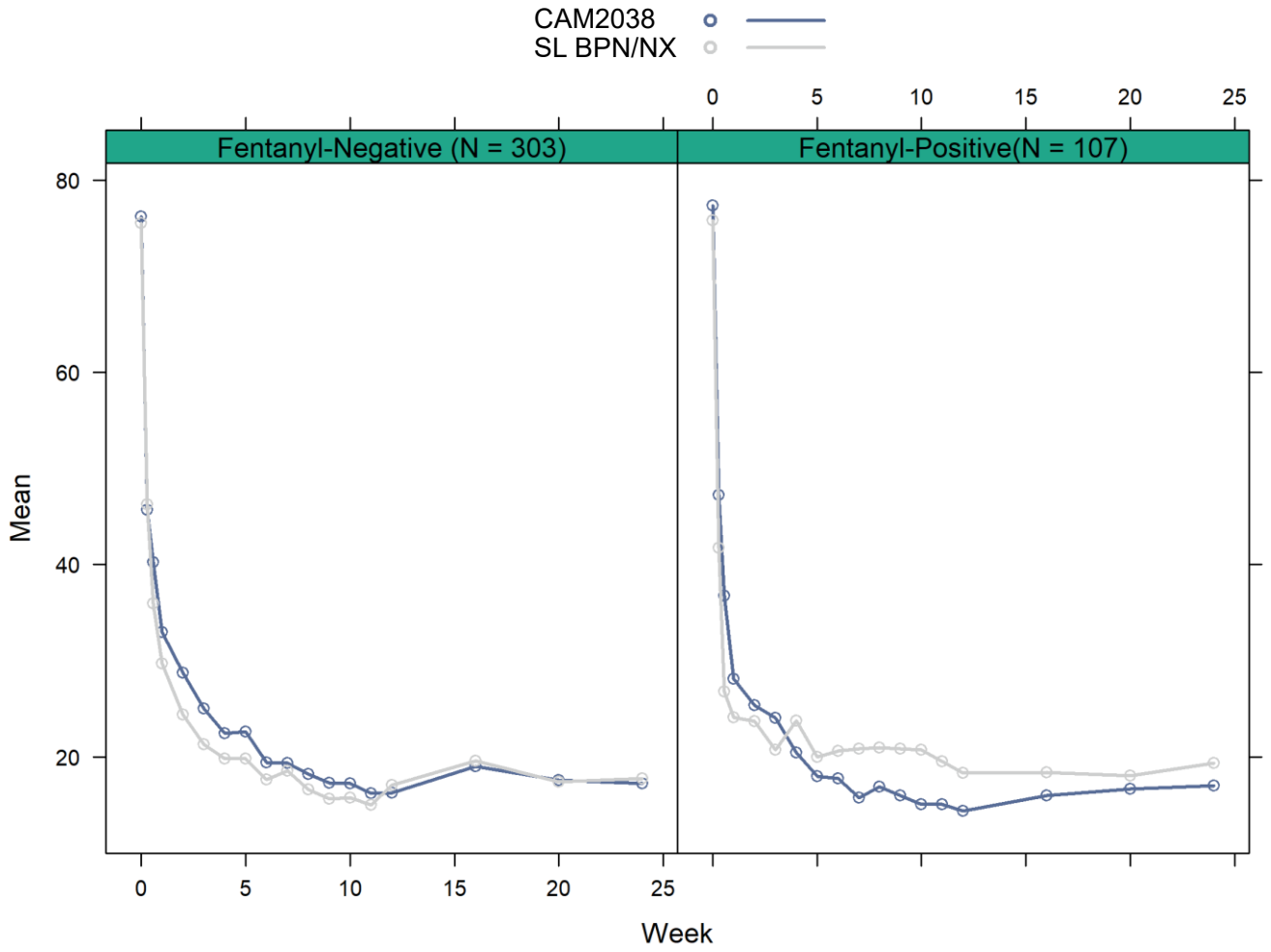
Mean Clinical Opioid Withdrawal Scale (COWS) total score over time in fentanyl-negative group and fentanyl-positive group



- For fentanyl-negative group, in both cohorts, opioid withdrawal, as evaluated by COWS, was suppressed from day 1 and throughout the study, including during transitions from weekly to monthly injections, without significant group differences.
- For fentanyl-positive group, opioid withdrawal was suppressed in both cohorts, however, COWS scores were lower for CAM2038 vs SL BPN/NX.

