INJECTABLE WEEKLY AND MONTHLY BUPRENORPHINE IN THE OUTPATIENT TREATMENT OF FENTANYL USERS WITH OPIOID USE DISORDER (OUD)

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DISCLOSURES

The study was funded and sponsored by Braeburn Inc.

Dr. Kim is an employee of Braeburn Inc.

The information presented today relates to the clinical data associated with CAM2038, an investigational product for the potential treatment of Opioid Use Disorder (OUD). The U.S. Food and Drug Administration (FDA) has granted tentative approval of CAM2038 (buprenorphine) extended-release weekly and monthly injections for the treatment of moderate to severe OUD in patients who have initiated treatment with a single dose of a transmucosal buprenorphine product or who are already being treated with buprenorphine.

With tentative approval, FDA has concluded that CAM2038 has met all required quality, safety and efficacy standards necessary for approval but is not eligible for marketing in the U.S. because of exclusivity considerations.

CAM2038 is approved by the European Medicines Agency as well as Australian Regulatory Agency under the brand name Buvidal.

CAM2038: INVESTIGATIONAL BUPRENORPHINE EXTENDED-RELEASE INJECTION FOR SUBCUTANEOUS USE

- Weekly or monthly formulations with multiple dose strengths
- Multiple subcutaneous injection sites (evaluated buttock, abdomen, arm, thigh)
- Low-volume (0.16mL to 0.64mL)
- Ready-to-use, pre-filled syringe
  - 23 gauge needle
- Stored at room temperature
- Administered by healthcare professional



4 Weekly Doses



3 Monthly Doses

Research

JAMA Internal Medicine | Original Investigation

Weekly and Monthly Subcutaneous Buprenorphine Depot Formulations vs Daily Sublingual Buprenorphine With Naloxone for Treatment of Opioid Use Disorder

A Randomized Clinical Trial

Michelle R. Lofwall, MD; Sharon L. Walsh, PhD; Edward V. Nunes, MD; Genie L. Bailey, MD; Stacey C. Sigmon, PhD; Kyle M. Kampman, MD; Michael Frost, MD; Fredrik Tiberg, PhD; Margareta Linden, PhD; Behshad Sheldon, BS; Sonia Oosman, BS; Stefan Peterson, PhD; Michael Chen, PhD; Sonnie Kim, PharmD

HS-11-421

JAMA Internal Medicine, 2018

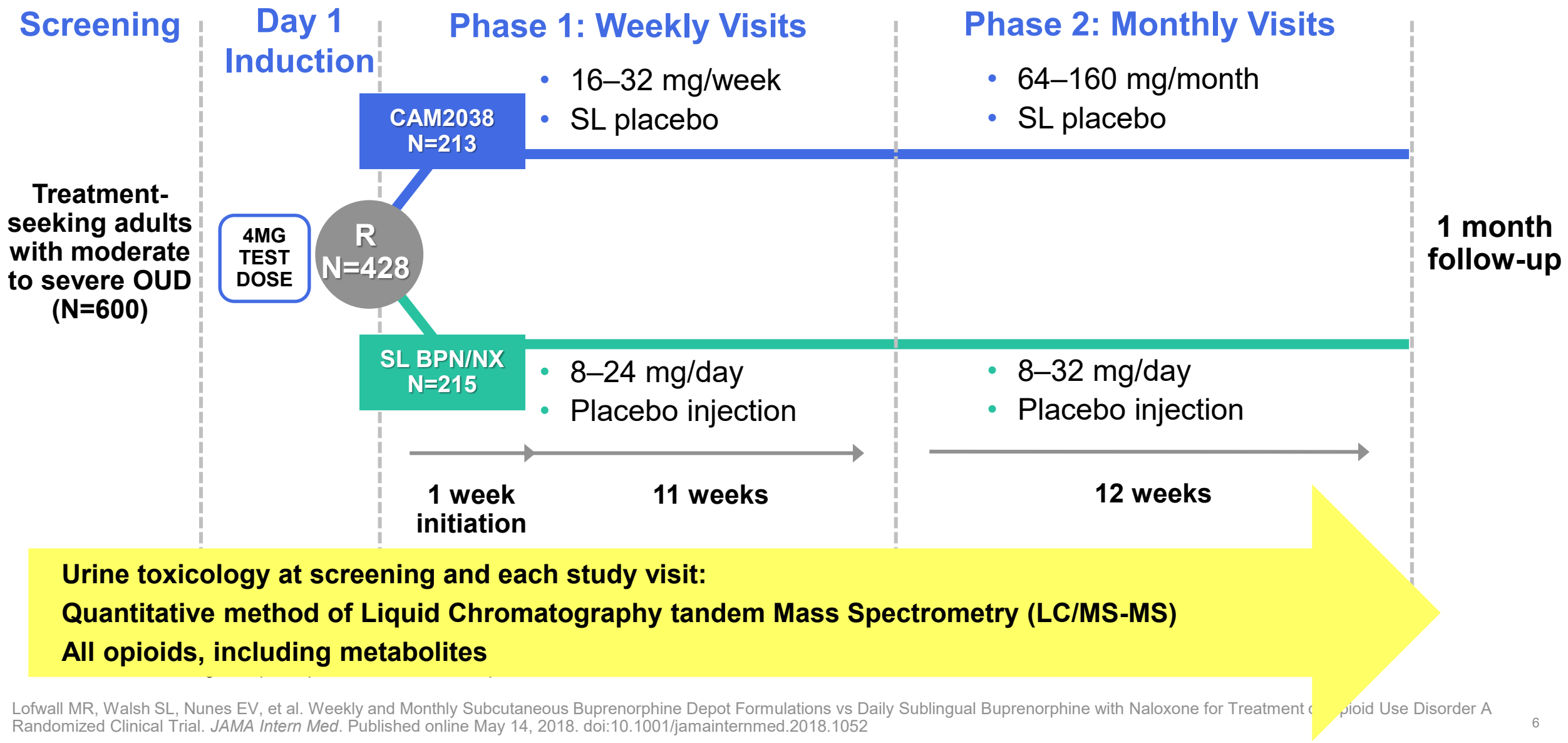
STUDY 421: PARTICIPANT DEMOGRAPHICS AND BASELINE CLINICAL CHARACTERISTICS (safety population)

