STATISTICAL ANALYSIS PLAN

PROTOCOL NO: HLAB-003

Human Laboratory Study of ASP8062 for Alcohol Use Disorder
Protocol Version No.: 6.0 Version Date: 13Jun2022

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1. ABBREVIATIONS

Abbreviation	Definition
ACQ-SF-R	Alcohol Craving Scale – Short Form
AE	Adverse event
AICc	Akaike Information Criterion corrected for finite samples
ALT	Alanine aminotransferase
ANCOVA	Analysis of covariance
AST	Aspartate aminotransferase
AUD	Alcohol Use Disorder
BAC	Blood alcohol concentration
CI	Confidence interval
CIWA-AR	Clinical Institute Withdrawal Assessment for Alcohol-revised
CrCl	Creatinine clearance
C-SSRS	Columbia-Suicide Severity Rating Scale
CTCAE	Common terminology criteria for adverse events
dL	Deciliter
DSM-5	Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EDMS	Electronic Data Management System
EOS	End of study
F	Fahrenheit
FDA	Food and Drug Administration
g	Gram
GGT	Gamma-glutamyl transferase
hr	Hour
ICH	International Conference on Harmonization
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
µg	Microgram
min	Minutes
MINI	MINI Neuropsychiatric Interview
mITT	Modified intention-to-treat
mL	Milliliter
mm	Millimeter
NHDD	No heavy drinking days
NIAAA	National Institutes on Alcohol Abuse and Alcoholism
oz	Ounce
PACS	Penn Alcohol Craving Scale
POMS	Profile of Mood State

Abbreviation	Definition
PROMIS	Patient Reported Outcomes Measurement Information System
PSNHDD	Percentage of subjects with no heavy drinking days
PSQI	Pittsburg Sleep Quality Index
PT	Preferred term
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SDU	Standard drinking unit
SOC	System Organ Class
THC	Tetrahydrocannabinol
TLFB	Timeline followback
TSH	Thyroid-stimulating hormone
ULN	Upper limit of normal
VAS	Visual analog scale
WHO	World Health Organization

2. INTRODUCTION

This statistical analysis plan (SAP) for Protocol No. HLAB-003, "Human Laboratory Study of ASP8062 for Alcohol Use Disorder" describes and expands upon the analytical plan presented in the protocol.

This document contains all planned analyses, reasons and justifications for these analyses for all study data. This plan also includes sample tables, figures, and listings that will be populated. The SAP will follow the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines as indicated in Topic E3 (Structure and Content of Clinical Study Reports), Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the FDA and ICH.

The following sources were used in preparation of this SAP:

- Protocol # HLAB-003, Protocol Version No.: 6.0; Version Date: 13 Jun 2022
- ICH Guidance Topics E9, E3 and E8

3. PROTOCOL SUMMARY

3.1. Study Objectives

3.1.1. Primary

The primary objective of this study is to evaluate the effects of ASP8062, 25 mg once a day and matched placebo, on alcohol cue-elicited alcohol craving during a human laboratory paradigm after 2 weeks of daily dosing among subjects with moderate to severe alcohol use disorder (AUD) as confirmed by the Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition (DSM-5™).

3.1.2. Secondary

Secondary objectives include evaluation of ASP8062, 25 mg once a day, and matched placebo on reduction of alcohol consumption, alcohol craving, cigarette smoking (among smokers) and nicotine use (among nicotine users), mood, sleep, alcohol use negative consequences, study retention, and safety and tolerability throughout the last 4 weeks of the treatment phase of the study.

3.2. Study Design

This study is a 2-arm, double-blind, randomized, placebo-controlled, parallel group, 3-site study designed to assess the effects of ASP8062 as compared with placebo on responses to *in vivo* alcohol cue exposure in the human laboratory setting. After signing informed consent, subjects will be screened for eligibility and have other baseline assessments. Screening is permitted over a 14-day period and most baseline assessments will be performed on the day of randomization. Assessments include alcohol breathalyzer test (before signing consent), medical history, physical examination, weight, vital signs, electrocardiogram (ECG), drinking history by the timeline follow-back (TLFB) method, Clinical Institute Withdrawal Assessment for Alcohol-revised (CIWA-AR), prior medication use, MINI neuropsychiatric interview, urine drug test, smoking quantity frequency and nicotine use interview, clinical laboratory tests including chemistry, hematology, medical urinalysis, alcohol craving responses during a baseline cue reactivity session, Columbia Suicide Severity Rating Scale (C-SSRS), drinking goal, Penn Alcohol Craving Scale (PACS), Pittsburg Sleep Quality Index (PSQI), PROMIS Alcohol Negative Consequences short form, Profile of Moods State (POMS), Hyperkatifeia Scale and confirmation that subjects are treatment seeking and desire a reduction or cessation of drinking. Women of child-bearing potential will have a pregnancy test.

If eligible for the study, 60 subjects will be randomized using a stratified permuted block randomization procedure with “clinical site” as the stratification variable in an approximate 1:1 ratio (targeting 30 subjects per group) to receive either ASP8062 25 mg once daily or matched placebo for 6 weeks.

Subjects will be seen in the clinic at screening, at randomization and 5 other times during the study. A final follow-up telephone interview will occur ~2 weeks after the end of study in-clinic visit. Two cue reactivity sessions will be conducted. The first will be during screening (named pretreatment session) and the second will be after two weeks of investigational product

administration at Study Week 3. During these cue sessions, subjects will be presented with water, followed by alcohol and will be asked to respond to 4 individual visual analog scales (VAS) items assessing alcohol craving and 1 item assessing beverage liking. Other assessments during the treatment period include TLFB, clinical laboratory tests, blood for serum levels of study drug for determining study drug compliance, vital signs, ECG, concomitant medications, CIWA-AR, C-SSRS, pregnancy test, male and female birth control methods, adverse events (AEs), PACS, smoking quantity/frequency, PSQI, and POMS. The end of study visit will include the other assessments performed during the treatment phase and an Exit Interview, PROMIS questionnaire, and a treatment referral.

Study assessments and procedures will be performed at the visits and time points outlined in the Schedule of Assessments (**Table 1**).

Table 1: Schedule of Assessments

Study Phase	**Screening**	**Treatment**					**End of Study[a]**	**Follow-up Call**
Clinic Visit #	**1**	**2**	**3**	**4**	**5**	**6**	**7**	
Study Week (Days)[b]	**-2 to -1 (-14 to -1)**	**1 (1 to 7)**	**2 (8 to 14)**	**3 (15 to 21)**	**4 (22 to 28)**	**5 (29 to 35)**	**7 (43 to 49)**	**9 (57 to 63)**
Informed Consent	X							
Alcohol Breathalyzer	X	X	X	X	X	X	X	
Urine Drug Test[c]	X	X	X	X	X	X	X	
Locator Form	X	Update	Update	Update	Update	Update	Update	
Demographics	X							
Medical History	X	Update						
Physical Exam	X	Update						
Body Weight	X				X		X	
MINI	X							
C-SSRS		X	X	X	X	X	X	
Clinical Chemistry[d]	X				X		X	
Hematology[e]	X				X		X	
Medical Urinalysis[f]	X				X		X	
Pregnancy Test	X	X					X	
Birth control methods (all subjects)	X	Update	Update	Update	Update	Update	Update	

Study Phase	**Screening**	**Treatment**					**End of Study[a]**	**Follow-up Call**
Clinic Visit #	**1**	**2**	**3**	**4**	**5**	**6**	**7**	
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Vital Signs[g]	X	X	X	X	X	X	X	
Eligibility Checklist	X	X						
Drinking Goal	X							
ECG	X				X		X	
Prior and Concomitant Meds	X	X	X	X	X	X	X	X
CIWA-AR	X	X	X	X	X	X	X	X
Screening Cue Reactivity Session: VAS Scales	X							
Randomization		X (Day 1)						
Blood for Drug Concentration					X		X	
Drug compliance/ accountability/ Review AiCure		Dispense Day 1	X	X	X	X	X	
AEs (open ended question)		X	X	X	X	X	X	X
Brief Telephone Interview[h]		once during the week	once during the week	As needed if the subject misses a clinic visit				
Take Control		X	X	X	X[i]	X	X	
Treatment Cue Reactivity Session: VAS Scales				X				

Study Phase	**Screening**	**Treatment**					**End of Study[a]**	**Follow-up Call**
Clinic Visit #	**1**	**2**	**3**	**4**	**5**	**6**	**7**	
Study Week (Days)[b]	**-2 to -1 (-14 to -1)**	**1 (1 to 7)**	**2 (8 to 14)**	**3 (15 to 21)**	**4 (22 to 28)**	**5 (29 to 35)**	**7 (43 to 49)**	**9 (57 to 63)**
TLFB	X	X	X	X	X	X	X	
Brief Drinking Questionnaire	as needed							
Exit Interview							X	
ACQ-SF-R	2X pre/post cue session			2X pre/post cue session				
PACS		X	X	X	X	X	X	
Cigarette smoking quantity/frequency and nicotine use		X				X	X	
PSQI		X				X	X	
POMS		X				X	X	
PROMIS Alcohol Negative Consequences		X					X	
Hyperkatifeia Scale		X						
Treatment Referral							X	
Follow-Up Telephone Interview								X
Final Subject Disposition								X

[a] EOS - end of study. These assessments are to be done at Week 7 or if the subject discontinues early and agrees to a final clinic visit.

[b] Within each study week, there should be a least two days elapsed since the visit in the prior week.

[c] Test for opiates (i.e., morphine test), cocaine, amphetamines, methamphetamine, THC, buprenorphine, methadone, benzodiazepines, oxycodone, barbiturates, 3,4-methylenedioxy-methamphetamine (MDMA – also known as ecstasy), and EtG.

[d] Creatinine, urea nitrogen, total bilirubin, ALT, AST, alkaline phosphatase, GGT, albumin, total cholesterol, triglycerides, sodium, potassium, and chloride

[e] Complete blood cell count including RBC, WBC, hemoglobin, hematocrit, and platelets.

[f] A dipstick urinalysis will be performed that tests for specific gravity, ketones, pH, protein, blood, glucose, nitrites, bilirubin, and leukocyte esterase. If the dipstick is positive for blood, leukocyte esterase, or protein, then a microscopic analysis will be performed at the discretion of the investigator.

[g] Sitting blood pressure and heart rate.

[h] Telephone calls after the Week 1 and 2 in clinic visits will collect AEs, concomitant medications, CIWA-AR, and give a drug compliance reminder. The call during Week 2 should be several days before the cue session to remind the subject of the planned visit.

[i] Two modules will be viewed this week.

3.3. Study Endpoints

3.3.1. Primary Efficacy Endpoint

The primary efficacy endpoint is the "strength" of alcohol craving VAS score (item 1 below) upon presentation of the first alcohol cue at Week 2 – after one week of investigational product treatment.

Confirmatory secondary endpoints include the VAS score for the other 3 VAS scales (items 2 through 4 below) for the first alcohol cue and the average score of the 4 VAS craving items; and the difference score (alcohol craving VAS scores minus the water craving VAS score). Tbeverage liking VAS item is also a confirmatory secondary endpoint. The 4 VAS craving items in the order of presentation are:

1. How strong is your craving to drink alcohol? - note this is the primary efficacy endpoint.
2. Having a drink would make things just perfect.
3. If I could drink alcohol now, I would drink it.
4. It would be hard to turn down a drink right now.

The beverage liking item is: How much did you like the beverage just given to you?

3.3.2. Secondary Efficacy Endpoints

Secondary efficacy endpoints will be analyzed over the last 4 weeks of the treatment period of treatment.

1. Percentage of subjects with no heavy drinking days. A "heavy drinking day" is 4 or more drinks per drinking day for women and 5 or more drinks per drinking day for men.
2. Percentage of subjects abstinent from alcohol
3. Percentage of subjects with at least a WHO 2-level decrease in alcohol consumption
4. Percentage of subjects with at least a WHO 1-level decrease in alcohol consumption
5. Percentage of days abstinent per week
6. Percentage of heavy drinking days per week
7. Percentage of very heavy drinking days per week. A "very heavy drinking day" is 8 or more drinks per drinking day for women and 10 or more drinks per drinking day for men.
8. Weekly mean number of drinks per week
9. Weekly mean drinks per drinking day
10. Cigarettes smoked per week among smokers
11. Percentage of subjects with no nicotine use among those reporting nicotine use at baseline
12. Alcohol craving score (PACS)
13. Sleep quality (PSQI) score

14. Profile of Mood States (POMS) score
15. PROMIS Alcohol Negative Consequences Score

3.3.3. Safety Endpoints

1. Vital signs
2. Body weight
3. Clinical laboratory parameters
4. BAC by breathalyzer
5. Urine drug tests
6. AEs
7. ECG results
8. CIWA-AR scores
9. Frequency of subjects with suicidal ideation at any time during the treatment period (C-SSRS)
10. Concomitant medication use
11. ACQ-SF-SR score (pre- and post-cue response sessions)

3.3.4. Compliance

Compliance will be assessed using the AiCure smart phone application and by tablet counts of returned blister packs at regular clinic visits. In addition, blood will be collected to determine plasma levels of ASP8062 and its metabolites. Compliance will be calculated as the percentage of investigational products taken as prescribed and by the total amount of study drug consumed. Participation in study visits will be evaluated as the percentage of subjects with complete drinking data. Compliance determined by ASP8062 plasma levels will be reported as number and percentage of subjects with a level above the limit of detection at each time point.

4. DEFINITION OF ANALYSIS SETS

The study analysis populations will consist of the following:

Modified Intention-to-Treat (mITT) Analysis Set: The mITT set is defined as subjects randomized to participate in the study that took at least one dose of investigational product and had a non-missing VAS craving primary endpoint.

Evaluable Analysis Set: The evaluable analysis set for the secondary endpoints is defined as those subjects randomized to the study who took at least 1 tablet per day for at least 80% of days in Weeks 1-6.

Safety Analysis Set: The safety analysis set includes all subjects who took at least one dose of investigational product.

The analysis of the primary and confirmatory efficacy endpoints will be conducted on both the mITT and evaluable analysis sets. All secondary endpoint analyses will be performed on the mITT set. Weekly percentage heavy drinking days, mean number of drinks per week, and PACS scores will also be performed on the evaluable analysis set. Safety analyses will be conducted on the safety analysis set.

5. ASSSESSMENT AND JUSTIFICATION OF STUDY ENDPOINTS

5.1. Alcohol Craving Visual Analog Scales

Alcohol craving in response to a water and typical alcohol beverage cue is assessed using 4 individual VAS items adapted from the ACQ (Singleton-1994).

The VAS craving scale items include in the following order:

1. How strong is your craving to drink alcohol?
2. Having a drink would make things just perfect.
3. If I could drink alcohol now, I would drink it.
4. It would be hard to turn down a drink right now.

Anchors (scores) for items 1, 3, and 4 are: Strongly Disagree (0) to Strongly Agree (20).

Anchors (scores) for question 2 are: None (0) to Extremely Strong (20).

There will be no imputation for missing values.

5.2. Alcohol Consumption Endpoints

5.2.1. Daily Quantity of Alcohol Consumption

Drinking will be assessed using the TLFB methodology and Form 90 structured assessment pattern chart. The TLFB is a semi-structured interview that provides estimates of the daily quantity of alcohol consumption during specified time periods. It uses a calendar prompt and a number of other memory aids (e.g., holidays, payday, and other personally relevant dates) to facilitate accurate recall of drinking or other drug use during the target period. The procedure has been widely used in clinical and research contexts. It has demonstrated adequate levels of reliability and validity when administered as an in-person interview, over the telephone, and when administered via computer (Carey-1997, Sobell et al-1988, Sobell et al-1996).

