SUMMITANALYTICAL	**STATISTICAL ANALYSIS PLAN** **CONFIDENTIAL**

Title: Phase I, Open-Label Trial to Evaluate the Safety and Immunogenicity of SNS-301 in Cancer Patients

Protocol: SNS0216

Compound: SNS-301

Phase: 1

Sponsor: Sensei Biotherapeutics, Inc.
620 Professional Drive
Gaithersburg, MD 20879 United States

Author: Summit Analytical
8354 Northfield Blvd.
Bldg. G Suite 3700
Denver, CO 80238

Date: December 21, 2018

Status: Final Version 2.0

Table of Contents

1 List of Abbreviations and Definition of Terms

Only abbreviations and terms relevant to the SAP are repeated herein. The reader is referred to the protocol for the complete and comprehensive list of abbreviations and definitions of terms for the study.

Abbreviation/Term	Definition
ADaM	Analysis data Model
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
CBC	Complete Blood Count
CDISC	Clinical Data Interchange Standards Consortium
CH50	Total Complement Activity
CTL	Cytotoxic CD8+ T-lymphocytes
DLT	Dose-limiting Toxicity
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Care Report Form
EDC	Electronic Data Capture
HAAH	Human aspartyl-asparaginyl-β-hydroxylase
MedDRA	Medical Dictionary for Regulatory Activities
MTD	Maximum Tolerated Dose
NCI-CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
SNS-301	HAAH bacteriophage lambda constructs: HAAH-1λ
PBMC	Peripheral Blood Mononuclear Cells
PD	Pharmacodynamic
PSA	Prostate-specific Antigen
PT	Preferred Term
RP2D	Recommended Phase 2 Dose
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD or sd	Standard Deviation
SDTM	Study Data Tabulation Model
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
WHO	World Health Organization

2 Introduction

This document presents a statistical analysis plan (SAP) for Sensei Biotherapeutics, Inc. Protocol SNS0216, Phase I, Open-Label Trial to Evaluate the Safety and Immunogenicity of SNS-301 in Cancer Patients.

Reference materials for this statistical plan include the Protocol SNS0216 Version 5.0 (dated 12 June 2018) and Electronic Case Report Forms (eCRF) (dated 07 August 2018).

3 Study Objectives

Primary:

To determine the maximum tolerated dose (MTD) of SNS-301 based on the incidence of dose-limiting toxicities (DLT) and the maximum administered dose of SNS-301, when administered every 21 days in patients with biochemically relapsed prostate cancer.

Secondary:

To assess the overall safety, immunogenicity and clinical activity of SNS-301.

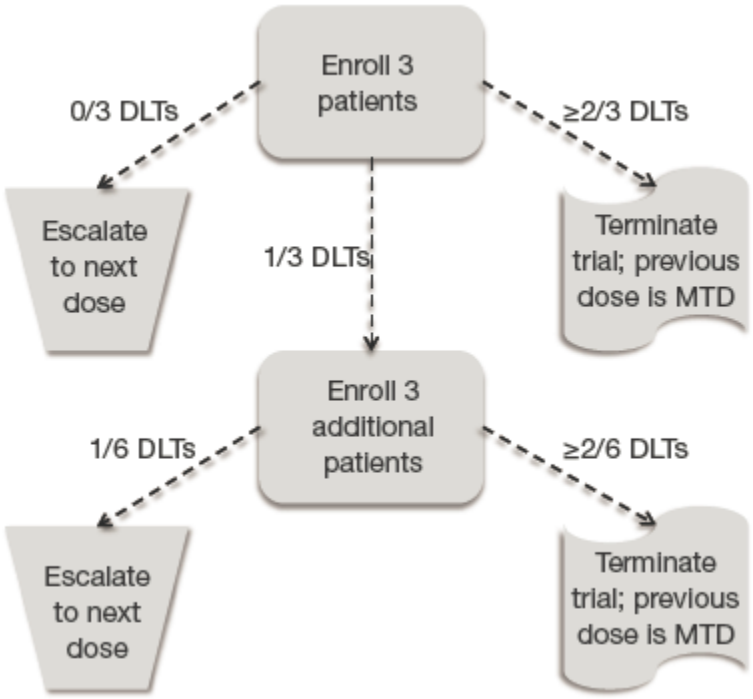
4 Study Design

As background for the statistical methods presented below, this section provides an overview of the study design. This overview is a summary only. The protocol is the definitive reference for all matters discussed in what follows.