	CAM2038 (N = 213), n (%)	SL BPN/NX (N = 215), n (%)
Age, years	39 (11.2)	38 (10.9)
Male	121 (57)	142 (66)
White	159 (75)	174 (76)
Employed full time or part time	76 (36)	72 (33)
Duration since Opioid Use Disorder diagnosis, years	4.3 (7.8)	4.7 (6.0)
History of injection opioid use at screening	114 (54)	110 (51)
Heroin as primary opioid of use	152 (71)	151 (70)
Fentanyl use	62 (29.1)	49 (22.8)
Non-opioid, poly-drug use at screening[a]	155 (73)	149 (69)

[a] For this study measure, 211 participants in the CAM2038 group were included; other substances=cocaine, amphetamines, PCP, THC, benzodiazepines

Lofwall MR, Walsh SL, Nunes EV, 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 Intern Med. Published online May 14, 2018. doi:10.1001/jamainternmed.2018.1052

STUDY 421: STUDY DESIGN



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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)
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)

HIGHEST DOSE ACHIEVED DURING FIRST WEEK OF INDUCTION AND THROUGHOUT THE STUDY PERIOD

Group		Buprenorphine Dose SL BPN equivalents* (mg)	CAM2038 (N=213)	SL BPN/NX (N=215)
			%	%
Fentanyl-Negative (N=317)	Week 1	8	0.7	1.8
		16	61.6	66.3
		24	26.5	24.1
	Study Period	8	13.2	9.0
		16	49.7	50
		24	33.1	36.1
		32	4.0	4.8