If a subject is withdrawn from the study early and is no longer participating in clinic visits or providing TLFB drinking data but is willing to be contacted by phone at the week most proximal to dropout, then they will be asked about any drinking and heavy drinking during the time since last contact. Phone calls will continue until the end of the treatment period, as deemed acceptable by the patient. The two questions cover whether the subject had any heavy drinking days or drinking days during the period covered and will be used to capture drinking data in the absence of individual daily TLFB drinking data.

5.2.2. Drinking Days

A drinking day is one calendar day in which the subject reported any alcohol consumption (i.e., > 0 standard drinking units [SDUs]). A standard drink contains approximately 0.6 fluid ounces (oz) of pure alcohol. The data given by the subjects on amount and type of alcoholic beverage(s) consumed will be converted to SDUs. Standard drink unit definitions are provided in **Table 2**.

Table 2: Standard Drink Unit Definitions

For Beer (~ 5% alcohol), the approximate number of SDUs in: • 12 oz = 1.0 • 16 oz = 1.3 • 24 oz = 2.0 • 40 oz = 3.3 For malt liquor (~ 7% alcohol), the approximate number of SDUs in**:** • 12 oz = 1.4 • 16 oz = 1.9 • 22 oz = 2.6 • 40 oz = 4.7
For table wine (~ 12% alcohol), the approximate number of SDUs in: • 750 mL bottle = 25oz = 5.0 • 5 oz glass = 1.0 • 10 oz glass = 2.0
For 80 proof spirits (~ 40% alcohol), or hard liquor, the approximate number of SDUs in: • 1.5 oz (mixed drink) = 1.0 • 16 oz (pint) = 8.5 • 25 oz (a fifth) = 17.0 • 1.75 L (59 oz) = 39.0

5.2.3. Very Heavy and Heavy Drinking Day

A very heavy drinking day is defined as 8 or more drinks per day for a woman, and 10 or more for men. A heavy drinking day is defined as a day with 5 or more drinks (SDUs) for males and 4 or more drinks (SDUs) for females.

5.2.4. Days at Risk

If a subject is being treated at an inpatient facility, is incarcerated, or otherwise under confinement, the days spent in under these conditions is considered a reduction in the days at risk for drinking and is deducted from the denominator in calculations of rates of drinking days.

5.2.5. Percentage of Subjects with No Heavy Drinking Days and Percentage of Subjects Abstinent from Alcohol

The percentage of subjects with no heavy drinking days is the number of subjects that have no heavy drinking days during the period of interest divided by the number of subjects with at least one day of non-missing drinking data during the period of interest, multiplied by 100.

The percentage of subjects abstinent from alcohol is calculated similarly, except the numerator is the number of subjects that have no drinking days during the period of interest.

5.2.6. Weekly Percentage of Heavy Drinking Days and Weekly Percentage of Days Abstinent

Weekly percentage of heavy drinking days is the number of heavy drinking days in a 7-day period divided by 7 then multiplied by 100. The TLFB permits capturing data in a subsequent visit if a visit is missed; however, if fewer than 7 days are observed then the denominator is the number of days observed in the 7-day period. At least 3 days in a week must be observed; otherwise, the week is considered missing.

Weekly percentage of days abstinent is similarly calculated by using the number of days abstinent instead of the number of heavy drinking days.

5.2.7. Weekly Mean Number of Drinks and Weekly Mean Number of Drinks per Drinking Day

Weekly mean number of drinks is the sum of SDUs calculated to the tenths over 7 calendar days divided by the number of days with non-missing data. The quotient is multiplied by 7. At least 3 days in a week must be observed; otherwise, the week is considered missing.

Weekly mean number of drinks per drinking days utilizes the same numerator, and the denominator is the number of days with greater than 0 SDUs. Weeks where all days within the week are abstinent are assigned a value of 0 for weekly drinks per drinking day.

5.2.8. World Health Organization Drinking Risk Categorical Scale

The WHO has developed a drinking risk categorical scale that can be used in a responder analysis approach to assess clinically relevant decreases in alcohol consumption (Aubin et al-2015). Two dichotomous endpoints will be analyzed: WHO 1-level and WHO 2-level decrease in alcohol consumption. The WHO 1-level and 2-level decrease endpoints are the percentage of subjects experiencing at least a 1-level or 2-level decrease in WHO levels of alcohol consumption, respectively, from the level at baseline (the period including the 28 days before screening) to the level during the last 4 weeks of the maintenance phase (Study Weeks 2-5). The WHO levels of average alcohol consumption per day are as follows:

	Males	**Females**
Low Risk	1 to 40g	1 to 20g
Medium Risk	41 to 60g	21 to 40g
High Risk	61 to 100g	41 to 60g
Very High Risk	101+g	61+g

where 14g = 1 SDU (WHO-2000). In computing the alcohol consumption level, average drinks per day will be used, computed as the sum of all drinking in the 28 day period divided by the number of days with non-missing drinking data in that period. Abstinent subjects will be included in a separate "Abstinent" category. A subject must have at least 1 week of data during the last 4 weeks of the maintenance phase to be considered non-missing.

5.3. Alcohol-Related Craving, Consequences, and Withdrawal

Alcohol-related craving is measured using the ACQ-SF-R scale and PACS; alcohol-related consequences are measured using the PROMIS Alcohol Negative Consequences scale; and alcohol-related withdrawal is measured using the CIWA-AR scale. The PACS and PROMIS

Alcohol Negative Consequences are used as efficacy endpoints, while the ACQ-SF-R and CIWA-AR scales are safety endpoints.

The ACQ-SF-R contains 12-items adapted from the 47-item ACQ-NOW developed by Singleton et al (1994) to assess craving for alcohol among alcohol users in the current context (right now). Items 3, 8, and 11 are reverse keyed. A general craving index is derived by summing all items and dividing by 12. If an item is missing, then the number of items is reduced by the number missing, and the sum is only the sum of the answered items. At least 10 items must be endorsed for the general craving index of ACQ-SF-R to be considered non-missing (i.e., scored).

The PACS is a five-item self-administered instrument for assessing craving (Flannery-1999). Frequency, intensity, and duration of thoughts about drinking are assessed along with ability to resist drinking. The final item asks the responder to provide an average rating of his/her craving over the course of the past week. The questions on the PACS use descriptors coupled with numerical ratings ranging from 0 to 6. The items are summed for a total score.

PROMIS Alcohol Negative Consequences scale is for negative consequences from alcohol use. The short form of the PROMIS Alcohol Negative Consequences questionnaire will be used to assess outcomes of alcohol use over the past 30 days (Pilkonis-2013).

The 7 PROMIS items include:

- Drinking created problems between me and others
- I disappointed others when I drank
- I was unreliable after I drank
- Others complained about my drinking
- I used poor judgment when I drank
- I said or did embarrassing things when I drank
- I had trouble getting things done after I drank

Each item is rated on a 5 point scale including: Never (1), Rarely (2), Sometimes (3), Often (4), and Almost Always (5) for the past 30 days. A subject's total score is converted to a T-score using scoring table provided by NIH PROMIS.

The CIWA-AR modified telephone version is an adaptation for telephone administration of the CIWA-AR a brief 10-item measure used to provide a quantitative index of the severity of the alcohol withdrawal syndrome (Sullivan et al-1989). The CIWA-AR has been used both in clinical and research applications and has demonstrated both reliability and validity (Sellers et al-1992, Stuppaeck et al-1994). The total score is the sum of the individual item scores. Since this is an interview scale, no missing items are anticipated. A score ≥ 10 is considered an indication that the subject is undergoing alcohol withdrawal.

5.4. Mood

Mood will be measured with the POMS, while negative emotional state will be measured using an exploratory measure of hyperkatifeia.

The POMS measures dimensions of affect or mood (McNair and Heuchert-2005). It consists of 65 adjectives to which the subject responds according to a 5-point scale ranging from "not at all (0)" to "extremely (5)." Six subscale scores will be computed for items grouped as follows: Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigor-Activity, Fatigue-Inertia, and Confusion-Bewilderment. A Total Mood Disturbance score will also be computed which consists of the sum of Tension-Anxiety, Depression-Dejection, Anger-Hostility, Fatigue-Inertia, and Confusion-Bewilderment scores then subtracting the Vigor-Activity subscale score. A missing value within a subscale will be replaced by the average score of the answered items within the subscale; if 2 or more items within a subscale are missing then the entire subscale is missing (Macefield et al-2010).

Hyperkatifeia is defined as a greater intensity of negative emotional/motivational signs and symptoms during withdrawal from drugs of abuse in the withdrawal/negative affect stage of the addiction cycle (Koob-2021). Hyperkatifeia or negative emotional state is considered to be one of stages of addiction in the context of drug withdrawal (Koob and LeMoal-1997, Koob-2019). NIAAA has developed a 24-item self-report Hyperkatifeia Scale to capture negative emotionality after stopping alcohol drinking that will be assessed for the first time in this study of heavy drinkers with a diagnosis of moderate to severe AUD. The items address four measures associated with negative emotional state including stress/anxiety, depression, stress, irritable and pain.

One difference between this scale and other negative emotional state scales is the pain questions. Pain may be particularly important in AUD as there is a positive association between pain severity and a higher risk for AUD (Lawton and Simpson-2009, Edlund et al-2013). Also, physical pain appears to be a significant predictor of alcohol use and heavy alcohol use and relapse to drinking after a period of abstinence (Larson et al-2007, Caldeiro et al-2008, Witkiewitz et al-2015).

5.5. Sleep Quality

Sleep quality will be measured using the PSQI. The PSQI is a 19-item questionnaire (Buysse et al-1989). The addition of all the scores permits an analysis of the subject's overall sleep experience in the past 30 days. The lower the overall score, the better the person sleeps. A score ≥ 5 is indictive of a sleep disturbance. If any of the items is missing, then the entire form is missing for that evaluation (PSQI website).

5.6. Cigarette Smoking Quantity-Frequency and Nicotine Use Questionnaire

A smoking quantity frequency and nicotine use interview will include 3 questions to assess nicotine use via cigarette smoking or via other products during the study: 1) Over the past week, on how many days did you smoke cigarettes?; 2) On the days you smoked during the past week, how many cigarettes did you smoke on average?; and 3) Over the past week, on how many days did you use other nicotine products (ex. chew, cigars, cigarellos, e-cigarettes, vape, gum, patch, etc...)? At baseline subjects that answer "0" to question #1 are considered non-smokers for the study. Cigarettes per week is the answer to question #1 multiplied by the answer to question #2. At baseline, subjects who report smoking (question #1) or the use of other nicotine product (question #3) will be considered nicotine users. The responses to questions #1 and #3 will be

used to calculate the percentage of subjects abstinent from nicotine use among nicotine users. No imputation for missing values will be used.

6. HYPOTHESES TO BE TESTED

6.1. Primary Efficacy Endpoint

Subjects treated with ASP8062 will report significantly lower VAS alcohol craving ratings in response to the *in vivo* alcohol cue during the treatment human laboratory cue session than placebo-treated subjects.

The hypotheses for the confirmatory secondary endpoints for the cue reactivity sessions are the same as for the primary endpoint.

6.2. Secondary Efficacy Endpoints

It is hypothesized that, during the last 4 weeks of the treatment period, ASP8062 as compared to the placebo, will:

1. Increase the percentage of subjects with no heavy drinking days. A "heavy drinking day" is 4 or more drinks per drinking day for women and 5 or more drinks per drinking day for men.
2. Increase the percentage of subjects abstinent from alcohol
3. Increase the percentage of subjects with at least a WHO 2-level decrease in alcohol consumption
4. Increase the percentage of subjects with at least a WHO 1-level decrease in alcohol consumption
5. Increase the percentage of days abstinent per week
6. Decrease the percentage of heavy drinking days per week
7. Decrease the percentage of very heavy drinking days per week
8. Decrease the weekly mean number of drinks per week
9. Decrease the weekly mean drinks per drinking day
10. Decrease the weekly mean cigarettes smoked per week among smokers
11. Increase the percentage of subjects abstinent from nicotine use among subjects who used any nicotine products in the week before randomization
12. Decrease the mean alcohol craving score (PACS)
13. Decrease the mean PSQI score
14. Decrease total mood disturbance (POMS)
15. Decrease in alcohol negative consequences (PROMIS)

7. SAMPLE SIZE CONSIDERATIONS

Analysis of covariance with clinical site and baseline cue as the covariates will be used to model the primary outcome – the VAS craving score for the alcohol cue. Statistical power was estimated using [PASS 13] with the following parameters. The treatment effect parameter—a maximal 3-point study drug-placebo difference on the strength of VAS craving in response to the alcohol cue—was obtained from Roberts (2017), which used a similar cue reactivity paradigm. The mean values on this outcome at Week 3 are assumed to be 11 for ASP8062 and 14 for placebo and a standard deviation between subjects of 4. Clinical site and the baseline VAS craving for the alcohol cue were assumed to have correlations of 0.13 and 0.39, respectively, with the primary outcome. These correlations, coupled with assumed standard deviations for site and baseline VAS craving for the alcohol cue of 0.82 and 4, respectively, yield explained variation of 26%. These assumptions, with a sample size of 30 subjects per arm (60 total subjects), provides 87% statistical power with a 0.05 two-sided significance level.

8. DATA QUALITY ASSURANCE

Data quality assurance will start with training of clinical investigative staff on data collection and assessment procedures including a Manual of Operations that describes what data to collect and procedures for completion of eCRFs. Completed eCRFs will be reviewed by Fast-Track Drugs and Biologics clinical monitors on a regular basis throughout the trial by comparison against the source documents.

Study data will come from the eCRFs, TLFB spreadsheets, coded AEs, coded medical history, AiCure Drug Compliance system outputs, and PK drug levels from the PK lab spreadsheets. eCRFs for this study were created using an electronic data management system (EDMS) based on IBM clinical development system. eCRFs were created using an established data dictionary for each variable including the field name, field type, field attributes, and coding for variables. Range checks, alpha-numeric requirements, and null/not null parameters were programmed as applicable. The back end database application is Oracle. Data entered into the EDMS system will be reviewed by Fast-Track clinical monitors and data managers. If incomplete or inaccurate data are found, the data will be queried in the system for site staff to address. The site will resolve data inconsistencies and errors using the EDMS with full audit trail of corrections being maintained within the system. Corrections and changes to the data will be reviewed by Fast-Track clinical monitors and data managers. TLFB spreadsheets have a double data entry check system and additionally, Fast-Track staff will verify the data entries with the drinking calandar to verify the correct percentages of alcohol by volume. QA review of laboratory data outputs is the responsibility of the individual testing laboratories; however, Fast-Track staff will verify that there is a result reported for each specimen that was recorded in the database as being collected. Coded AEs and medical history terms will be cross checked by a second trained MedDRA coder.

Additional edit checks will be written to detect anomalies in the database. These checks will address inconsistencies (within visits, across visits), invalid/unusual values, missing values, and protocol violations. Edit checking will be validated on test data or actual clinical trial data. In addition to programmed edit checks, quality control examination of data will also be performed on reviews of data listings.