This is a Phase I, open-label study of SNS-301, an HAAH (Human aspartyl-asparaginyl-β-hydroxylase)-directed nanoparticle vaccine, given intradermally in cohorts of patients with biochemically relapse prostate cancer, using a fixed dose-escalation schema every 21 days to establish the MTD.

Following informed consent and screening, patient serum will be tested for the expression of HAAH. Patients who test positive for HAAH expression in fresh serum may be continued in the study. Baseline biochemical testing (chemistry, complete blood count [CBC], coagulation panel, total complement activity [CH50], and prostate-specific antigen [PSA]) will be obtained prior to study treatment administration.

Figure 4-1. DOSE-ESCALATION STUDY DESIGN (3+3 SCHEMA)



Treatment will consist of single repeated doses of SNS-301 administered every 21 days. A traditional 3+3 dose-escalation schema will be used to determine the MTD of SNS-301 for the first 2 doses and a modified dose-escalation schema with 6 patients per dose level for the remaining dose (Figure 4-1). Planned doses of SNS-301 are 2.0 x 10^{10}, 1.0 x 10^{11} and

3.0 x 10^{11} particles per administration diluted to 1 mL and administered intradermally. Additional patients will be enrolled at the highest dose level until at least 6 patients can be evaluated even if no DLTs are observed at the dose. Planned treatment may continue for two additional doses of SNS-301 administered every 21 days. Serum and whole blood samples will be obtained on the day of study treatment administration (Day 1) and 21 days thereafter. In patients who continue to receive study treatment, biochemical and immunologic testing will continue every 21 days.

The MTD will be determined over the first 21-day interval following a single dose of SNS-301 in 3 consecutive dose cohorts. The MTD will be considered the dose level lower than that dose which produces ≥2 DLTs in 3 or 6 patients. A DLT will be considered a protocol-specified drug related grade 3-4 (National Cancer Institute Common Terminology Criteria for Adverse Events [NCI-CTCAE] V 4.03) adverse experience). The recommended Phase 2 dose (RP2D) will be the highest dose administered if no MTD is observed.

Dose cohorts will be enrolled sequentially.

Dose-escalation will proceed once all patients in a cohort (unless the MTD is observed) have completed a 21-day safety evaluation following the first dose of study treatment in the cohort. Planned treatment may continue for an additional 2 extra doses of SNS-301 administered every 21 days. Additional patients will be enrolled at the highest dose level until at least 6 patients can be evaluated even if no DLTs are observed at the dose. In patients who tolerate SNS-301, additional treatment may be continued with single doses of SNS-301 at their current dose level to maintain geometric mean titer (GMT) of HAAH antibodies to no less than 4 times the baseline value for at least six months (9 injections). Treatment will be terminated with the 9th injection or will otherwise be terminated at any time upon the observance of PSA doubling < 90 days or occurrence of unacceptable toxicity as determined by the Investigator (either for that patient or in their dose cohort). After termination, patients will be followed for an additional 6 months with monthly PSA levels and imaging studies as needed.

Once the MTD/RP2D is determined, patients receiving ongoing treatment may be escalated to that dose for subsequent treatments and receive a maximum of 9 injections. Patients who have received more than 9 injections due to the timing of the amendment limiting therapy to 6 months (9 doses), will be stopped at their last dose received and be followed for 6 months as with other patients. These subjects will continue to be followed for safety and biochemical PSA monitoring on a monthly basis for 6 months and are eligible to resume SNS-301 in case of increases in PSA doubling to < 90 days or other evidence of disease progression and decline in immunological parameters.

Exploratory pharmacodynamic (PD) analysis will be performed using dose, vaccine-specific antibody response (geometric mean titer), antigen-specific T and B cell indices, and the relative expression of HAAH in each patient's tumor. The PD will be balanced and optimized to the degree of antigen-specific immune response and minimized for the production of regulatory immune processes.