Sublingual buprenorphine/naloxone (SL BPN/NX)

Mean craving assessed by need to use VAS* by treatment week and treatment group in fentanyl-negative group and fentanyl-positive group



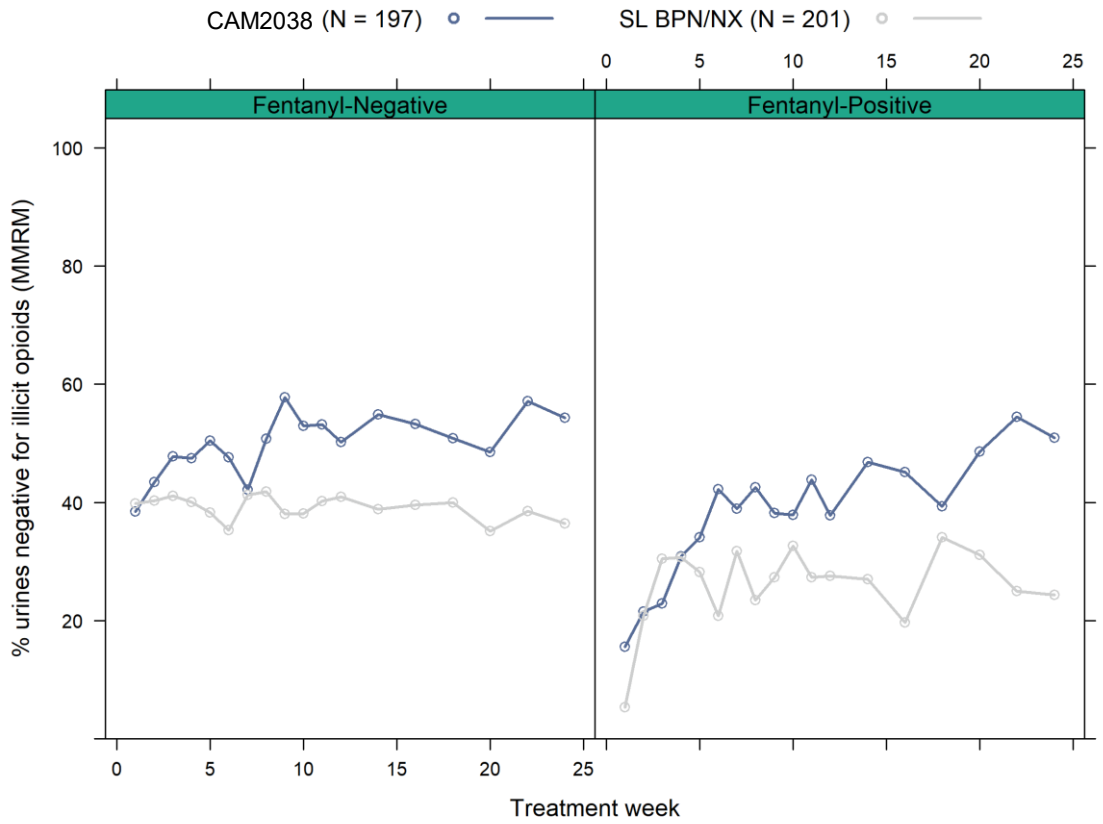
- For fentanyl-negative group, in both cohorts, ratings of opioid cravings were suppressed at treatment initiation on day 1 and throughout the study, including during transitions from weekly to monthly injections, without significant group differences.
- For fentanyl-positive group, ratings of opioid cravings were suppressed for both cohorts, however, ratings of opioid cravings were lower for CAM2038 vs SL BPN/NX.