9. STATISTICAL CONSIDERATIONS

9.1. General Considerations

For descriptive purposes, dichotomous and categorical variables will be presented as number of observations and percentages; continuous variables will be given as means, standard deviations (SD), median, miniumum (min) and maximum(max). Statistical tests will be two-tailed at a 0.05 Type I error rate. P-values for the primary and secondary endpoints of < 0.05 will be considered statistically significant. Endpoint data will also be screened for outliers and skewness. Appropriate non-parametric tests will be used to compare treatment groups on continuous baseline characteristics that are not normally distributed. Continuous endpoint data that are not normally distributed will be transformed using either a square root, logarithmic, or inverse transformation, the selection of which is determined by skewness and kurtosis statistics with values closest to zero. Cohen's d will be used to calculate the effect size for means and Cohen's h or odds ratios will be used to calculate the effect size for proportions. Descriptive statistics – mean, SD, median, min and max – of all endpoint data will be provided for each assement point or summarized at each week for drinking endpoints. All data will be presented in listings.

9.2. Participant Accountability and Protocol Deviations

A summary will be prepared to show dropouts/retention over time in each group, along with the reason for early discontinuation. The number of missing observations will be presented between groups. Protocol deviations will be presented as summaries by type of deviation.

9.3. Demographics and Other Baseline Characteristics

Summaries of the characteristics of the subjects in each of the study groups at baseline will be prepared for the mITT, and evaluable analysis sets. Demographic characteristics (e.g., age, gender, race, and ethnicity) and other baseline characteristics, coded medical history terms, screening cue session VAS scale scores and ACQ-SF-R pre and post session score, mood scales (e.g., POMS total and subscale scores), Hyperkatifeia Scale scores, PSQI, and drinking goal, MINI AUD scores and other DSM-5 diagnoses will be summarized by treatment group for the mITT and evaluable subjects. Chi-square tests or t-tests will be used on baseline characteristics to test the hypothesis of effective randomization. Imbalance in any of these factors is an indication of ineffective randomization which may bias the results observed on any of the endpoints.

Baseline drinking parameters in the 28-days prior to the start of screening, will be summarized by treatment group for the mITT subjects. t-tests will be used for baseline drinking paramenters to test the hypothesis of effective randomization. The number and percentage of subjects with mild, moderate and severe symptoms of AUD and summary statistics for total number of symptoms will also be presented.

The quantity of cigarettes smoked per week in the week prior to randomization will be presented for those subjects who reported any smoking. The numbers and percentages of subjects who report other nicotine product use at baseline, any nicotine use, and who test positive for THC will also be presented. Because smoking, any nicotine use, and positive THC are subsets and are not

controlled by randomization, balance across treatment groups will be assessed using t-test and chi-square tests.

Baseline drinking-associated consequences (CIWA-AR and PROMIS Alcohol Negative Consequences scores) and drinking-associated-craving (PACS) total score and subscales will be summarized in the tables. t-test will be used to test for balance across the treatment groups and evaluate the hypothesis of ineffective randomization.

Continuous variables will be summarized using means, standard deviations, medians, minimum, and maximum values. Categorical variables will be summarized using counts and percentages.

9.4. Efficacy Analysis

9.4.1. Primary Analysis of the Primary Efficacy Endpoint

Each subject will have an initial alcohol cue for "strength" of craving score from the VAS that is the primary endpoint. Analysis of covariance (ANCOVA) with the "strength" of alcohol craving value as the dependent variable and the pretreatment "strength' of alcohol craving score from the alcohol cue as an independent fixed effect. Treatment and clinical site will also be included as independent factors.

No imputation for missing endpoint data will be performed.

9.4.2. Confirmatory Secondary Endpoints

There are 3 additional VAS craving questions and a beverage liking question asked during the human lab session. Each of these questions will be analyzed in the same manner as listed in Section 9.4.1. An overall mean of the 4 VAS craving items will also be analyzed similarly for just the alcohol beverage cue. The difference between the alcohol cue and water cue for each VAS item will be computed at both the pre and post treatment time points. The difference values for each VAS item and the average difference will be analyzed similarly to the primary endpoint.

9.4.3. Analysis of the Secondary Efficacy Endpoints

Secondary efficacy endpoints will also be analyzed based on data collected during the last 4 weeks of the maintenance period (Weeks 3 through 6), including TLFB and other questionnaire data assessed at Week 7 that reflect data collected during this period. Note that the data collected at Week 7 reflect drinking and other questionnaire items that occurred during Week 6.

In general, every continuous secondary efficacy endpoint is analyzed using a repeated measures mixed effects model where subjects are random effects; factors and covariates are fixed effects. The analyses will be performed using SAS PROC MIXED procedure. The information criterion is requested from every mixed effects model. Subjects are treated as a class variable and not continuous. The week (Weeks 3 through 6), treatment group, and clinical site are also treated as class variables.

The primary analysis model for all continuous endpoints is:

- Appropriately transformed endpoint = treatment + week + treatment*week + clinical site + baseline equivalent of endpoint + other covariates (identified in Section 9.4.4)

This model will also be created for the untransformed endpoint. The solution statement from SAS PROC MIXED is requested to provide the solution for the fixed effects parameters. A

REPEATED statement specifies that values are repeated each week and subjects are nested within treatment group. The covariance structure is specified.

The selection of the covariance structure is performed using a simple repeated mixed effects model that includes treatment group as the only fixed effect and subject nested within treatment group as the only random effect. The covariance structure for each continuous secondary endpoint is selected from autoregressive, compound symmetry, Toeplitz, and unstructured. The Akaike Information Criterion (AICc) corrected for a finite sample is obtained from each of the four models for the four possible covariance structures to determine model fit. The smallest (minimum) AICc associated with one of the covariance structurs is selected and the difference for each of the other three covariance structures are calculated. A graph is produced of the model fit statistics and relative difference for the four possible covariance structures. The graphs across the continuous endpoints are compared to determine which covariance structure will be selected for all continuous endpoints or if one or more models need different covariance structures.

Results based on the primary analysis model and the model of the untransformed endpoint will be presented in tabular form. The overall least squares means and least square means for each time point along with the 95% confidence intervals (CI) will be presented for the untransformed endpoint only, while two-tailed p-values and Cohen's d will be presented for both the untransformed and transformed data. Inference and Cohen's d will be based upon the results using appropriately transformed data. Graphs of all secondary endpoints will be produced.

9.4.3.1. Secondary Drinking Endpoints

Percentage of days abstinent per week, percentage of subjects abstinent, percentage of heavy drinking days per week, percentage of very heavy drinking days, weekly mean number of drinks per week, and weekly mean number of drinks per drinking day will be analyzed using the mixed effects model specified in Section 9.4.3. Covariates for these models will be identified as in Section 9.4.4.

Percentage of subjects with a WHO 1-level decrease, and WHO 2-level decrease in alcohol consumption risk category will be analyzed during the last 4 weeks of the maintenance period (Weeks 2 through 5) using a logistic regression model. Covariates for the logistic regression will be identified as in Section 9.4.4. 2x2 contingency tables will report the WHO 1-level decrease, and WHO 2-level decrease along with Cohen's h, odds ratios and 95% CIs. The Wald statistic will be used to test for treatment differences.

No adjustment for multiple comparisons and no imputation will be used for these endpoints.

9.4.3.2. Alcohol Consequences and Craving Scales

The PACS is assessed weekly and will be analyzed similarly to the drinking endpoint (Section 9.4.3.1). PROMIS alcohol negative consequences scale is assessed at baseline and Study Week 7 which will be used for the secondary endpoint. Analysis of covariance will be used to analyze the PROMIS scale similarly to the primary endpoint (Section 9.4.1).

No imputation or multiplicity adjustment will be used for this endpoint.

9.4.3.3. Smoking and Any Nicotine Use

The mean number of cigarettes smoked in the past week is measured weekly. The sample is the mITT subjects who smoked at baseline. The data will be analyzed as described in Section 9.4.3. Covariates for this endpoint will be identified in Section 9.4.4. Amount of other nicotine products is not captured, only number of days of use of other nicotine products. The analysis of days of use in subjects using other nicotine products at baseline will use the same method as cigarettes smoked. In addition, 2 tables will examine the number of subjects that are abstinent from cigarettes and any nicotine product use. There will be one logistic regression, if there are sufficient number of subjects abstaining from nicotine use, with abstaining as the dependent variable and covariates as described in Section 9.4.4. No imputation will be used for these endpoints.

9.4.3.4. Sleep and Mood Scales

The PSQI total score, POMS 6 subscales and total disturbance score are continuous variables. The data will be analyzed as described in Section 9.4.3. Covariates for these models will be identified as in Section 9.4.4.

No imputation or multiplicity adjustment will be used for these endpoints.

9.4.4. Covariate Adjustment for the Analysis of Secondary Efficacy Endpoints

Covariates for continuous secondary efficacy endpoints include the baseline equivalent of the endpoint, clinical site, treatment, time and the treatment by time interaction. Additional covariates for the secondary efficacy endpoints may include baseline characteristics with a theoretical and/or empirical basis for a relationship with a particular secondary endpoint. Such characteristics may include, but are not limited to, drinking goal (stop drinking versus reduce drinking but not stop), age, and baseline alcohol craving scale total score. Prior to the unblinding of the data, matrices of correlations between these baseline characteristics and each of the secondary efficacy endpoints, pooled across blinded treatment assignment, will be produced (using Pearson for continuous variables, Spearman for categorical outcomes). Selection of baseline variables to include as covariates in the models will be based on consideration of the following criteria: at least modest correlation with outcome (i.e., $r \geq 0.20$) and clinical expertise. Each endpoint may have a unique set of covariates. Care is taken to only select a limited number of covariates such that the models are not over fitted.

Covariates for the dichotomous secondary endpoints, percentage of subjects abstinent, WHO 1-level risk category decrease, and WHO 2-level risk category decrease in alcohol consumption, will use phi correlation with dichotomous variables, chi-square statistic for categorical variables, and biserial correlation. Fewer covariates for the logistic regression may be used depending upon the number of events. If the number of events permits the inclusion of a baseline drinking covariate, the percentage of days abstinent will be used as the covariate for the percent subjects abstinent endpoint and the percent heavy drinking days will be used as the covariate for the percent subjects with no heavy drinking days endpoint; however, no baseline drinking covariate will be employed for the endpoint, percent subjects with a WHO decrease in alcohol consumption, as this endpoint already adjusts for baseline drinking in its calculation.

9.5. Handling of Missing Data

The primary endpoint of craving cannot be imputed; likewise, for the other craving questions given during the human lab session. Secondary endpoints analyzed with mixed effects or logistic regression models are capable of handling missing data, so no imputation will be utilized. PROMIS scores are analyzed using ANCOVA which cannot handle missing data; therefore, only subjects with an assessment during the treatment period will be used and no imputation.

9.6. Safety Analysis

9.6.1. Adverse Events

AEs will be coded using the most recent version of the Medical Dictionary for Regulatory Activities (MedDRA) and will be grouped by system, organ, and class (SOC) and preferred term (PT) designation. The severity, frequency, and relationship of AEs to investigational product will be presented by SOC and PT groupings. Listings of each individual AE including start date, stop date, severity, relationship, outcome, and duration will be provided. Each AE (based on PT) will be counted once only for a given study subject. If the same AE occurred on multiple occasions, the highest severity will be assumed. Thus, study subjects are not counted multiple times in a given numerator in the calculation of frequencies for a specific AE. C-SSRS reports of suicidality or suicidal ideation will be reported as AEs and analyzed as AEs if the investigator determines after an interview with the subject, that the responses are consistent with suicidal ideation or attempt.

9.6.2. Clinical Laboratory and Point of Care Tests

For clinical laboratory data, descriptive statistics will be generated for all tests performed at screening and at each clinic visit. If a laboratory analysis is repeated, the last measurement performed prior to the clinic visit will be used in the summary statistics for that clinic visit. If an unscheduled clinical laboratory visit occurs prior to a scheduled visit that is missed due to dropout, then the unscheduled visit will be used in the summary statistics for the missed scheduled clinical visit. If an unscheduled clinical laboratory visit occurs between two scheduled clinical visits, then the data from the unscheduled visit only be presented in the listings and not in summary statistics. In addition, at each post-randomization clinic visit descriptive statistics for change from baseline will be generated. Laboratory values will be plotted as mean ± standard error over time. All laboratory measurements will be presented in the listings.

Number and percentage of positive urine drug tests and pregnancy tests for screening visits and all treatment and follow-up visits will be tabulated. Results of all urine drug tests and pregnancy tests will be presented in the listings. The percentage of subjects with a positive urine drug test at any time post start of treatment will also be presented by test type and treatment group.

9.6.3. Vital Signs, ECG, and Body Weight

Vital signs will be presented as summary statistics and change from baseline. The percentage of ECG results considered abnormal and clinically significant will be provided. Body weight will be presented as summary statistics and change from screening. Vital signs, ECG results, and weight measurements for all visits will be presented in the listings.

9.6.4. CIWA-AR Scores

The number and percentage of subjects who reported CIWA-AR scores ≥ 10 at any time after the start of dosing will be presented.

9.6.5. ACQ-SF-R Scores

Summary statistics for ACQ-SF-R raw scores prior to after each cue session will be presented. The number and percentage of subjects with a higher ACQ-SF-R score post each cue session will be provided by treatment group.

9.7. Drug Exposure and Retention Analyses

Drug exposure will be presented for each treatment group as the mean number of tablets taken by week and overall through AiCure during the entire treatment phase. The analysis will include the total number of tablets taken and the percent compliance. AiCure data will also be used for the number subjects receiving reminder intervention (phone calls, texts, or in person visits). Compliance will also be evaluated by determining the proportion of subjects who were prescribed ASP8062, reported taking ASP8062 (by AiCure assessment), and had a plasma sample with detectable ASP8062. Compliance by ASP8062 plasma levels will be reported as number and percentage of subjects with a level above the limit of detection at each time point. Descriptive statistics of plasma levels of ASP8062 and metabolites will also be provided. Samples with levels below of limit of quantitation will not be included in the summary statistics and the N will reflect the number with a detectable level at each timepoint.

The participation rate is the percentage of subjects with complete drinking data. Dropouts by week with cumulative percentages will be provided by treatment arm.

9.8. Blood Alcohol Content

The number and percentage of subjects at any clinic visit that have a BAC > 0 will be tabulated. All BAC measurements will be presented in the listings.

9.9. Exploratory and Ad Hoc Analyses

9.9.1. Hyperkatifeia Scale

There is interest in exploring the use of a new Hyperkatifeia Scale as a predictor of drug response and possibly as an outcome measure. *Ad hoc* analyses will be performed on this scale as a planned part of exploring the utility of this scale including subscales and individual items. *Ad hoc* analyses may include: 1) examining the association between cue outcomes and naturalistic outcomes; 2) conducting of moderator analyses; and 3) examining the treatment goal assessment and its relationship between outcomes. The data from this study could be used for combined analyses with results of other studies conducted in the future.

9.9.2 Supplemental Exploratory Analysis

The exploratory analysis are defined as: Explore moderators of the treatment effect on primary and secondary outcomes. The exploratory endpoint will not be analyzed at the same time as the primary and secondary endpoints.

10. VALIDATION OF PROGRAMMING CODE

All SAS codes used to generate tables and listings will be validated and reviewed before being finalized. The validation process will be used to determine that the numbers are produced by a statistically valid method and that the execution of the computations is correct. Qualified personnel who have not previously been involved in the production of the original programming codes will perform the validation procedures. Methods of validation include independent programming and comparison to data listings. Tables will be reviewed for accuracy, consistency with this plan, consistency within tables, and consistency with corresponding output. Once validation is complete, a quality control reviewer will perform a final review of the documents for accuracy and consistency. Upon completion of validation and quality review procedures, all documentation will be collected and filed in the study documentation files at Fast-Track.