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

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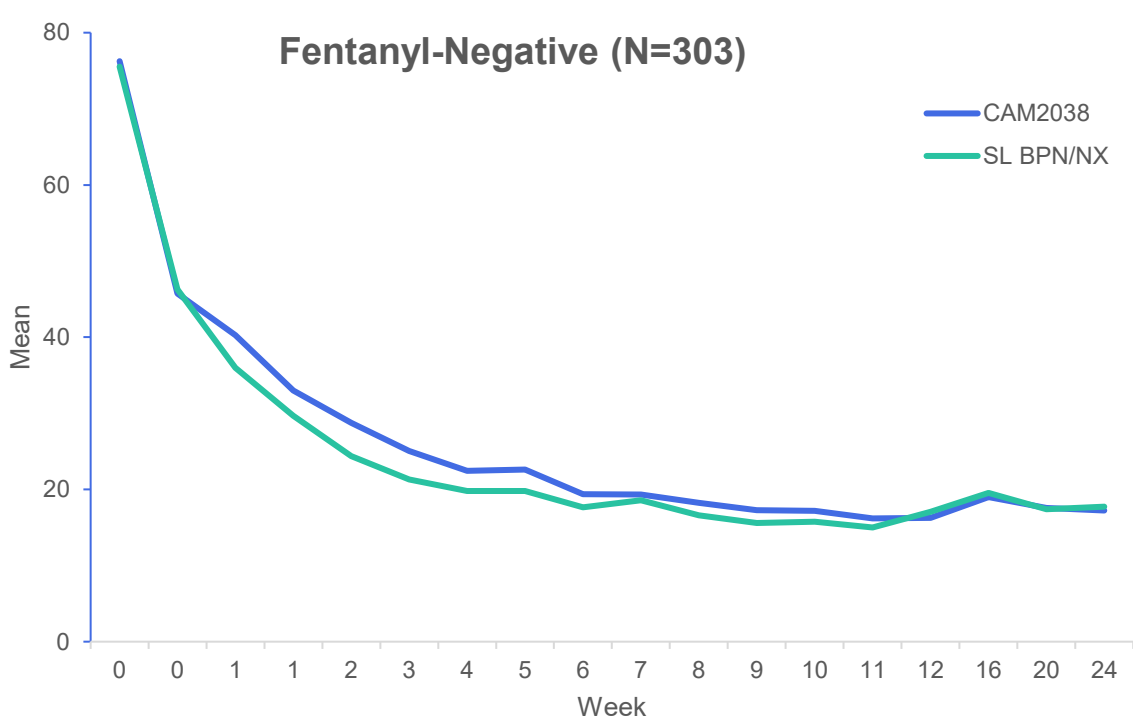
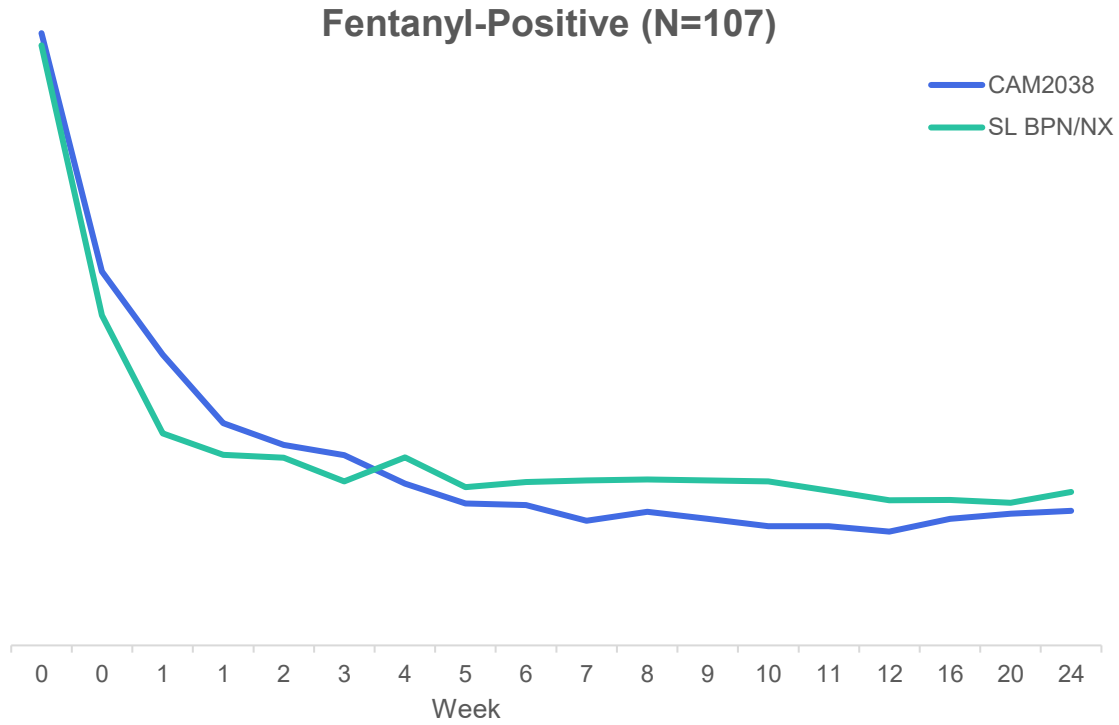
Mean Craving Assessed by Need to Use Visual Analog Scale (VAS)