*Need to Use (opioid cravings) were assessed using unipolar 100 mm VAS ("Since your last scheduled assessment visit, indicate your worst or strongest desire/need to use opioids, where 0 = No desire to use and 100 mm = Strongest possible desire, and from 0 = No need to use and 100 mm = Strongest possible need, respectively")

Sublingual buprenorphine/naloxone (SL BPN/NX)

Any Opioid Use

Weekly percentage of urine samples negative for any illicit opioids by treatment and fentanyl use at screening/ baseline (MMRM)



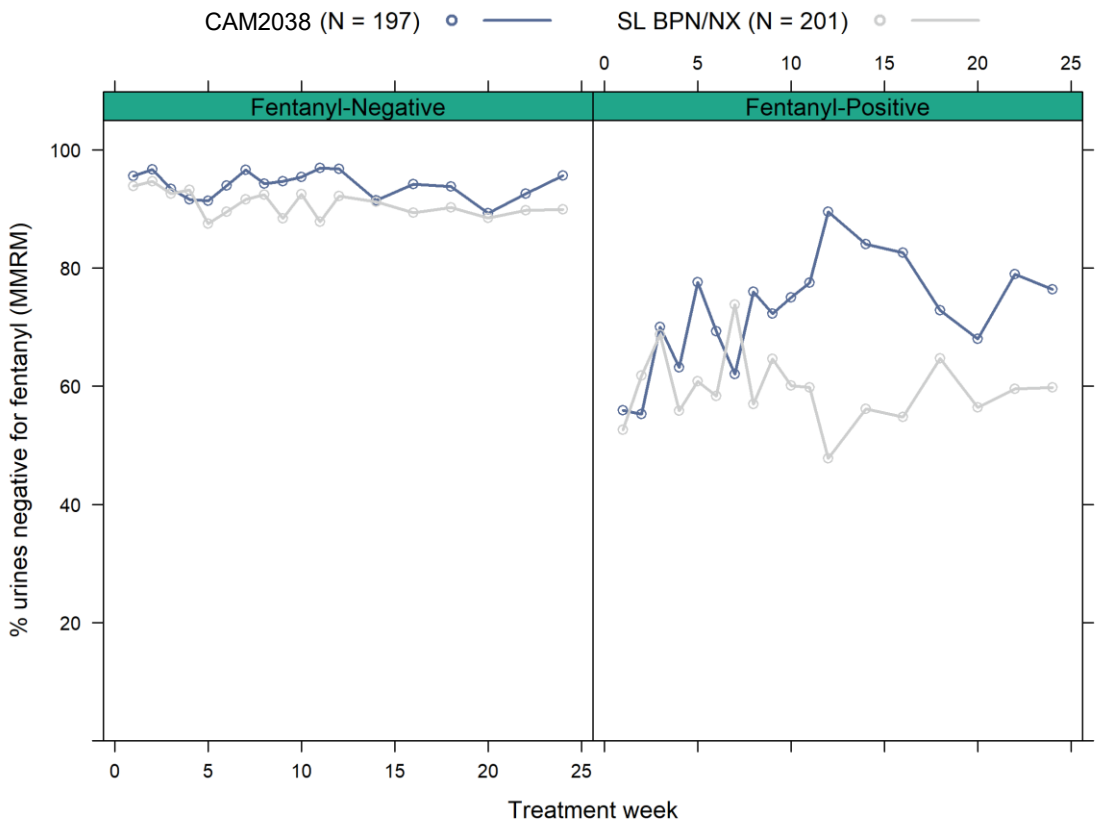
Sublingual buprenorphine/naloxone (SL BPN/NX)

Percent urine samples negative for any illicit opioids by fentanyl use at screening/baseline (weeks 1-24; not imputed)