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12. TABLE, LISTING, AND FIGURE SHELLS

12.1. Tables

12.1.1. Subject Disposition, Participation, Compliance

Table 1: Subject Disposition - All Randomized Subjects

	ASP8062	Placebo	Total	
	n (%)	n (%)	n (%)	p-value[1]
Number of Subjects Consented			xx	
Number of Subjects Screen Failed			xx	
Number of Subjects Randomized[2]	xx	xx	xx	0.xxx
Number of Subjects Randomized not Receiving Study Drug	x (xx.x)	x (xx.x)	x (xx.x)	0.xxx
Number of mITT Subjects	xx (xx.x)	xx (xx.x)	xxx (xx.x)	0.xxx
Number of Completed[3] Subjects	xx (xx.x)	xx (xx.x)	xxx (xx.x)	0.xxx
Number of Evaluable Subjects	xx (xx.x)	xx (xx.x)	xxx (xx.x)	0.xxx
Number of Subject Completing Study & Drug	xx (xx.x)	xx (xx.x)	xx (xx.x)	0.xxx
Number of Subjects Discontinuing Study Drug, Remaining in Study	xx (xx.x)	xx (xx.x)	xx (xx.x)	0.xxx
Number of Subjects Withdrawn Early (did not provide any data at Week 7)	xx (xx.x)	xx (xx.x)	xx (xx.x)	0.xxx
Reason for Early Withdrawal[4]				
Subject withdrew consent	xx (xx.x)	xx (xx.x)	xx (xx.x)	
Investigator withdrew subject	xx (xx.x)	xx (xx.x)	xx (xx.x)	
Lost-to-followup	xx (xx.x)	xx (xx.x)	xx (xx.x)	
Adverse Event	xx (xx.x)	xx (xx.x)	xx (xx.x)	
Increased drinking	xx (xx.x)	xx (xx.x)	xx (xx.x)	
Psychiatric crisis	xx (xx.x)	xx (xx.x)	xx (xx.x)	
Died	xx (xx.x)	xx (xx.x)	xx (xx.x)	
Absent from the protocol due to confinement in a controlled environment	xx (xx.x)	xx (xx.x)	xx (xx.x)	
Determined after randomization to be ineligible	xx (xx.x)	xx (xx.x)	xx (xx.x)	

Notes: [1] p-value from Fisher's exact test.
[2]The following percentages are based upon number randomized
[3]Completed is defined as attending all clinical visits through Week 7 making the subject available for all endpoint analyses
[4]The following categories sum to the number of early withdrawals

Programmer Notes: The discontinuation reasons are as given on the CRF. Include only the reasons actually used for the subjects in the study. If a subject discontinued, but the specific reason is missing, include 'Missing' as a row in the table. Use the order of discontinuation reasons as presented on the CRF page.

Table 2: Exposure to Investigational Products Using AICure Data – mITT Subjects

	Number of Tablets Taken								
	ASP8062 N=XX				Placebo N=XX				
	N	**Mean (SD[3])**	**Med**	**(Min-Max)**	**N**	**Mean (SD)**	**Med**	**(Min-Max)**	**p-value[1]**
Week 1	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	0.xxx
Week 2	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	0.xxx
Week 3	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	0.xxx
Week 4	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	0.xxx
Week 5	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	0.xxx
Week 6	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	0.xxx
Total Dose[2]	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	0.xxx

[1] p-value from t-test

[2] Dose is the total number of tablets taken, maximum prescribed is 42 tablets

[3] SD is standard deviation

Table 3: Total Exposure to Investigational Products Using AICure Data – Evaluable Subjects

Same as Table 2 only using evaluable subjects

Table 4: Compliance to Investigational Products Using AICure Data – mITT Subjects

Same analysis as Table 2 using compliance rather than dose. Compliance is the number of capsules taken/number of capsules prescribed.

Table 5: Compliance to Investigational Products Using AICure Data – Evaluable Subjects

Same analysis as Table 4 using evaluable subjects

Table 6: AiCure Interventions mITT Subjects

	ASP8062		Placebo	
	N	**# Receiving ≥ 1**	**N**	**# Receiving ≥ 1**
Interventions[1]	xx	xx	xx	xx

[1] Interventions includes texts, emails, and phone calls

Table 7: AiCure Interventions – Evaluable Subjects

Same as Table 6 only using evaluable subjects

Table 8: Summary of ASP8062 and Metabolite Plasma Levels – ASP8062 Arm Only (mITT Subjects)

	ASP8062			
	N	**% > LLD[1]**	**Mean (SD[2])**	**(Min-Max)**
Week 4	xx	xx.x	xx.x (xx.x)	(xx.x-xx.x)
Week 7	xx	xx.x	xx.x (xx.x)	(xx.x-xx.x)
	AS3486189			
	N	**% > LLD[1]**	**Mean (SD[2])**	**(Min-Max)**
Week 4	xx	xx.x	xx.x (xx.x)	(xx.x-xx.x)
Week 7	xx	xx.x	xx.x (xx.x)	(xx.x-xx.x)
	AS3486191			
	N	**% > LLD[1]**	**Mean (SD[2])**	**(Min-Max)**
Week 4	xx	xx.x	xx.x (xx.x)	(xx.x-xx.x)
Week 7	xx	xx.x	xx.x (xx.x)	(xx.x-xx.x)
	AS3486192			
	N	**% > LLD[1]**	**Mean (SD[2])**	**(Min-Max)**
Week 4	xx	xx.x	xx.x (xx.x)	(xx.x-xx.x)
Week 7	xx	xx.x	xx.x (xx.x)	(xx.x-xx.x)

[1] LLD is lowest level of detection[2] SD is standard deviation

Table 9: Summary of ASP8062 Plasma Levels – ASP8062 Arm Only (Evaluable Subjects)

Same as Table 8 only using evaluable subjects.

Table 10: AiCure Report of ASP8062 Versus ASP8062 Plasma Levels – mITT Subjects

		AiCure Report Indicates Drug Taken (pill count must = 1, on the day before the blood sample was drawn)			
Timing	**Plasma level Indicates Drug Taken**[a]	**Yes, n (%)**	**No, n (%)**	**p-value**[b]	**kappa**[c]
Week 4	Yes				
	No				
Week 7	Yes				
	No				
Overall	Yes				
	No				

[a] Blood level of ≥xx ng/mL indicates drug taken
[b] Chi-square test for independence
[c] Kappa test for agreement

Table 11: AiCure Report of ASP8062 Versus ASP8062 Plasma Levels – Evaluable Subjects

Repeat of Table 10 using evaluable subjects

Table 12: Exit Interview – mITT Subjects

	ASP8062	**Placebo**	**Total**	

Question	(N=xx)	(N=xx)	(N=xxx)	p-value[1]
Did you think you were receiving the study drug or the placebo?				0.xxx
Placebo	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Study Drug	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Don't know; No idea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Refuse to answer	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
What is your desire to please people?				0.xxx
More than average	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Average	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Less than average	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Refuse to answer	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Take the study drug again, for more than 6 weeks?				0.xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Refuse to answer	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Did you ever miss a dose of medication to avoid these effects?				
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Refuse to answer	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Did you use any other services during the study to help you reduce drinking?				0.xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Refuse to answer	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

[1] p-value from chi-squared test (c) unless one of the cells expected is less than 5 then Fisher's exact test is used (f). Refuse to answer is not included in statistical test.

Table 13: Exit Interview – Evaluable Subjects

Same as Table 12

Table 14: Dropouts by Treatment Group and Week – mITT Subjects

	ASP8062 N=XX		Placebo N=XX		Total N=XX		
Study Week[2]	**n**	**Cumulative n (%)**	**n**	**Cumulative n (%)**	**n**	**Cumulative n (%)**	**p-value[1]**
Week 1	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	0.xxx
Week 2	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	0.xxx
Week 3	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	0.xxx
Week 4	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	0.xxx
Week 5	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	0.xxx
Week 6	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	0.xxx
Week 6	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	0.xxx

[1] Fisher's exact test

[2]Subjects are considered dropouts when they stop providing TLFB and other data. Subjects that discontinue study drug but provide data are not considered dropouts.

Table 15: Number and Percent of Subjects Using Brief Drinking Questions after Discontinuing TLFB – mITT Subjects

	ASP8062	Placebo	Total	
Study Week	**n (%)**	**n (%)**	**n (%)**	**p-value[1]**
Week 3	xx (xx.x)	xx	xx.x	0.xxx
Week 4	xx	xx	xx.x	0.xxx
Week 5	xx	xx	xx.x	0.xxx
Week 6	xx	xx	xx.x	0.xxx
Week 6	xx	xx	xx.x	0.xxx
Overall	xx	xx	xx.x	0.xxx

[1]Fisher's exact test is used because frequencies are expected to be low

Note only rows with values above 0 will be presented

12.1.2. Demographic and Baseline Characteristics

Table 16: Demographic Characteristics - mITT Subjects

Characteristic	ASP8062	Placebo	Total	p-value[1]
Age (years)				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD[2]	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Gender				0.xxx
N				
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Race				0.xxx
N	xx	xx	xx	
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
African-American or Black	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Native Hawaiian or Other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
American Indian or Alaskan Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Ethnicity				0.xxx
N	xx	xx	xx	
Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Not Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

[1]c = chi-squared test, f=Fisher's exact test, w=Wilcoxon signed rank test

[2] SD is standard deviation

Table 17: Demographic Characteristics – Evaluable Subjects

Same as Table 16

Table 18: Screening Cue Reactivity – mITT Subjects

			ASP8062 **N=xx**	**Placebo** **N=xx**	**Total** **N=xx**	**p-value**[1]
Cue	Question	Statistic				
Water	*Craving Strength*					0.xxx
		Mean (SD[2])	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
	Drinking makes things perfect					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
	Drink now					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	

			ASP8062 **N=xx**	**Placebo** **N=xx**	**Total** **N=xx**	**p-value[1]**
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
	Turn down drink					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
	Average					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Alcohol	*Craving Strength*					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	

			ASP8062 **N=xx**	**Placebo** **N=xx**	**Total** **N=xx**	**p-value**[1]
	Drinking makes things perfect					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
	Drink now					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
	Turn down drink					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
	Average					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	

			ASP8062 **N=xx**	**Placebo** **N=xx**	**Total** **N=xx**	**p-value[1]**
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Alcohol - Water	*Craving Strength*					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
	Drinking makes things perfect					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
	Drink now					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
	Turn down drink					0.xxx

			ASP8062 **N=xx**	**Placebo** **N=xx**	**Total** **N=xx**	**p-value**[1]
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
	Average					0.xxx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx	xx	xx	
		Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	

[1] t-test is used to examine balance across treatment groups

[2] SD is standard deviation

Table 19: Screening Cue Reactivity – Evaluable Subjects

Same as Table 18

Table 20: Psychiatric Baseline Characteristics – mITT Subjects

	ASP8062	Placebo	Total
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xxx)**
DSM-5 Disorders			
Depression	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Suicidality	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Manic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hypomanic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Bipolar	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Panic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Agoraphobia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Social Phobia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Obsessive Compulsive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Posttraumatic Stress	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Substance Abuse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Psychotic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mood	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Anorexia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Bulemia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Binge-eating	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Generalized Anxiety	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Medical Organic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Antisocial Personality	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 21: Medical History – mITT Subjects

Medical History SOC and Preferred Term	**ASP8062 (N=xx)**	**Placebo (N=xx)**	**Total (N=xx)**
SOC	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term name	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 22: Baseline POMS – mITT Subjects

Characteristic	ASP8062 (N=xx)	Placebo (N=xx)	Total (N=xx)	p-value[1]
Tension-Anxiety				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD[2]	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Depression-Dejection				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Anger-Hostility				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Fatigue-Inertia				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Confusion-Bewilderment				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	

Characteristic	ASP8062 (N=xx)	Placebo (N=xx)	Total (N=xx)	p-value[1]
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Vigor-Activity				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Total Mood Disturbance				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	

[1] t-test
[2]SD is standard deviation

Table 23: Baseline POMS – Evaluable Subjects

Same as Table 22

Table 24: Baseline PSQI – mITT Subjects

Characteristic	ASP8062	Placebo	Total	p-value[1]
Overall Sleep Experience				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD[2]	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	

Characteristic	ASP8062	Placebo	Total	p-value[1]
Scale Min-Max			(xx-xx)	

[1] t-test
[2] SD is standard deviation

Table 25: Baseline PSQI – Evaluable Subjects

Same as Table 24

Table 26: Baseline Drinking-related Behavior and Characteristics – mITT Subjects

	ASP8062	Placebo	Total	
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xx)**	**p-value[1]**
Drinking Goal (n, %)				
Stop Drinking	xx (xx.x)	xx (xx.x)	xx (xx.x)	
Reduce but not stop	xx (xx.x)	xx (xx.x)	xx (xx.x)	
Goal of no heavy drinking days (n, %)				
Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	
No	xx (xx.x)	xx (xx.x)	xx (xx.x)	
# Drinks/Week Goal in Subjects that Want to Reduce Drinking				
N	xx	xx	xx	0.xxx
Mean	xx.x	xx.x	xx.x	
SD[2]	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Motivation to achieve goal				
N	xx	xx	xx	0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Confidence in achieving goal				
N	xx	xx	xx	0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
AUD Symptom Severity (n, %)				0.xxx
Moderate (4 or 5 symptoms)	xx (xx.x)	xx (xx.x)	xx (xx.x)	
Severe (6 or more symptoms)	xx (xx.x)	xx (xx.x)	xx (xx.x)	
AUD Number of Symptoms (n, %)				
4	xx (xx.x)	xx (xx.x)	xx (xx.x)	
5	xx (xx.x)	xx (xx.x)	xx (xx.x)	
6	xx (xx.x)	xx (xx.x)	xx (xx.x)	
7	xx (xx.x)	xx (xx.x)	xx (xx.x)	
8	xx (xx.x)	xx (xx.x)	xx (xx.x)	
9	xx (xx.x)	xx (xx.x)	xx (xx.x)	
10	xx (xx.x)	xx (xx.x)	xx (xx.x)	

	ASP8062	Placebo	Total	
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xx)**	**p-value[1]**
11	xx (xx.x)	xx (xx.x)	xx (xx.x)	
AUD Number of Symptoms (continuous)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	

Note: Percentages are based on the number of non-missing values in each variable.
[1] t-test
[2]SD is standard deviation

Table 27: Baseline Drinking-related Behavior and Characteristics – Evaluable Subjects

Same as Table 26

Table 28: Baseline Drinking by TLFB – mITT Subjects

	ASP8062	Placebo	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Drinks/Week (Pre-screening Days -1 to -28)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD[2]	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Drinks/Week (7 Days Prior to Randomization)				0.xxx
Mean	xx.x	xx.x	xx.x	

	ASP8062	Placebo	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Drinks/Week (Percent Change Pre-screening Days -1 to -28 to 7 Days Prior to Randomization)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Drinks/Drinking Day (Pre-screening Days -1 to -28)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Drinks/Drinking Day (7 Days Prior to Randomization)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Drinks/Drinking Day (Percent Change Pre-screening Days -1 to -28 to 7 Days Prior to Randomization)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Percentage of Heavy Drinking Days (Pre-screening Days -1 to -28)				0.xxx
Mean	xx.x%	xx.x%	xx.x%	
SD	xx.x%	xx.x%	xx.x%	
Median	xx.x%	xx.x%	xx.x%	
Min-Max	(xx%-xx%)	(xx%-xx%)	(xx%-xx%)	
Percentage of Very Heavy Drinking Days (Pre-screening Days -1 to -28)				0.xxx
Mean	xx.x%	xx.x%	xx.x%	