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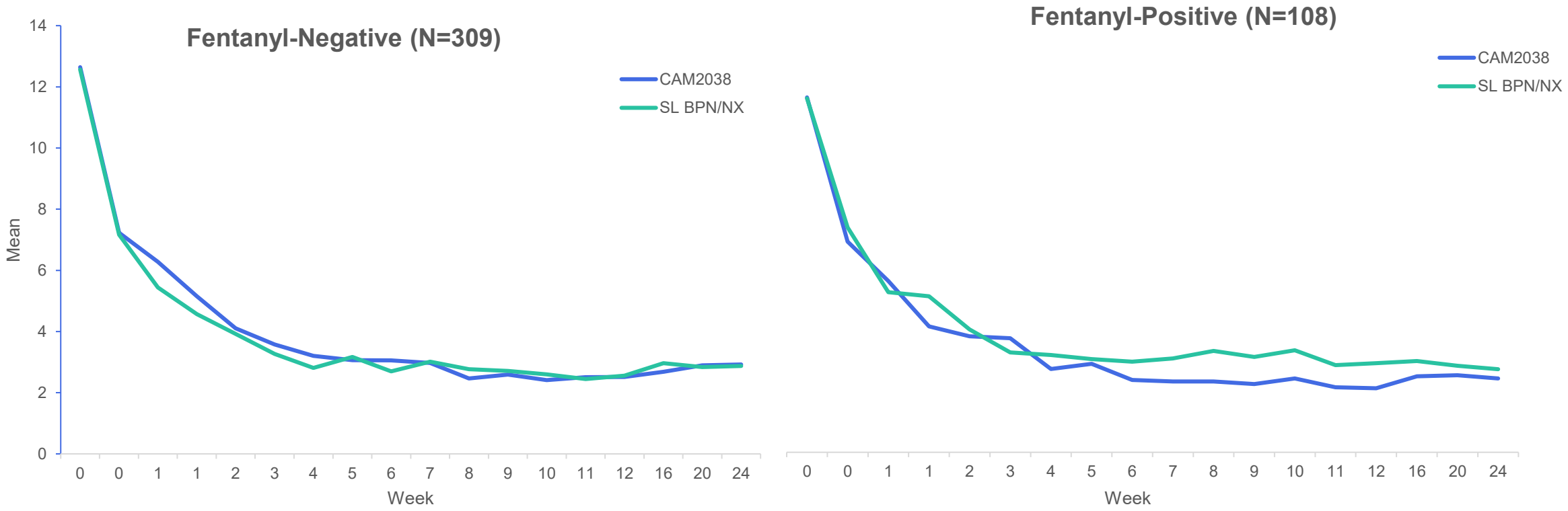
Mean Clinical Opioid Withdrawal Scale (COWS) Total Score