Safety endpoints will be evaluated by the incidence and severity of administration site reactions, changes in biochemical safety measures, general incidence and types of AEs, serious adverse events (SAEs), and other overt toxicities.

The duration of the study for each patient will include an up to 8-week screening phase, 21-day study treatment cycles for 9 cycles and 6 months of follow up including monthly PSAs, and an end of study visit (28 days post last dose of study treatment). Patients may continue to receive single repeated doses of SNS-301 at their original dose level (or at the MTD when it is determined) every 21 days or until the observance of PSA doubling < 90 days or unacceptable toxicity (either for that patient or in their dose cohort).

A complete schedule of procedures and assessments is in Table 4-1.

Table 4-1. TIME AND EVENTS SCHEDULE

Assessment	Screen (D-56+7[e] to D0)	Cycle 1 Assessments			Cycle 2-3		Additional Treatments	Follow-up/End of study
		D1	D8 ± 2	D15± 2	D22 ± 3	D43 ± 3	Every 21 ± 3 day	Every 28 ± 3 days after final treatment for 6 Months
Signed Informed Consent	X							
HAAH assessment[a]	X							
Demographics	X							
Medical/Oncology History	X							
Tumor Burden Evaluation[d]	X							
Baseline Signs and Symptoms	X							
Physical Examination	X							X
Symptom-Directed Physical Examination		X	X	X	X	X	X	
Vital Signs	X	X	X	X	X	X	X	X
ECOG Performance Score	X	X	X	X	X	X	X	X
ECG	X	X			X	X	X	X
PSA	X	X			X	X	X	X
Hematology[b]	X	X	X	X	X	X	X	
Chemistry[b]	X	X	X	X	X	X	X	
Coagulation, CH50[b]	X	X	X	X	X	X	X	
Study Treatment administration		X			X	X	X	
Physician Administration Site Assessment		X	X		X	X	X	
Immunologic Blood Collection[c]		X			X	X	X	X
Cohort enrollment evaluation					X			
Concomitant Medications Collection		X	X	X	X	X	X	X
Adverse Events Assessments[f]		X	X	X	X	X	X	X

a HAAH assessment: following informed consent, archived prostate tumor tissue and patient serum will be tested for the expression of HAAH. Only patients who test positive for HAAH expression in archived tumor tissue (if available) or fresh serum may be continued in the study. HAAH assessments are not subject to the 56-day screening window and are valid for 6 months. Patients who are negative for HAAH may be followed for 6 months and if PSA rises over that period time, they can enroll in the study provided that tissue or fresh serum is positive for HAAH

b Biochemical testing (chemistry, complete blood count, coagulation, and total complement CH50,) to be obtained within 14 days prior to study drug administration if screening period is between 3 and 8 weeks. PSA levels are also to be evaluated at screening and within 14 days prior to study drug administration if screening period is between 3 and 8 weeks.

c Immunologic blood collection: to be taken pre-dose on the day of study drug administration (Day 1) and every 21 days thereafter. Following the 9th dose (or last dose otherwise), PSA levels and other assessments will be followed on a monthly basis for 6 months. Patients with evidence of progression and declining HAAH immune parameters will have the option of resuming therapy on the study protocol.

d Baseline radiological tumor burden evaluation consists of a baseline pelvic MRI or CT scan in addition to bone scan. These studies will need to be performed within 56 days (+ 7 days) prior to the start of the study.

e Patients that have a delay in screening beyond 56-days may be re-screened for randomization.

f Adverse events that occur post patient receiving study drug. Should Adverse event occur prior to patient receiving study drug they will be captured as Medical History.

5 Analysis Populations

There will be two analysis populations defined for this study. All populations will be analyzed as treated.

1. The "Safety Population" will be comprised of all subjects who received a study treatment administration.

2. The "Immunologic Population" will be comprised of all subjects who received a study treatment administration and for whom any follow-up immunologic data were recorded for a specific immunological analysis.

6 Analysis Variables

In what follows, variables to be analyzed have been grouped under the headings 6.1 to 6.5. Additional variables may be added as further drafts of the eCRF and this SAP are developed and/or as discussion unfolds concerning the usefulness of *derived* variables formulated using the information presented below.