	ASP8062	Placebo	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
SD	xx.x%	xx.x%	xx.x%	
Median	xx.x%	xx.x%	xx.x%	
Min-Max	(xx%-xx%)	(xx%-xx%)	(xx%-xx%)	
Percentage Days Abstinent (Pre-screening Days -1 to -28)				0.xxx
Mean	xx.x%	xx.x%	xx.x%	
SD	xx.x%	xx.x%	xx.x%	
Median	xx.x%	xx.x%	xx.x%	
Min-Max	(xx%-xx%)	(xx%-xx%)	(xx%-xx%)	
WHO Risk Level				0.xxx
High Risk	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Very High Risk	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

Note: Percentages are based on the number of non-missing values in each variable.
[1]Chi-square test for categorical variables and t-test for continuous variables
[2] SD is standard deviation

Table 29: Baseline Drinking by TLFB – Evaluable Subjects

Same as Table 28

Table 30: Baseline Alcohol-Related Craving, Consequences, Withdrawal and Hyperkatifeia – mITT Subjects

	ASP8062	Placebo	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Pre-cue ACQ-SF-R[2]				0.xxx
Mean	xx.x	xx.x	xx.x	
SD[3]	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	
Post-cue ACQ-SF-R				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Pre-Post ACQ-SF-R				
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
PROMIS[4] Alcohol Negative Consequences (T-scores)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
PACS[5]				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	
CIWA-AR[6]				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	

	ASP8062	Placebo	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Withdrawal Symptoms (CIWA ≥ 10)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Hyperkatifeia				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	
Stress Anxiety				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	
Depression				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	
Irritable				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	
Pain				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	

[1] t-test for continuous variables and chi-square test for categorical

[2]ACQ-SF-R is Alcohol Craving Questionnaire – Short Form – Revised

[3] SD is standard deviation

[4] PROMIS is short form of Patient-reported Outcomes Information System

[5] PACS is Penn Alcohol Craving Scale [6] CIWA-AR is Clinical Institute Withdrawal Assessment for Alcohol-revised

Table 31: Baseline Alcohol-Related Craving, Consequences, Withdrawal and Hyperkatifeia – Evaluable Subjects

Same as Table 30

Table 32: Baseline Other Substance Use – mITT Subjects

	ASP8062	Placebo	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Smoker (n, %)	xx (xx)	xx (xx)	xx (xx)	0.xxx
Days Smoked in the Past Week				
Mean	xx.x	xx.x	xx.x	
SD[2]	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
(Min-Max)	(xx-xx)	(xx-xx)	(xx-xx)	
Average Cigarettes Smoked Per Week (among Smokers)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Any Other Nicotine Product Use (doesn't include cigarettes) (n, %)	xx (xx)	xx (xx)	xx (xx)	0.xxx
Days Used Other Nicotine Products Per Week				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Any Nicotine Use (cigarettes + other) (n, %)	xx (xx)	xx (xx)	xx (xx)	0.xxx
THC				0.xxx
Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

Note: Percentages are based on the number of non-missing values in each variable.

[1]t-test for continuous variables and chi-square test for categorical

[2] SD is standard Deviation

Table 33: Baseline Other Substance Use – Evaluable Subjects

Same as Table 32

12.1.3. Primary Efficacy Endpoint

Table 34: Week 3 Strength of Craving Scores – mITT Subjects

		ASP8062 N=xx	**Placebo N=xx**	**Total N=xx**
Cue	Statistic			
Water				
	Mean (SD[1])	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx
	Min-Max	(xx-xx)	(xx-xx)	(xx-xx)
Alcohol				
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx
	Min-Max	(xx-xx)	(xx-xx)	(xx-xx)
Alcohol - Water				
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx
	Min-Max	(xx-xx)	(xx-xx)	(xx-xx)

[1] SD is standard deviation

Table 35: Week 3 Strength of Craving Scores – Evaluable Subjects

Same as Table 34

Table 36: ANCOVA Strength of Craving – mITT Subjects

Type III Wald Tests

Parameter	**Num DF[1]**	**Den DF[2]**	**F Value**	**p-value**
Arm	1	xx	xxx.xx	0.xxx
Site	xx	xx	xxx.xx	0.xxx
Baseline Cue[3]	1	xx	xxx.xx	0.xxx

[1]Numerator degrees of freedom; [2] Demonimator degrees of freedom

[3] Baseline Cue is the baseline equivalent of the outcome obtained after the presentation of the first alcohol cue at baseline

Least Squares Means

			95% CI					
Arm	**Estimate**	**SE[1]**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value[2]**	**Cohen's d**
ASP8062	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	xx.xx	0.xxx	0.xxx	0.xxx				

[1] SE is standard error; [2] Wald test;

Table 37: ANCOVA Strength of Craving – Evaluable Subjects

Follow the same analysis as Table 36

12.1.4. Confirmatory Secondary Efficacy Endpoints

Table 38: ANCOVA Strength of Craving (Difference Alcohol-Water) – mITT Subjects

Type III Wald Test

Parameter	Num DF[1]	Den DF[2]	F Value	p-value
Arm	**1**	**xx**	**xxx.xx**	**0.xxx**
Site	**xx**	**xx**	**xxx.xx**	**0.xxx**
Baseline Cue[3]	**1**	**xx**	**xxx.xx**	**0.xxx**

[1]Numerator degrees of freedom; [2] Demonimator degrees of freedom

[3] Baseline Cue is the baseline equivalent of the outcome obtained after the presentation of the first alcohol cue at baseline

Least Squares Means

			95% CI					
Arm	**Estimate**	**SE[1]**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value[2]**	**Cohen's d**
ASP8062	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	xx.xx	0.xxx	0.xxx	0.xxx				

[1] SE is standard error; [2] Wald test;

Table 39: ANCOVA Strength of Craving (Difference Alcohol-Water) – Evaluable Subjects

Same as Table 38

Table 40: Drinking Makes Things Perfect Scores – mITT Subjects

		ASP8062 N=xx	**Placebo N=xx**	**Total N=xx**
Cue	Statistic			
Water				
	Mean (SD[1])	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx
	Min-Max	(xx-xx)	(xx-xx)	(xx-xx)
Alcohol				
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx
	Min-Max	(xx-xx)	(xx-xx)	(xx-xx)
Alcohol- Water				
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx
	Min-Max	(xx-xx)	(xx-xx)	(xx-xx)

[1] SD is standard deviation

Table 41: Drinking Makes Things Perfect Scores – Evaluable Subjects

Same as Table 40

Table 42: ANCOVA Drinking Makes Things Perfect – mITT Subjects

Type III Wald Test

Parameter	**Num DF[1]**	**Den DF[2]**	**F Value**	**p-value**
Arm	**1**	**xx**	**xxx.xx**	**0.xxx**
Site	**2**	**xx**	**xxx.xx**	**0.xxx**
Baseline Cue[3]	**1**	**xx**	**xxx.xx**	**0.xxx**

[1]Numerator degrees of freedom; [2] Demonimator degrees of freedom

[3] Baseline Cue is the baseline equivalent of the outcome obtained after the presentation of the first alcohol cue at baseline

Least Squares Means

			95% CI					
Arm	**Estimate**	**SE[1]**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value[2]**	**Cohen's d**
ASP8062	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	xx.xx	0.xxx	0.xxx	0.xxx				

[1] SE is standard error; [2] Wald test;

Table 43: ANCOVA Drinking Makes Things Perfect – Evaluable Subjects

Same analysis as Table 42

Table 44: ANCOVA Drinking Makes Things Perfect (Difference Alcohol-Water) – mITT Subjects

Type III Wald Test

Parameter	Num DF[1]	Den DF[2]	F Value	p-value
Arm	**2**	**xx**	**xxx.xx**	**0.xxx**
Site	**2**	**xx**	**xxx.xx**	**0.xxx**
Baseline Cue[3]	**1**	**xx**	**xxx.xx**	**0.xxx**

[1]Numerator degrees of freedom; [2] Demonimator degrees of freedom

[3] Baseline Cue is the baseline equivalent of the outcome obtained after the presentation of the first alcohol cue at baseline

Least Squares Means

			95% CI					
Arm	**Estimate**	**SE[1]**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value[2]**	**Cohen's d**
ASP8062	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	xx.xx	0.xxx	0.xxx	0.xxx				

[1] SE is standard error; [2] Wald test;

Table 45: ANCOVA Drinking Makes Things Perfect (Difference Alcohol-Water) – Evaluable Subjects

Same analysis as Table 44

Table 46: Drink Now Scores– mITT Subjects

		ASP8062 **N=xx**	**Placebo** **N=xx**	**Total** **N=xx**
Cue	Statistic			
Water				
	Mean (SD[1])	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx
	Min-Max	(xx-xx)	(xx-xx)	(xx-xx)
Alcohol				
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx	xx	xx
	Min-Max	(xx-xx)	(xx-xx)	(xx-xx)
Alcohol - Water				
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)

		ASP8062 N=xx	**Placebo N=xx**	**Total N=xx**
	Median	xx	xx	xx
	Min-Max	(xx-xx)	(xx-xx)	(xx-xx)

[1] SD is standard deviation

Table 47: Drink Now Scores – Evaluable Subjects

Same as Table 46

Table 48: ANCOVA Drink Now – mITT Subjects

Type III Wald Test

Parameter	**Num DF[1]**	**Den DF[2]**	**F Value**	**p-value**
Arm	**1**	**xx**	**xxx.xx**	**0.xxx**
Site	**xx**	**xx**	**xxx.xx**	**0.xxx**
Baseline Cue[3]	**1**	**xx**	**xxx.xx**	**0.xxx**

[1]Numerator degrees of freedom; [2] Demonimator degrees of freedom

[3] Baseline Cue is the baseline equivalent of the outcome obtained after the presentation of the first alcohol cue at baseline

Least Squares Means

			95% CI					
Arm	**Estimate**	**SE[1]**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value[2]**	**Cohen's d**
ASP8062	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	xx.xx	0.xxx	0.xxx	0.xxx				

[1] SE is standard error; [2] Wald test;

Table 49: ANCOVA Drink Now – Evaluable Subjects

Same analysis as Table 48

Table 50: ANCOVA Drink Now (Difference Alcohol-Water) – mITT Subjects

Same analysis as Table 44 with difference as the dependent variable

Table 51: ANCOVA Drink Now (Difference Alcohol-Water) – Evaluable Subjects

Same analysis as Table 50

Table 52: Turn Down Drink Scores – mITT Subjects

Same analysis as Table 46

Table 53: Turn Down Drink Scores – Evaluable Subjects

Same analysis as Table 52

Table 54: ANCOVA Turn Down Drink – mITT Subjects

Same analysis as Table 48

Table 55: ANCOVA Turn Down Drink – Evaluable Subjects

Same analysis as Table 54

Table 56: ANCOVA Turn Down Drink (Difference Alcohol-Water) – mITT Subjects

Same analysis as Table 44

Table 57: ANCOVA Turn Down Drink (Difference Alcohol-Water) – Evaluable Subjects

Same analysis as Table 56

Table 58: Average of Cue Scores – mITT Subjects

Same analysis as Table 46

Table 59: Average of Cue Scores – Evaluable Subjects

Same as Table 58

Table 60: ANCOVA Average of Cue Scores – mITT Subjects

Same analysis as Table 48

Table 61: ANCOVA Average of Cue Scores – Evaluable Subjects

Same analysis as Table 60

Table 62: ANCOVA Average of Cue Scores (Difference Alcohol-Water) – mITT Subjects

Same analysis as Table 44

Table 63: ANCOVA Average of Cue Scores (Difference Alcohol-Water) – Evaluable Subjects

Same analysis as Table 62

Table 64: Beverage Liking Scores – mITT Subjects

Same analysis as Table 46

Table 65: Beverage Liking Scores – Evaluable Subjects

Same analysis as Table 64

12.1.5. Secondary Efficacy Endpoints

Table 66: Percentage of Subjects No Heavy Drinking Days Weeks 3-6 – mITT Subjects

	ASP8062	Placebo	Total
	(N=xx)	(N=xx)	(N=xxx)
No Heavy Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 67: Percentage of Subjects with No Heavy Drinking Days Weeks 3-6 – Full Model Logistic Regression (mITT)

									95% CI[3]	
Parameter		**DF[1]**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**Cohen's h**	**OR[2]**	**Upper**	**Lower**
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Overall	X	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment[4]	ASP8062	X	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	X	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site[5]	1	X	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2	X	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

									95% CI[3]	
Parameter		**DF[1]**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**Cohen's h**	**OR[2]**	**Upper**	**Lower**
Cov		X	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

[1] DF is degrees of freedom; [2] OR is odds ratio; [3] CI is confidence interval; [4] Comparison to placebo;

[5] Site 3 is reference for the OR

Programming note: COV is baseline equivalent of dependent variable and any other covariate(s) which have not been specified at the time of writing of SAP

Table 68: Percentage of Subjects Abstinent from Alcohol Weeks 3-6 – mITT Subjects

Presented in same manner as Table 66

Table 69: Percentage of Subjects Abstinent from Alcohol Weeks 3-6 – Full Model Logistic Regression (mITT)

Prented in same manner as Table 67 *programming note: baseline PDA is a covariate for PSA outcome*

Table 70: WHO 1-Level Decrease in Alcohol Consumption (mITT) – Weeks 3-6

	ASP8062	Placebo	Total
	(N=xx)	(N=xx)	(N=xxx)
WHO 1-Level Decrease			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 71: WHO 1-Level Decrease in Alcohol Consumption (mITT) – Full Model, Logistic Regression, Weeks 2-5

									95% CI[3]	
Parameter		**DF[1]**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**Cohen's h**	**OR[2]**	**Upper**	**Lower**
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Overall	X	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment[4]	ASP8062	X	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	X	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site[5]	1	X	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2	X	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Cov		X	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

[1] DF is degrees of freedom; [2] OR is odds ratio; [3] CI is confidence interval; [4] Comparison to placebo;

[5] Site 3 is reference for the OR

Programming note: COV is baseline equivalent of dependent variable and any other covariate(s) which have not been specified at the time of writing of SAP

Table 72: WHO 2-Level Decrease in Alcohol Consumption (mITT) – Weeks 3-6

Same as Table 70

Table 73: WHO 2-Level Decrease in Alcohol Consumption (mITT) – Full Model, Logistic Regression, Weeks 3-6

Same as Table 71

Table 74: Percentage of Days Abstinent per Week (mITT) – Weeks 3-6

	ASP8062					Placbo		
Study Week	**N**	**Mean (SD[1])**	**Median**	**(Min-Max)**	**N**	**Mean (SD)**	**Median**	**(Min-Max)**
3	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)
4	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)
5	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)
6	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)
Overall	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)

[1] SD is standard deviation

Table 75: Percentage of Days Abstinent per Week (mITT) -- Full Model, Mixed Effects, Weeks 3-6

Type III Wald Tests

Parameter	Num DF[1]	Den DF[2]	F Value	p-value
Arm	1	xxx	xxx.xx	0.xxx
Week	3	xxx	xxx.xx	0.xxx
Site	xx	xxx	xxx.xx	0.xxx
Cov	x	xxx	xxx.xx	0.xxx
Arm*Week	5	xxx	xxx.xx	0.xxx

[1] Numerator degrees of freedom; [2] Denominator degrees of freedom

Programming note: Cov is the baseline equivalent of the dependent variable and any additional covariates included in the model.