Group	Treatment	Mean (%)	95% CI	p-value (ANOVA)
Fentanyl-negative	CAM2038 (N=139)	48.7	0.2, 18.6	0.05
	SL BPN/NX (N=156)	39.3		
Fentanyl-positive	CAM2038 (N=58)	34.8	-3.3, 24.6	0.13
	SL BPN/NX (N=45)	24.2		

Fentanyl Use

Weekly percentage of urine samples negative for fentanyl/norfentanyl by treatment and fentanyl use at screening/ baseline (MMRM)



Sublingual buprenorphine/naloxone (SL BPN/NX)

Percent urine samples negative for a) Fentanyl and b) Norfentanyl by fentanyl use at screening/baseline (weeks 1-24; not imputed)

Group	Treatment	Mean (%)	95% CI	p-value (ANOVA)
Fentanyl-negative	CAM2038 (N=139)	94.2	-2.5, 8.1	0.30
	SL BPN/NX (N=156)	91.4		
Fentanyl-positive	CAM2038 (N=58)	69.9	2.0, 20.1	0.01
	SL BPN/NX (N=45)	58.9		

Group	Treatment	Mean (%)	95% CI	p-value (ANOVA)
Fentanyl-negative	CAM2038 (N=139)	91.0	-0.9, 11.9	0.09
	SL BPN/NX (N=156)	85.5		
Fentanyl-positive	CAM2038 (N=58)	56.0	2.9, 24.6	0.01
	SL BPN/NX (N=45)	42.2		

Buprenorphine Dosing

Highest dose achieved week 1

Group	Dose*	CAM2038 (N=213)		SL BPN/NX (N=215)	
		n (N=151)	%	n (N=166)	%
Fentanyl-negative (N=317)	8mg	1	0.7	3	1.8
	16mg	93	61.6	110	66.3
	24mg	40	26.5	40	24.1
	Other	17**	11.2	13***	7.8
		n (N=62)	%	n (N=49)	%
Fentanyl-positive (N=111)	8mg	1	1.6	1	2.0
	16mg	41	66.1	34	69.4
	24mg	14	22.6	10	20.4
	Other***	6	9.7	4	8.2

*CAM2038 doses were converted to SL BPN/NX dose equivalents based on the following conversions: CAM2038 weekly 16, 24, and 32 mg was converted to SL BPN/NX daily doses of 8, 16, and 24 mg, respectively.

**One participant achieved a dose of CAM2038 8mg weekly and 16 were not dosed

***Not dosed

Highest dose achieved

Group	Dose* (SL BPN dose equivalents)	CAM2038 (N=213)		SL BPN/NX (N=215)	
		n (N=151)	%	n (N=166)	%
Fentanyl-negative	8mg	20	13.2	15	9.0
	16mg	75	49.7	83	50
	24mg	50	33.1	60	36.1
	32mg	6	4.0	8	4.8
		n (N=62)	%	n (N=49)	%
Fentanyl-positive	8mg	7	11.3	4	8.2
	16mg	28	45.2	24	49.0
	24mg	24	38.7	20	40.8
	32mg	3	4.8	1	2.0

*CAM2038 doses were converted to SL BPN/NX dose equivalents based on the following conversions: CAM2038 weekly 16, 24, 32 mg and CAM2038 monthly 64, 96 and 128 mg were converted to SL BPN/NX daily doses of 8, 16, and 24 mg, respectively. CAM2038 monthly 160mg was converted to SL BPN/NX 32 mg daily.