6.1 Study Drug Dosing

- Study treatment administered
- Treatment dose

6.2 Demographics and Baseline Characteristics

- Gender
- Age
- Race
- Ethnicity
- Weight
- Height
- Body mass index (BMI)
- Medical/oncologic history
- Prior medications

6.3 Primary Endpoints

Primary endpoints are derived at the end of each cohort and are not within the scope of the SAP.

- Determine the MTD
- Determine the RP2D if different than the MTD
- Determine the DLTs possibly-, probably-, or definitely related to SNS-301 (based on the NCI-CTCAE V4.03 criteria):
    - Grade 4 non-hematological toxicities (excluding alopecia) of any duration
    - Grade 3 non-hematologic (non-laboratory) toxicity lasting > 3 days despite optimal supportive care
    - Any Grade 3 or Grade 4 non-hematologic laboratory value if: a). Medical intervention is required to treat the subject; b), the abnormality leads to hospitalization; c). The abnormality persists for >1 week.
    - Grade 4 hematologic toxicity, other than those specified in criteria 5 and 6 below, lasting > 7 days
    - Grade 3 or Grade 4 febrile neutropenia of any duration
    - Grade 3 thrombocytopenia in combination with a grade 3 or greater blood and lymphatic system disorder

- Grade 3 AST or ALT that is associated with a grade 2 rise in bilirubin

6.4 Secondary Endpoints

- Incidence of administration site reactions
- Biochemical safety and tolerability (hematology, serum chemistry, coagulation, CH50)
- Geometric mean titers of anti-HAAH antibodies by dose
- Antigen-specific Cytotoxic CD8+ T-lymphocytes (CTL) responses by dose
- Production of B cell and T cell response of interest

Clinical Secondary Endpoints:

- Change in the prostate-specific antigen (PSA) velocity
- Reduction in the PSA doubling time from pre-baseline

Pharmacodynamic Secondary Endpoints:

- Duration of antigen-specific anti-HAAH antibody titers
- Changes in the amplitude or duration of the production of anti-HAAH antibodies
- Correlation of anti-HAAH titers and serum HAAH levels

6.5 Safety Variables

In addition to the assessments listed as endpoints above, safety assessments include the following:

- AEs and SAEs
- Vital signs (blood pressure, heart rate, body temperature)
- Eastern Cooperative Oncology Group (ECOG) performance score
- ECG (heart rate, PR interval, QRS interval, QT interval, QTcF interval, atrial rate, ventricular rate)
- Concomitant medications
- Physical examination

7 Statistical Methodology

7.1 Sample Size

Cohorts of 3 or 6 patients will be screened and treated at each dose level. The actual sample size may vary depending on the incidence of DLT during the first cycle at a given dose level.

Approximately 18 patients will be included and treated in the trial.

7.2 Randomization

Not applicable.

7.3 Interim Analysis

No interim analysis is planned for this study.

7.4 Analysis of the Study

All statistical tests will be two-sided and a difference resulting in a p-value of less than or equal to 0.05 will be considered statistically significant. All p-values will be rounded to and displayed in four decimals. If a p-value less than 0.0001 occurs it will be shown in tables as <0.0001.

There will be no multiplicity adjustments.

Descriptive summaries of variables will be provided where appropriate. For continuous variables, the number of non-missing values (n) and the median, mean, standard deviation, minimum, and maximum will be tabulated by dosage group. For categorical variables, the counts and proportions of each value will be tabulated by dosage group. Since this study allows for subjects to change their dose level during additional treatment visits after Day 43, the dose level can change over the course of the study; see Section 8 for how summaries by dosage group will be handled when dose levels vary.

Expansion of descriptive table categories within each treatment may occur if such elaborations are thought to be useful.

Assessments completed during the 6-month follow up period after study treatment will not appear in any tables or graphs (unless noted otherwise), but will be included in the data listings, classified under the last dose level the subject took at the last treatment visit prior to the end of study.

All collected data will be presented in listings. Data not subject to analysis according to this plan will not appear in any tables or graphs but will be included in the data listings.