Least Squares Means

				95% CI[2]				Model	
Arm	**Week**	**Estimate**	**SE[1]**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**
ASP8062	3	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	3	xx.xx	0.xxx	0.xxx	0.xxx				
ASP8062	4	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	4	xx.xx	0.xxx	0.xxx	0.xxx				
ASP8062	5	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	5	xx.xx	0.xxx	0.xxx	0.xxx				
ASP8062	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx				
ASP8062	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx				

[1] SE is standard error; [2] CI is confidence interval

Programming note:If a transformation of the dependent variable is used add 2 columns: p-value and Cohen's d for the transformed model.

Table 45 is the template for Tables 76, 78, 80, 82, 84, and 86. Table 75 is the template for Tables 77, 79, 81, 83, 85, and 87.

Table 76: Percentage of Heavy Drinking Days per Week (mITT) – Weeks 3-6

Table 77: Percentage of Heavy Drinking Days per Week (mITT) – Full Model, Mixed Effects, Weeks 3-6

Table 78: Percentage of Very Heavy Drinking Days per Week (mITT) – Weeks 3-6

Table 79: Percentage of Very Heavy Drinking Days per Week (mITT) – Full Model, Mixed Effects, Weeks 3-6

Table 80: Drinks per Week (mITT) – Weeks 3-6

Table 81: Drinks per Week (mITT) – Full Model, Mixed Effects, Weeks 3-6

Table 82: Drinks per Drinking Day (mITT) – Weeks 3-6

Table 83: Drinks per Drinking Day (mITT) – Full Model, Mixed Effects, Weeks 3-6

Table 84: Mean Cigarettes Smoked Among Smokers (mITT) – Weeks 3-6

Table 85: Mean Cigarettes Smoked Among Smokers (mITT) – Full Model, Mixed Effects, Weeks 3-6

Table 86: PACS (mITT) – Weeks 3-6

Table 87: PACS (mITT) – Full Model, Mixed Effects, Weeks 3-6

Table 88: Percentage of Subjects Abstinent from Nicotine Use[1] Weeks 3-6 – Among Subjects that Used Nicotine Products at Baseline

	ASP8062	Placebo	Total
	(N=xx)	(N=xx)	(N=xxx)
No Nicotine Use			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] Nicotine use includes cigarettes or other nicotine products

Table 89: Percentage of Subjects Abstinent from Nicotine Use[1] Weeks 3-6 – Full Model Logistic Regression (Among Nicotine Users at Baseline)

									95% CI[4]	
Parameter		**DF[2]**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**Cohen's h**	**OR[3]**	**Upper CI**	**Lower CI**
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				

									95% CI[4]	
Parameter		**DF[2]**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**Cohen's h**	**OR[3]**	**Upper CI**	**Lower CI**
Treatment[5]	ASP8062	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site[6]	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

[1] Nicotine use includes either cigarettes or other nicotine products; [2] DF is degrees of freedom; [3] OR is odds ratio; [4] CI is confidence interval; [5] Comparison to placebo for each active treatment;[6] Site 3 is reference for the OR

Programming note: COV is baseline equivalent of dependent variable and any other covariate(s) which have not been specified at the time of writing of SAP

Table 90: Percentage of Subjects Abstinent from Smoking Weeks 3-6 – Among Baseline Smokers

Same analysis as Table 88

Table 91: Percentage of Subjects Abstinent from Smoking Weeks 3-6 – Full Model Logistic Regression (Among Baseline Smokers)

Same analysis as Table 89

Table 92: PSQI Scores – mITT Subjects

	ASP8062					Placebo		
Study Week	**N**	**Mean (SD[1])**	**Median**	**(Min-Max)**	**N**	**Mean (SD)**	**Median**	**(Min-Max)**
1	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)
5	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)
7	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)

[1] SD is standard deviation

Table 93: PSQI Scores (mITT) – Full Model, Mixed Effects, Weeks 5 & 7

Type III Wald Tests

Parameter	**Num DF[1]**	**Den DF[2]**	**F Value**	**p-value**
Arm	1	xx	xxx.xx	0.xxx
Site	xx	xx	xxx.xx	0.xxx
Baseline PSQI	1	xx	xxx.xx	0.xxx

[1] Numerator degrees of freedom; [2] Denominator degrees of freedom

Least Squares Means

				95% CI[2]				Model	
Arm	**Week**	**Estimate**	**SE[1]**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**
ASP8062	5	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	5	xx.xx	0.xxx	0.xxx	0.xxx				
ASP8062	7	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	7	xx.xx	0.xxx	0.xxx	0.xxx				

[1] SE is standard error; [2] CI is confidence interval

Programming note:If a transformation of the dependent variable is used add 2 columns: p-value and Cohen's d for the transformed model.

Table 94: POMS Total Mood Disturbance Score – mITT

	ASP8062				Placebo			
Study Week	**N**	**Mean (SD[1])**	**Median**	**(Min-Max)**	**N**	**Mean (SD)**	**Median**	**(Min-Max)**
1	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)
5	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)
7	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)

[1] SD is standard deviation

Table 95: POMS Total Mood Disturbance Score (mITT) – Full Model, Mixed Effects, Weeks 5 & 7

Type III Wald Tests

Parameter	**Num DF[1]**	**Den DF[2]**	**F Value**	**p-value**

Parameter	Num DF[1]	Den DF[2]	F Value	p-value
Arm	1	xxx	xxx.xx	0.xxx
Week	1	xxx	xxx.xx	0.xxx
Site	2	xxx	xxx.xx	0.xxx
Cov	x	xxx	xxx.xx	0.xxx
Arm*Week	x	xxx	xxx.xx	0.xxx

[1] Numerator degrees of freedom; [2] Denominator degrees of freedom

Programming note: Cov is the baseline equivalent of the dependent variable and any additional covariates included in the model.

Least Squares Means

				95% CI[2]				Model	
Arm	**Week**	**Estimate**	**SE[1]**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**
ASP8062	4	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	4	xx.xx	0.xxx	0.xxx	0.xxx				
ASP8062	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx				
ASP8062	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx				

[1] SE is standard error; [2] CI is confidence interval

Programming note:If a transformation of the dependent variable is used add 2 columns: p-value and Cohen's d for the transformed model.

Table 94 is the template for Tables 96, 98, 100, 102, 104, and 106. Table 95 is the template for Tables 97, 99, 101, 103, 105, and 107

Table 96: POMS Tension-Anxiety Score – mITT Subjects

Table 97: POMS Tension-Anxiety Score (mITT) – Full Model, Mixed Effects, Weeks 5 & 7

Table 98: POMS Anger-Hostility Score – mITT Subjects

Table 99: POMS Anger-Hostility Score (mITT) – Full Model, Mixed Effects, Weeks 5 & 7

Table 100: POMS Vigor-Activity Score – mITT Subjects

Table 101: POMS Vigor-Activity Score (mITT) – Full Model, Mixed Effects, Weeks 5 & 7

Table 102: POMS Fatigue-Inertia Score – mITT Subjects

Table 103: POMS Fatigue-Inertia Score (mITT) – Full Model, Mixed Effects, Weeks 5 & 7

Table 104 POMS Confusion-Bewilderment Score – mITT Subjects

Table 105: POMS Confusion-Bewilderment Score (mITT) – Full Model, Mixed Effects, Weeks 5 & 7

Table 106: POMS Depression-Dejection Score – mITT Subjects

Table 107: POMS Depression-Dejection Score (mITT) – Full Model, Mixed Effects, Weeks 5 & 7

Table 108: PROMIS Negative Consequences of Alcohol Scores – mITT Subjects

	Placebo					ANS-6637 200mg		
Study Week	N	Mean (SD[1])	Median	(Min-Max)	N	Mean (SD)	Median	(Min-Max)

1	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)
7	xx	xxx (xx)	xxx	(xx-xx)	xx	xxx (xx)	xxx	(xx-xx)

[1] SD is standard deviation

Table 109: ANCOVA PROMIS Negative Consequences of Alcohol – mITT Subjects

Type III Wald Test

Parameter	**Num DF[1]**	**Den DF[2]**	**F Value**	**p-value**
Arm	1	xx	xxx.xx	0.xxx
Site	2	xx	xxx.xx	0.xxx
Baseline PROMIS	1	xx	xxx.xx	0.xxx

[1] Numerator degrees of freedom; [2] Demonimator degrees of freedom

Least Squares Means

				95% CI[2]				**Model**	
Arm	**Week**	**Estimate**	**SE[1]**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**

				95% CI[2]				Model	
Arm	**Week**	**Estimate**	**SE[1]**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**
ASP8062	7	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	7	xx.xx	0.xxx	0.xxx	0.xxx				

[1] SE is standard error; [2] CI is confidence interval

Programming note:If a transformation of the dependent variable is used add 2 columns: p-value and Cohen's d for the transformed model.

12.1.6. Safety Analyses

Table 110: Overall Summary of Adverse Events – Safety Subjects

	ASP8062	Placebo	Total	
	(N=xx)	(N=xx)	(N=xxx)	p-value[1]
Number of AEs	xx	xx	xx	
Number of SAEs	xx	xx	xx	
Number (%) of subjects with at least one AE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Number (%) of subjects with at least one SAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Number (%) of subjects with at least one AE related[2] to study product	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Number of AEs by severity				
Mild	xx	xx	xx	
Moderate	xx	xx	xx	
Severe	xx	xx	xx	
Life-threatening	xx	xx	xx	
Number of AEs by relationship to study product				
At least possibly related	xx	xx	xx	
Unrelated	xx	xx	xx	
Number of AEs by SAE status				
No	xx	xx	xx	
Yes	xx	xx	xx	

[1]p-value from chi-square test [2] Related is possible, probable, or definite

Table 111: Number and Percentage of Subjects with Adverse Events - Safety Subjects

MedDRA System Organ Class/	ASP8062	Placebo
Preferred Term	(N=xx)	(N=xx)
- Any Adverse Events -	xx (xx.x%)	xx (xx.x%)
SOC		
- Overall -	xx (xx.x%)	xx (xx.x%)
Preferred term 1	xx (xx.x%)	xx (xx.x%)
Preferred term 2	xx (xx.x%)	xx (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.

Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 112: Summary of Subjects with Adverse Events by Severity and Relationship – ASP8062

Number of Subjects (%) (N=x)												
		Mild		Moderate		Severe		Life-threatening		All Grades		
SOC	MedDRA PT	R	NR	R	NR	R	NR	R	NR	R	NR	R + NR
		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Events are counted once per subject at the highest severity grade and closest relationship to the investigational product. R= related to investigational product (possibly, probably, definitely). NR = not related to investigational product (unrelated, unlikely).

Table 113: Summary of Subjects with Adverse Events by Severity and Relationship – Placebo

Number of Subjects (%) (N=x)												
		Mild		Moderate		Severe		Life-threatening		All Grades		
SOC	MedDRA PT	R	NR	R	NR	R	NR	R	NR	R	NR	R + NR
		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Events are counted once per subject at the highest severity grade and closest relationship to the investigational product. R= related to investigational product (possibly, probably, definitely). NR = not related to investigational product (unrelated, unlikely).

Table 114: Number and Percentage of Subjects with Adverse Events by Maximum Severity - Safety Subjects

MedDRA SOC/ Preferred Term	ASP8062 (N=xx)				Placebo (N=xx)			
	Mild	Moderate	Severe	Life-threatening	Mild	Moderate	Severe	Life-threatening
- Any Adverse Events -	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
SOC								
- Overall -	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
Preferred term 1	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 115: Number and Percentage of Subjects Adverse Events by Relatedness - Safety Subjects

MedDRA SOC/	ASP8062		Placebo	
Preferred Term	(n=xx)		(n=xx)	
	Related[1]	Not-Related[2]	Related	Not-Related
SOC	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
- Overall -				
Preferred term 1	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)

[1]Related are possibly, probably or definitely related to investigational product

[2] Not Related to investigational product (not related or unlikely)

Table 116: Number and Percentage of Subjects with Treatment-Related Adverse Events by Maximum Severity- Safety Subjects

MedDRA SOC/	ASP8062				Placebo			
Preferred Term	(N=xx)				(N=xx)			
	Mild	Moderate	Severe	Life-threatening	Mild	Moderate	Severe	Life-threatening
SOC	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
- Overall -								
Preferred term 1	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 117: Number and Percentage of Subjects with Adverse Events Occurring in >= 5% of Subjects in Any One Group - Safety Subjects

MedDRA SOC/ Preferred Term	ASP806 (N=xx)	Placebo (N=xx)	p-value[1]
SOC	nn (xx.x%)	nn (xx.x%)	x.xxx
- Overall -			
Preferred term 1	nn (xx.x%)	nn (xx.x%)	x.xxx
Preferred term 2	nn (xx.x%)	nn (xx.x%)	x.xxx

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term. At least % occurring in either arm to be included in the table.
[1]p-value from Fisher's exact test
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 118: Number and Percentage of Subjects with Adverse Events Leading to Discontinuation of Study - Safety Subjects

MedDRA SOC/ Preferred Term	ASP8062 (N=xx)	Placebo (N=xx)
SOC		
- Overall -	nn (xx.x%)	nn (xx.x%)
Preferred term 1	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 119: Number and Percentage of Subjects with Adverse Events Leading to Discontinuation of Study Drug – Safety Subjects

MedDRA SOC/ Preferred Term	ASP8062 (N=xx)	Placebo (N=xx)
SOC		
- Overall -	nn (xx.x%)	nn (xx.x%)
Preferred term 1	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 120: CIWA-AR Score ≥ 10 at Least Once During Treatment – Safety Subjects

	ASP8062	Placebo				95% CI[2]	
	(N=xx)	(N=xx)	p-value[1]	Cohen's h	Odds Ratio	OR[3] Lower CI	OR Upper CI
CIWA-AR Score >= 10							
Never	xx (xx.x%)	xx (xx.x%)					
At Least Once	xx (xx.x%)	xx (xx.x%)	0.xxx				
ASP8062 vs Placebo				0.xx	xx.xxx	xx.xxx	xx.xxx

1 Chi-squared test; [2] CI is confidence interval; [3] OR is odds ratio

Table 121: Summary of Vital Signs and Body Weights – Safety Subjects

		ASP8062					Placebo	
Parameter	**N**	**Mean (SD)**	**Med**	**Min-Max**	**N**	**Mean (SD)**	**Med**	**Min-Max**
Vital Sign (units)								
Screening	xx	xx.x (xx.xx)	xx.x	(xx.x – xx.x)	xx	xx.x (xx.xx)	xx.x	(xx.x – xx.x)
Week 1	xx	xx.x (xx.xx)	xx.x	(xx.x – xx.x)	xx	xx.x (xx.xx)	xx.x	(xx.x – xx.x)
Change from Baseline	xx	xx.x (xx.xx)	xx.x	(xx.x – xx.x)	xx	xx.x (xx.xx)	xx.x	(xx.x – xx.x)
Weeks 2,3,4,5,6,7								

Programmers note: vital signs include pulse rate, systolic blood pressure, and diastolic blood pressure. Body weight (kg) will also be presented.