Summary of treatment-emergent adverse events (AEs)

Adverse event characteristic	Fentanyl-positive			Fentanyl-negative		
	SL BPN/NX N = 49	CAM2038 N = 62	Total N=111	SL BPN/NX N = 166	CAM2038 N = 151	Total N=317
Participants with any TEAEs	25 (51.0)	32 (51.6)	57 (51.3)	94 (56.6)	96 (63.6)	190 (59.9)
Number of TEAEs	155	147	302	407	326	733
Participants with serious AEs	3 (6.1)	0	3 (2.7)	10 (6.0)	5 (3.3)	15 (4.7)
Participants with AEs that led to drug discontinuation	0	0	0	3 (1.8)	7 (4.6)	10 (3.1)
Participants with suspected to be drug-related AEs	16 (32.7)	21 (33.9)	37 (33.3)	48 (28.9)	49 (32.5)	97 (30.6)
Participants with AEs that resulted in death	0	0	0	0	1 (0.7)*	1 (0.3)
Occurred in ≥5% of study participants	22 (44.9)	25 (40.3)	47 (42.34)	70 (42.2)	66 (43.7)	136 (42.9)
Injection-site pain	3 (6.1)	4 (8.2)	7 (6.3)	14 (9.3)	15 (9.9)	29 (9.1)
Headache	1 (2.0)	3 (6.1)	4 (3.6)	16 (10.6)	13 (8.6)	29 (9.1)
Constipation	6 (12.2)	5 (10.2)	11 (9.9)	10 (6.6)	11 (7.3)	21 (6.6)
Nausea	5 (10.2)	7 (14.3)	12 (10.8)	12 (7.9)	8 (5.3)	20 (6.3)
Injection-site pruritus	4 (8.2)	3 (6.1)	7 (6.3)	9 (6.0)	10 (6.6)	19 (6.0)
Injection-site erythema	3 (6.1)	3 (6.1)	6 (5.4)	9 (6.0)	9 (6.0)	18 (5.7)

- Three non-fatal accidental overdoses involving heroin were reported, all occurred in the fentanyl-negative SL BPN/NX group; 1 overdose occurred in the context of withdrawal after being jailed without study medication.
- There were no clinically meaningful differences between the treatments for SAEs; however, all SAEs in the Infections and Infestations System Organ Class occurred in the SL BPN/NX group, suggesting ongoing IV drug use. For fentanyl-negative group, this included acute hepatitis C (n = 1), cellulitis (n = 1), osteomyelitis (n = 1), pneumonia (n = 1), and sepsis (n = 1). For fentanyl-positive group, this included abscess (n = 1, limb; n = 1 subcutaneous), and localized infection (n = 1).
- With the exception of injection site AEs, the safety profile observed with CAM2038 was consistent with the known safety profile of SL BPN with no unexpected AEs observed.

*Participant was hit by a car and died; the death was assessed as unlikely related to the study drug

Conclusions

- In this diverse sample of participants seeking treatment for OUD, the subgroup with exposure to fentanyl prior to randomization exhibited markers of greater severity of illness at baseline (more heroin use, more co-occurring non-opioid drug use) and fewer opioid negative urine results during treatment.

- Consistent with previous post-hoc analyses of subgroups reporting heroin or intravenous drug use at baseline,[1,2] treatment with CAM2038 resulted in a greater percentage of urine samples negative for illicit opioids in participants with evidence of fentanyl use prior to randomization vs SL BPN/NX. These findings are consistent with the primary and secondary endpoints of the total study population from this Phase 3 study.[1]

- The long-acting weekly and monthly injectable BPN, CAM2038, may have an advantage over SL BPN/NX on illicit opioid use outcome among difficult-to-treat patient population, including those who test positive for fentanyl at treatment initiation.

- As these are post-hoc analyses from a randomized study, results should be interpreted with caution as further studies are needed to confirm the improved effectiveness of CAM2038 in these subgroups.

[1]Lofwall et al. Weekly and Monthly Subcutaneous Buprenorphine Depot Formulations vs Daily Sublingual Buprenorphine With Naloxone for Treatment of Opioid Use Disorder, A Randomized Clinical Trial. JAMA Internal Medicine. 2018;178(6):764-773; [2]Frost M, et al. Phase 3 trial comparing depot buprenorphine (CAM2038) to SL BPN/NX for OUD treatment: subanalysis among persons with heroin as the primary opioid of abuse. Presented at the 80th Annual Scientific Meeting of CPDD, June 13, 2018; San Diego, CA