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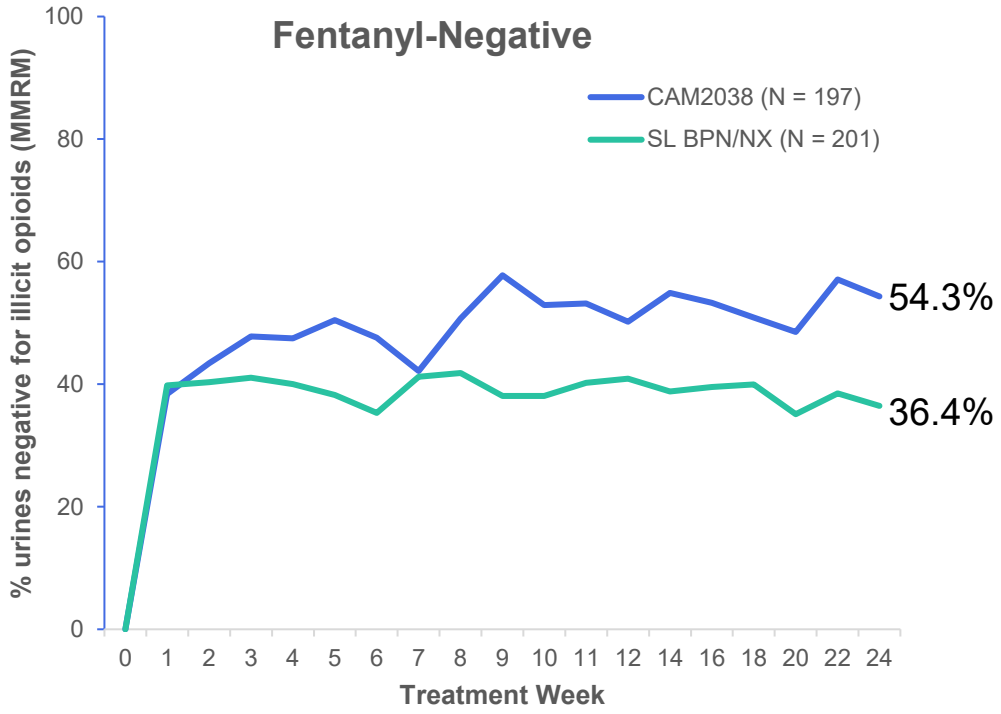
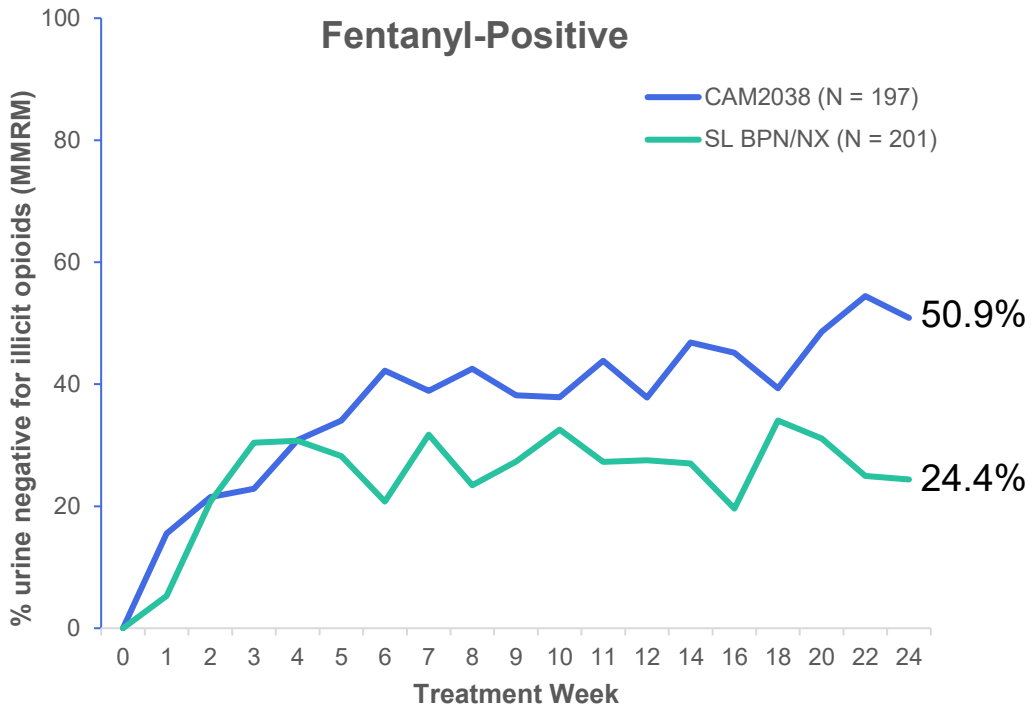
Weekly Percentage of Urine Samples Negative for Illicit Opioids in Patients with Positive Fentanyl Prior to Treatment Initiation





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SUMMARY OF TREATMENT-EMERGENT ADVERSE EVENTS (TEAEs)

	FENTANYL-POSITIVE			FENTANYL-NEGATIVE		
Adverse Event Characteristic	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	51.0	51.6	51.3	56.6	63.6	59.9
Participants with serious AEs	6.1	0	2.7	6.0	3.3	4.7
Participants with AEs that led to drug discontinuation	0	0	0	1.8	4.6	3.1
Death	0	0	0	0	0.7*	0.3
Occurred in ≥5% of study participants	44.9	40.3	42.34	42.2	43.7	42.9
Injection-site pain	6.1	8.2	6.3	9.3	9.9	9.1
Headache	2.0	6.1	3.6	10.6	8.6	9.1
Constipation	12.2	10.2	9.9	6.6	7.3	6.6
Nausea	10.2	14.3	10.8	7.9	5.3	6.3
Injection-site pruritus	8.2	6.1	6.3	6.0	6.6	6.0
Injection-site erythema	6.1	6.1	5.4	6.0	6.0	5.7

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

HS-11-421 Clinical Study Report Data on File

CONCLUSIONS

- Positive urines for fentanyl at baseline exhibit greater severity of illness compared to negative fentanyl exposure participants. (initially longer to stabilize based on urine toxicology)
- Compared to SL BPN/NX, CAM2038 resulted in higher proportions of participants with negative illicit opioid use by urine toxicology over time
  - Both fentanyl negative and fentanyl positive groups
- No differences in highest dose achieved between SL BPN/NX and CAM2038 groups
- No differences in highest dose achieved between fentanyl negative and positive groups
- Extended-release weekly and monthly injectable CAM2038, may have an advantage over daily SL BPN/NX on illicit opioid use outcome among difficult-to-treat patient population, including those who test positive for fentanyl at treatment initiation.
- **Limitations:**
  - Post-hoc clinical data analysis
  - Additional clinical studies are needed to confirm the results and impact of extended-release BPN injections in participants with fentanyl use

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Study volunteers

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