Table 122: Summary of ECG Results - Safety Subjects

	ASP8062	Placebo
Result	**(N=xx)**	**(N=xx)**
Screening		
Normal	nn (xx.x%)	nn (xx.x%)
Abnormal, Not Clinically Significant	nn (xx.x%)	nn (xx.x%)

Abnormal, Clinically Significant	nn (xx.x%)	nn (xx.x%)
Week 4		
Normal	nn (xx.x%)	nn (xx.x%)
Abnormal, Not Clinically Significant	nn (xx.x%)	nn (xx.x%)
Abnormal, Clinically Significant	nn (xx.x%)	nn (xx.x%)
Week 7		
Normal	nn (xx.x%)	nn (xx.x%)
Abnormal, Not Clinically Significant	nn (xx.x%)	nn (xx.x%)
Abnormal, Clinically Significant	nn (xx.x%)	nn (xx.x%)

Table 123: Summary of Blood Chemistries and Hematology – Safety Subjects

	ASP8062				**Placebo**			
	N	**Mean (SD)**	**Med**	**(Min-Max)**	**N**	**Mean (SD)**	**Med**	**(Min-Max)**
Chemistry (units)								
Baseline Value	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)
Week 4	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)
Change from baseline	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)
Week 7	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)
Change from baseline	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)

Programmers note: table will include creatinine, ALT, AST, total bilirubin, alkaline phosphate, albumin, CrCl, GGT, *RBC, WBC, hematocrit, hemoglobin, platelets*.

Table 124: Summary of Urinalysis Continuous Data – Safety Subjects

	ASP8062	**Placebo**

	N	Mean (SD)	Med	(Min-Max)	N	Mean (SD)	Med	(Min-Max)
Urinalysis (units)								
Baseline Value	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)
Week 4	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)
Change from baseline	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)
Week 7	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)
Change from baseline	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)	xx	xx.x (xx.x)	xx.x	(xx.x-xx.x)

Programmers note: table will PH, specific gravity, and glucose result, .

Table 125: Summary of Urine Glucose and Nitrites – Safety Subjects

	ASP8062		Placebo	
	Positive	Negative	Positive	Negative
	n (%)	n (%)	n (%)	n (%)
Glucose				
Baseline	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Week 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Week 7	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Nitrites				

Baseline	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Week 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Week 7	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Table 126: Summary of Urine Protein, Ketones, Billirubin, Leukocyte Esterace, and Blood – Safety Subjects

	ASP8062			**Placebo**		
	Baseline	**Week 4**	**Week 7**	**Baseline**	**Week 4**	**Week 7**
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Blood						
Negative	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Trace	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1+	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
2+	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
3+	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
4+	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Ketones						
Negative	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Trace	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1+ (small)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
2+ (medium)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
3+ (large)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Protein						
Negative	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Trace	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1+	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
2+	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
3+	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
4+	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Programmer Note: Billirubin and Leukocyte Esterace follow the same as Protein

Table 127: Summary of Positive Urine Drug Tests, Preganancy Test or BAC > 0.02 Any Time During the Study– Safety Subjects

Test	**ASP8062**	**Placebo**

	(N=xx)	(N=xx)
THC	xx (xx%)	xx (xx%)
Cocaine	xx (xx%)	xx (xx%)
Opioids	xx (xx%)	xx (xx%)
Methamphetamine	xx (xx%)	xx (xx%)
Amphetamine	xx (xx%)	xx (xx%)
MDMA	xx (xx%)	xx (xx%)
Benzodiazapines	xx (xx%)	xx (xx%)
Buprenorphine	xx (xx%)	xx (xx%)
Methadone	xx (xx%)	xx (xx%)
Oxycodone	xx (xx%)	xx (xx%)
Ethylglucuronide (EtG)	xx (xx%)	xx (xx%)
Pregnancy	xx (xx%)	xx (xx%)
BAC > 0.02	xx (xx%)	xx (xx%)

Table 128: Frequency of Subjects with Suicidal Ideation Any Time During the Study – Safety Subjects

ASP8062	Placebo	p-value
(N=xx)	(N=xx)	
xx (xx.x%)	xx (xx.x%)	0.xxx

Table 129: Return to Baseline ACQ-SF-R Scores – Safety Subjects

	ASP8062	Placebo
Test	(N=xx)	(N=xx)
Screening		
Increased Craving, n (%)	xx (xx%)	xx (xx%)
Week 3		
Increased Craving, n (%)	xx (xx%)	xx (xx%)

12.2. Listings

Listing 1: Subject Disposition - All Subjects

Subject ID	Date of Consent	Treatment Group	mITT	Eval-uable	Safety	Study Completion	(Day) Date of Study Completion or Early Withdrawal	Reason for Early Withdrawal	Subject confined	Start Date/ End Date of confinement
xxx	ddmmmyyyy	ASP8062	Yes	Yes	Yes	Yes	(xx) ddmmmyyyy	xxxxxx	Yes	ddmmmyyyy / ddmmmyyyy
		Placebo	No	No	No	No			No	
		None								

Note: Day is relative to Study Day 0.

Listing 2. Enrollment and Randomization – All Consented Subjects

Subject ID	Treatment Group	Did the subject meet all eligibility criteria?	Randomized?	Date of Randomization	Kit Number
xxx	ASP8062	Yes	Yes	ddmmmyyyy	xxx
	Placebo	No	No		

Listing 3: Reason not Eligible – Screen Failures

Subject ID	Criterion Type	Criterion
xxx	Inclusion Criteria	
	Exclusion Criteria	

Listing 4: Protocol Deviations – Safety Subjects

Subject ID	Treatment Group	Deviation Date	Protocol Deviation	Details
xxx	ASP8062	ddmmmyyyy	Subject Failed to Meet the Inclusion/Exclusion Criteria	
	Placebo		Source Documentation was Not Available	
			Pregnancy Test Not Performed	
			Required study data was not obtained or obtained	

			late due to site error	
			Informed Consent Deviation	
			AE/SAE Reporting Deviation	
			Other Deviation:	xxxxxxxxxxxxxx

Note: Only subjects with protocol deviation are listed.

Listing 5: Subjects Excluded from the Efficacy Analysis or Evaluable Set

Subject ID	Treatment Group	Reason for Exclusion from mITT	Reason for Exclusion from Evaluable Set
xxx	ASP8062	xxxxxx	
	Placebo		

Note: Only subjects excluded from the efficacy analysis or evaluable set are listed.

Listing 6: Demographics Data – Safety Subjects

Subject ID	Treatment Group	Gender	Age (yrs)	Ethnicity	Race
xxx	ASP8062	Male	xx	Hispanic or Latino	American Indian or Alaska Native
	Placebo	Female		Not Hispanic or Latino	Asian
				Unknown	Native Hawaiian or Other Pacific Islander
					Black or African American
					White
					Other
					Unknown

Listing 7: Baseline Drinking Characteristics – mITT Subjects

Subject ID	Treatment Group	Drinks/Day (Days -1 to -28)	Drinks/Day (Days -1 to -14 Pre-randomization)	Drinks/ Drinking Day (Days -1 to -28)	Drinks/Drinking Day (Days -1 to -14 Pre-randomization)	Weekly % Heavy Drinking Days (Days -1 to -28)	Weekly % Heavy Drinking Days (Days -1 to -14 Pre-randomization)
xxx	ASP8062	xxx.x	xxx.x	xxxx	xxx.x	xxx.x	xxx.x
	Placebo						

Subject	Treatment	Weekly %Very	Weekly % Very	Weekly % Days	Weekly % Days

ID	Group	Heavy Drinking Days (Days -1 to -28)	Heavy Drinking Days (Days -1 to -14 Pre-randomization)	Abstinent (Days -1 to -28)	Abstinent (Days -1 to -14 Pre-randomization)
xxx	ASP8062	xxx.x	xxx.x	xxx.x	xxx.x
	Placebo				

Note: Exclude the three abstinent days during pre-randomization period.

Listing 8: Baseline Smoking Characteristics – mITT Subjects

Subject ID	Treatment Group	Over the past week, how many days did you smoke cigarettes?	How many cigarettes on average per day?	Over the past week, how many days did you use nicotine products?
xxx	ASP8062	None	xxx	None
	Placebo	1, 2, 3, 4, 5		1, 2, 3, 4, 5
		6, 7		6, 7
		Refused to answer		Refused to answer

Listing 9: MINI DSM-5 Disorders – Safety Subjects

Subject ID	Treatment Group	Visit Date	Diagnosis	Timeframe
xxx	ASP8062	ddmmmyyyy	xxxxxx	Current (2 weeks)
	Placebo			Past
				Recurrent

Note: Only subjects with a diagnosis of a disorder will be listed.

Listing 10: MINI DSM-5 AUD – Safety Subjects

Subject ID	Treatment Group	Visit Date	# of Symptoms
xxx	ASP8062	ddmmmyyyy	xx
	Placebo		

Listing 11: Medical History – Safety Subjects

Subject ID	Treatment Group	Medical History Verbatim Term/ Preferred Term/ SOC	Start Date	Ongoing
xxx	ASP8062	xxxxxxxxxx	ddmmmyyyy	No
	Placebo			Yes

Programming note: Only identify items that were scored "yes"

Listing 12: Drinking Goal – mITT Subjects

Subject ID	Treatment Group	Visit Date	Time	What goal have you chosen for yourself about drinking by the end of the study?	What might a typical week look like at the end of the study having achieved your goal? (number of drinks per day)	Motivation to reach goal	Confidence to reach goal
xxx	ASP8062	ddmmmyyyy	hh:mm	To stop drinking	xx	xx	xx
	Placebo			Reduce drinking but not stop			

Listing 13: Physical Exam – Safety Subjects

Subject ID	Treatment Group	Exam Date	Finding	Any abnormal finding during the physical exam?
xxx	ASP8062	ddmmmyyyy	xxxxxxxxxx	Yes
	Placebo			No

Programming Note: Only report the items that are abnormal

Listing 14: Daily and Weekly Standard Drink Units (TLFB) During Treatment – mITT Subjects

Subject ID	Treatment Group	Week	D1	D2	D3	D4	D5	D6	D7	Mean drinks/day	Mean drinks/ drinking day	Heavy drinking days	% days abstinent
xxx	ASP8062	1	xx	xx	xx	xx	xx	xx	xx				
	Placebo	2											
		3, etc											

Listing 15: Brief Drinking Questionnaire – mITT Subjects

Subject ID	**Treatment Group**	**Date of Assessment**	**Date that the last day of non-missing drinking data was collected by TLFB**	**This is a period of XX days since the last day of drinking data that was collected by TLFB**	**Did the subject drink during this period?**	**How many days during this period did the subject drink?**
xxx	ASP8062	ddmmmyyyy	ddmmmyyyy	xx	Yes	xx
	Placebo				No	

Subject ID	Treatment Group	Date of Assessment	How many alcoholic drinks on a typical day?	How many heavy drinking days?	Maximum number of drinks on any one day?	How many days did you drink this maximum number?
xxx	ASP8062	ddmmmyyyy	xx	xx	xx	xx
	Placebo					

Listing 16: Cue Reactivity – mITT Subjects

Subject ID	Treatment Group	Visit	Date of Assessment	Assessment Time	Cue	How strong is your craving to drink alcohol?	Having a drink would make things just perfect	If I could drink alcohol now, I would drink it
xxx	ASP8062	Screening	ddmmmyyyy	hh:mm	Water	xx	xx	xx

	Placebo	Week 2			Alcohol			

Subject ID	Treatment Group	Visit	Cue	It would be hard to turn down a drink right now	How much did you like the beverage just given to you?	Sum of first 4 questions
xxx	ASP8062	Screening	Water	xx	xx	xx
	Placebo	Week 2	Alcohol			

Listing 17: Drinking Consequences and Craving Scores – mITT Subjects

								Hyperkatifeia				
Subject ID	**Treatment Group**	**Week**	**CIWA-AR**	**ACQ-SF-R Pre**	**ACQ-SF-R Post**	**PACS**	**PROMIS Negative Consequences**	**Total**	**Stress**	**Depression**	**Irritable**	**Pain**
xxx	ASP8062		xxx	xxx	xxx	xxx	xxx	xxx				
	Placebo											

Listing 18: Pittsburg Sleep Quality Index Scores – mITT Subjects

Subject ID	Treatment Group	Week	Total score
xxx	ASP8062	Screening	xx
	Placebo	Week 6	

		Week 7	

Listing 19: Smoking and Other Nicotine Use Data– mITT Subjects

Subject ID	Treatment Group	Week	Visit Date	Over the past week, how many days did you smoke cigarettes?	On the days you smoked, how many cigarettes did you smoke on average?	How many days use nicotine products during the past week?
xxx	ASP8062		ddmmmyyyy	x	xx	x
	Placebo					

Listing 20: **MINI AUD– Safety Subjects**

Subject ID	**Treatment Group**	**Item**											**# of Symptoms**
		1	2	3	4	5	6	7	8	9	10	11	
xxx	ASP8062	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
	Placebo	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	
		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	

Item #	**List of Items**
1	a. During the times when you drank alcohol, did you end up drinking more than you planned when you started?
2	b. Did you repeatedly want to reduce or control your alcohol use? Did you try to cut down or control your alcohol use, but failed? IF YES TO EITHER, MARK YES.
3	c. On the days that you drank, did you spend substantial time obtaining alcohol, drinking, or recovering from the effects of alcohol?
4	d. Did you crave or have a strong desire or urge to use alcohol?
5	e. Did you spend less time meeting your responsibilities at work, at school, or at home, because of your repeated drinking?
6	f. If your drinking caused problems with your family or other people, did you still keep on drinking?
7	g. Were you intoxicated more than once in any situation where you or others were physically at risk, for example, driving a car, riding a motorbike, using machinery, boating, etc.?
8	h. Did you continue to use alcohol, even though it was clear that the alcohol had caused or worsened psychological or physical problems?
9	i. Did you reduce or give up important work, social or recreational activities because of your drinking?
10	j. Did you need to drink a lot more in order to get the same effect that you got when you first started drinking or did you get much less effect with continued use of the same amount?
11	K1. When you cut down on heavy or prolonged drinking did you have any of the following: [increased sweating or heart rate; hand tremor or “the shakes”; trouble sleeping; nausea or vomiting; hearing or seeing things other people could not see or hear or having sensations in your skin for no apparent reason; agitation; anxiety; seizures] (If yes to 2 or more of these, check yes for this question), OR K2. Did you drink alcohol to reduce or avoid withdrawal symptoms or to avoid being hung over? If K1 or K2 = yes, then score as yes.

Listing 21. Exit Interview – mITT Subjects

Subject ID	Treatment Group	Visit Date	Did you think you were receiving the study drug or the placebo?	What is your desire to please people?	If you had the opportunity in the future to take the study drug again, would you continue to take it for more than 5 weeks?	Did you limit your drinking because of flushing (a heat reaction or facial redness)?
xxx	ASP8062	ddmmmyyyy	Placebo	More than average	Yes	Yes
	Placebo		Study Drug	Average	No	No
			Don't know	Less than average	Refuse to answer	Refuse to answer
			Refuse to answer	Refuse to answer		

Subject ID	Treatment Group	Visit Date	Did you limit your drinking because of nausea or other effects?	Did your friends or family notice flushing?	If your friends or family noticed flushing, did this change your drinking?	Did you ever miss a dose of medication to avoid these effects?	Did you use any other services during the study to help you reduce drinking?
xxx	ASP8062	ddmmmyyyy	Yes	Yes	Yes	Yes	Yes
	Placebo		No	No	No	No	No
			Refuse to answer	Refuse to answer	Refuse to answer	Refuse to answer	Refuse to answer

Listing 22: Drug Exposure from AiCure– mITT Subjects

			Pills Taken								
Subject ID	**Treatment Group**	**Study Week**	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**	**Total Taken**	**Total Expected**
xxx	ASP8062	1, 2, 3, 4, 5,6	x	x	x	x	x	x	x	xx	xx
	Placebo										

Listing 23: Drug Accountability – Safety Subjects

Subject ID	**Treatment Group**	**Blister Pack #**	**Date Dispensed**	**Date Returned**	**# Pills Returned**
xxx	ASP8062	1, 2, 3, 4	ddmmmyyyy	ddmmmyyyy	xx
	Placebo				

Listing 24: Take Control – mITT Subjects

		Dates Modules Viewed

Subject ID	**Treatment Group**	**1**	**2**	**3**	**4**	**5**	**6**	**7**
xxx	ASP8062	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy
	Placebo							

Listing 25: Adverse Events – Safety Subjects

Subject ID	Treatment Group	Adverse Event (Verbatim) S: SOC P: PT Term	Start Date/ Day	Stop Date/ Day	Duration in Days	Severity	Relation -ship	Actions Taken	Outcome	Serious
xxx	ASP8062	Verbatim	ddmmmyyyy/ xx	ddmmmyyyy/ xx		1	1	1	1	Yes
	Placebo	S: xxxx	xx	xx		2	2	2	2	No
		P: xxxx				3	3	3	3	
						4	4	4	4	
							5	5	5	
								6		

Notes: Day is relative to Study Day 0.
Severity: 1=Mild; 2=Moderate; 3=Severe; 4=Potentially Life-threatening.
Relationship: 1= Unrelated; 2=Unlikely; 3=Possibly; 4=Probably; 5=Definitely
Action Taken Due to AE: 1=None; 2=Treated with Drugs; 3=Non-drug treatment; 4=ER/Outpatient visit; 5=Hospitalization; 6=Referral for treatment
Outcome: 1=Resolved; 2=Recovered with sequelae; 3=Ongoing; 4=Required treatment; 5=Unknown

Programmer's Note: If "Were any AEs reported?" checkbox=No, then display "None Reported" in the Adverse Event column and SOC/PT column. If an AE started and stopped the same day, the duration is 1 day.

Listing 26: Serious Adverse Events – Safety Subjects

Subject ID	**Treatment Group**	**SAE Verbatim S: SOC P: PT**	**Start Date/ Day**	**Stop Date/ Day**	**SAE Category**	**SAE Description**	**Relevant tests/ laboratory data**
xxx	ASP8062	Verbatim	ddmmmyyyy	ddmmmyyyy	Results in Death		xxxxxx
	Placebo	S: XXX	Xx	Xx	Life-threatening		

		P: XX			Requires or Prolongs Hospitalization		
					Disability		
					Congenital Anomaly/Birth Defect		
					Required Intervention to Prevent Persistant or Significant Disability / Incapacity		
					Other		

Subject ID	**SAE**	**Date of death**	**Cause of death**	**Hospitalization Date/Discharge Date**	**Comments**
xxx	Verbatim	ddmmmyyyy	xxxxxx	ddmmmyyyy	xxxxxxxxxxxxxxxxxxxxxx
				ddmmmyyyy	

Notes: Day is relative to Study Day 0.
Severity: 1=Mild; 2=Moderate; 3=Severe; 4=Potentially Life-threatening.
Relationship: 1= Unrelated; 2=Unlikely; 3=Possibly; 4=Probably; 5=Definitely
Outcome: 1=Recovered/Resolved; 2=Recovering/Resolving; 3=Not Recovered/Not Resolved; 4=Recovered/Resolved With Sequelae; 5=Fatal (Date of Death)

Listing 27: POMS Scores – mITT Subjects

			Scores						
Subject ID	**Treatment Group**	**Week**	**Total Mood Disturbance**	**Tension**	**Depression**	**Anger**	**Fatigue**	**Confusion**	**Vigor**
xxx	ASP8062		xxx	xxx	xxx	xxx	xxx	xxx	xxx
	Placebo								

Listing 28. Columbia-Suicide Severity Scale – Safety Subjects

				Response to Question:												
Subject ID	**Treatment Group**	**Visit Date**	**Study Week**	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**	**Q9**	**Q10**	**Q11**	**Q12**	**Q13**
xxx	ASP8062	ddmmmyyyy		Yes	Yes	Yes	Yes	Yes	Yes	Type 1	1	1	0	0	0	Yes
	Placebo			No	No	No	No	No	No	Type 2	2	2	1	1	1	No
										Type 3	3	3	2	2	2	
										Type 4	4	4	3	3	3	
										Type 5	5	5	4	4	4	
													5	5	5	

Suicide Ideation

1. Have you wished you were dead or wished you could go to sleep and not wake up?
2. Have you actually had any thoughts of killing yourself?
3. Have you been thinking about how you might do this?
4. Have you had these thoughts and had some intention of acting on them?
5. Have you started to work out or worked out the details of how to kill yourself?
6. Do you intend to carry out this plan?

Intensity of Ideation

7. The following features should be rated with respect to the most severe type of ideation (i.e. 1-5 with 1 being the least severe and 5 being the most severe)
8. How many times have you had these thoughts?1=Less than once a week; 2=Once a week; 3=2-5 times a week; 4=Daily or almost; 5=Many times each day
9. When you have the thoughts, how long do they last? 1=Fleeting-few seconds or minutes; 2=Less than 1 hr-some of the time; 3=1-4 hrs/a lot of time; 4=4-8 hrs/most of day; 5=More than 8 hours/persistent or continuous
10. Could/can you stop thining about killing yourself or wanting to die if you want to? 1=Easily; 2=Little Difficulty; 3=Some Difficulty; 4=Lot of Difficulty; 5=Unable to control; 0=Does not attempt to control
11. Are there things that stop you from wanting to die or acting on thoughts of committing suicide? 1=Definite deterrents; 2=Probably Deterrents; 3=Uncertain Deterrents; 4=Unlikely Deterrents; 5=No Deterrents; 0=Does not apply
12. What sort of reasons did you have for thinking about wanting to die or killing yourself? Was it to end pain or stop the way you were feeling or to get attention, revenge or reaction from others 1=Completely to get attention or revenge or reaction; 2=Mostly to get attention or revenge or reaction; 3=Equally to get attention or revenge or reaction and stop pain; 4=Mostly to stop pain; 5=Completely to stop pain; 0=Does not apply

Suicidal Behavior

13. Have you made a suicide attempt?

			Response to Question:										
Subject ID	**Treatment Group**	**Study Week**	**Q14**	**Q15**	**Q16**	**Q17**	**Q18**	**Q19**	**Q20**	**Q21**	**Q22**	**Q23**	**Q24**
xxx	ASP8062		xx	Yes	Yes	xx	Yes	xx	Yes	Yes	Yes	0	0
	Placebo			No	No		No		No	No	No	1	1
												2	2
												3	
												4	
												5 (date ddmmmyyyy)	

14. Number of attempts
15. Has the subject engaged in non-suicidal self-injurious behavior?
16. Has there been a time when you started to do something to end your life but someone or something stopped you before actually did anything?
17. Number interrupted
18. Has there been a time when you stared to do something to try to end your life but you stopped yourself before you actually did anything?
19. Number aborted
20. Have you taken any step towards making a suicide attempt or preparing to kill yourself?
21. Suicidal behavior was present during the assessment period
22. Completed suicide?
23. Actual Lethality/Medical Damage; 0=No physical damage; 1=Minor physical damage; 2=Moderate physical Damage; 3=Moderately severe physical damage; 4=Severe physical damage; 5=Death
24. Potential Lethality; 0=Behavior not likely to result in injury; 1=Behavior likely to result in injury, but not death; 2=Behavior likely to result in death

Listing 29: Blood Chemistries – Safety Subjects

Subject ID	Treatment Group	Visit Date	Test Name	Result	Units	Flag	Evaluation
xxxx	ASP8062	ddmmmyyyy	Creatinine	x.xx	mg/dL	H (high)	WNL
	Placebo		Total Bilirubin	xxx	mg/dL	L (low)	Abnormal, NCS
			ALT	xx.x	U/L		Abnormal, CS
			AST	x.xx	U/L		
			BUN	Xx	mg/dL		
			Creatinine Clearance	xxx.xx	mL/min		
			Akaline Phosphate	xxx.x	U/L		

Subject ID	Treatment Group	Visit Date	Test Name	Result	Units	Flag	Evaluation
			Albumin	xx.x	g/dL		
			GGT	xx.x	U/L		
			Total Cholesterol	xxx	mg/dL		
			Triglycerides	xx	mg/dL		
			Chloride	xxx	mmol/L		
			Sodium	xxx	mmol/L		
			Potasium	xx.x	mmol/L		

Listing 30: Hematology – Safety Subjects

Subject ID	Treatment Group	Visit Date	Test Name	Result	Units
xxxx	ASP8062	ddmmmyyyy	Hematocrit	xxx.xx	%
	Placebo		Hemoglobin	xxx	g/dL
			RBC	xx.x	mil/uL
			WBC	x.xx	thous/uL
			Platelets	xxx.xx	thous/uL
			Neutrophils	xxx.x	%
			Monocytes	xx.x	%
			Eosinophils	xx.x	%

Subject ID	Treatment Group	Visit Date	Test Name	Result	Units
			Basophils	xx.x	%

Listing 31: Urinalysis – Safety Subjects

Subject ID	Treatment Group	Visit Date	Study Week	pH	Specific Gravity	Glucose	Glucose Result (mg/dL)	Protein	Ketones	Blood	Nitrites	Bilirubin	Leukocyte Esterase
xxx	ASP8062	ddmmmyyyy	Screen	xx.x	x.xxx	Negative	xxxx	Negative	Negative	Negative	Negative	Negative	Negative
	Placebo		x			Positive		Trace	Trace	Trace	Positive	Trace	Trace
								1+	1+	1+		1+	1+
								2+	2+	2+		2+	2+
								3+	3+	3+		3+	3+
								4+	4+	4+		4+	4+

Listing 32: Urinalysis Microscopy[1] – Safety Subjects

Subject ID	Treatment Group	Visit Date	Test Name	Result (cells/HPF)
xxxx	ASP8062	ddmmmyyyy	Microscopic RBC	xx
	Placebo		Microscopic WBC	xx
			Epithelial Cells	xx
			Hyaline Casts	xx

[1]Only subjects that had microscopy

Listing 33: Pregnancy Test/Birth Control Data – Safety Subjects

Subject ID	Treatment Group	Gender	Pregnancy Test Performed?	Pregnancy Test / Visit Date	Pregnancy Result	Methods of birth control
xxx	ASP8062	Male	Not Done	ddmmmyyyy	Negative	Oral Contraceptive
	Placebo	Female	Yes		Positive	Vasectomy
						Contraceptive Skin Patch
						Intrauterine
						Medroxyprogesterone
						Complete Abstinence
						Tubal Ligation or Postemopausal
						Other : xxxxxxxxxxxxxxx

Programming note: Only indicate birth control methods that were indicated as Yes

Listing 34: Blood Alcohol Concentration – Safety Subjects

Subject ID	Treatment Group	Visit Date	Study Week	BAC Performed	Time of BAC	BAC %
xxx	ASP8062	ddmmmyyyy	x	Done	hh:mm	x.xxx
	Placebo			Not Done		

Listing 35. Urine Drug Screen – Safety Subjects

Subject ID	Treatment Group	Visit Date	Study Week	AMP[1]	Benzos[2]	Coc[3]	Bup[4]	Meth[5]	Methadone	Opioids	THC	Barb[6]	MDMA	EtG[7]
xxx	ASP8062	ddmmmyyyy	Screen	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg
	Placebo		x	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos

[1]AMP = Amphetamine; [2]Benzos = Benzodiazapines; [3] Coc = Cocaine; [4] Bup = Buprenorphine; [5] Methamphetamine; [6]Barb = Barbituates;
[7] EtG = Ethyl Glucuronide; Note: Neg=negative; Pos=positive

Listing 36: Vital Signs and Body Weights– Safety Subjects

Subject ID	Treatment Group	Visit Date	Study Week	Weight (Kg)	Heart Rate (beats/min)	Systolic Pressure (mmHg)	Diastolic Pressure (mmHg)
xxx	ASP8062	ddmmmyyyy	Screening	xxx	xxx	xxx	xxx
	Placebo		x				

Listing 37. ECG – Safety Subjects

Subject ID	Treatment Group	Visit Date	Study Week	Result	If abnormal, specify finding
xxx	ASP8062	ddmmmyyyy	Screen 1	Normal	xxxxxxxxxxx
	Placebo		x	Abnormal, NCS	
				Abnormal, CS	

Listing 38. Prior and Concomitant Medications – Safety Subjects

Subject ID	Treatment Group	Prohibited Med	Verbatin Med	Indication	Route	Frequency	Dose	Start Date/ Stop Date	Study Day	Continuing?
xxx	ASP8062	Yes	xxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx	ddmmmyyyy	xxx	Yes
	Placebo									
		No	xxx							No

Prohibited meds include CYP3A4 inhibitors, CYP3A4 inducers, Benzodiazepines sedatives/hypnotics/anxiolytics, Monoamine oxidase inhibitors, Opioids, Opioid partial agonist-antagonists/opioid antagonists, and Drugs approved or have clinical data supporting their use for the treatment of AUD.

Listing 39: Blood for Drug Concentrations – Safety Subjects

Subject ID	Treatment Group	Sample Collected?	Date	Time	ASP8062 Plasma Level (ng/mL)	AS3486189 Plasma Level (ng/mL)	AS3486191 Plasma Level (ng/mL)	AS3486192 Plasma Level (ng/mL)
xxx	ASP8062	Yes	ddmmmyyyy	hh:mm	xxx	xxx	xxx	xxx
	Placebo	No						

Listing 40: **Comments – Safety Subjects**

Subject ID	Treatment Group	Comments
xxx	ASP8062	xxxxxxxxxxxxx
	Placebo	

12.3. Figures

Figure 1: Percentage of Subjects No Heavy Drinking Days Weeks 3-6

*Programmer note: Use percent on y-axis, bar graph of PSNHDD add Cohen's h, * a significant p-value, put values on graph*

Figure 2: Percentage of Subjects Abstinent Weeks 3-6

*Programmer note: bar graph of PSA add Cohen's h, * a significant p-value, put values on graph*

Figure 3: Weekly Percentage of Subjects No Heavy Drinking Days (mITT)

*Programmer note: graph of estimates out to 5 weeks. Include 95% confidence intervals for each estimate and * on statistically significant differences between treatment groups.*

Figure 4: Weekly Percentage of Subjects Abstinent (mITT)

Figure 5: Weekly Percentage WHO 1-Level Decrease in Alcohol Consumption (mITT)

Figure 6: Weekly Percentage WHO 2-Level Decrease in Alcohol Consumption No Imputation (mITT)

Figure 7: Percentage Days Abstinent per Week Least Squares Means – (mITT)

Figure 8: Percent Heavy Drinking Days per Week Lease Squares Means –(mITT)

Figure 9: Mean Drinks per Week Lease Squares Means – (mITT)

Figure 10: Mean Drinks per Drinking Day by Week Least Squares Means – (mITT)

Figure 11: Weekly Number of Cigarettes Smoked in Smokers Over Entire Treatment Period – Least Squares Means (mITT)

Figure 12: Clinical Chemistry, Urinalysis, and Hematology Values Over Time