Post-hoc exploratory analyses not identified in this SAP may be performed to further examine the study data. These analyses will be clearly identified as such in the final clinical study report.

7.4.1 Changes in Analysis in Comparison to Study Protocol

The analyses described in this analysis plan are consistent with the analyses described in the study protocol.

7.4.2 Study Data

Study data identified in the schedule for time and events (Table 4-1) are collected, and source verified, on the electronic data capture (EDC) product Medrio. HAAH tissue, HAAH serum, PBMC, and immunological blood testing results are not collected in the EDC tool and are provided by Sensei Biotherapeutics.

All study data will be formulated into regulatory compliant data sets to provide transparency, traceability, and integrity of trial analysis results from the collection source. Observed study data will be mapped to the CDISC Study Data Tabulation Model (SDTM) and serve as the source data from the trial. All study analyses will be completed using analysis data sets that are derived from the SDTM and follow the CDISC Analysis Data Model (ADaM) architecture. All planned analyses will be performed using the ADaM data sets developed for this study.

7.4.3 Coding

Coding of AEs will be performed on an ongoing basis throughout the study by Accelovance Safety. Verbatim terms that are entered into the database by the site will be coded manually; if necessary a query will be created to obtain clarification from the site. These events will be mapped to the MedDRA (Version 18.1) system for reporting (preferred term [PT] and system organ class [SOC]).

Concomitant medications will be coded using World Health Organization (WHO) Drug Dictionary (B Format – June 2015). Medical history data will not be coded.

7.4.4 Statistical Software

Data manipulation, tabulation of descriptive statistics, calculation of inferential statistics, and graphical representations will be performed primarily using SAS (release 9.2 or higher) for Windows. If the use of other software is warranted, the final clinical study report will detail what software was used and for what purposes.

7.4.5 Derived Variables

- *Non Treatment Emergent Adverse Events* include all AEs that stopped the day prior to the first vaccination, started prior to the first vaccination but did not increase in severity or relationship during treatment, or started more than 30 days after *the final study treatment administration* date.
- *Treatment Emergent Adverse Events* (TEAEs) include all AEs that start on or after the first study treatment administration, or AEs that are present prior to the first administration, but their severity or relationship increases after the first administration up to and including 30 days after the final administration date.
- *Change from baseline* will be calculated as the observed value at the current visit or time point minus the observed value at baseline.
- *Number of doses administered* will be calculated for each subject by summing the number of doses administered over all visits.
- *Prior medications* include all medications that have a start date prior to the date of first study treatment administration.
- *Concomitant medications* include all medications that are taken on or after the date of first study treatment administration.
- *The end of treatment phase visit* will be the visit immediately after the last visit where treatment was administered. This visit will be the first follow up visit for subjects who have any follow up visits, or the End of Study visit for all other subjects.

7.4.6 Data Handling

Any administration site reaction found in the AE log that is also captured on the Physician Administration Site Assessment eCRF page will not be counted as an (unsolicited) AE to avoid duplication.

Unscheduled or repeated laboratory results will not be analyzed for the summary of continuous values.

7.4.7 Handling of Early Termination Visits and Additional Treatments

Early termination visit data (on or prior to Day 43) for safety variables will be analyzed at the closest scheduled visit. If the closest visit has valid data, the early termination data will be assigned to the next available visit.

Any safety or immunologic data collected for additional treatments (after Day 43) will be summarized as visits separate from the scheduled visits (up to and including Day 43 and End of Study).

7.4.8 Handling of Missing Values

Partial or Missing Dates

The following conventions will be used to impute missing portions of dates for AEs and concomitant medications. Note that the imputed values outlined here may not always provide the most conservative date. In those circumstances, the imputed value may be replaced by a date that will lead to a more conservative analysis.

A. Start Dates

1) If the year is unknown, then the date will not be imputed and will be assigned a missing value.

2) If the month is unknown, then:

   i) If the year matches the first dose date year, then impute the month and day of the first dose date.

   ii) Otherwise, assign 'January.'

3) If the day is unknown, then:

   i) If the month and year match the first dose date month and year, then impute the day of the first dose date.

   ii) Otherwise, assign the first day of the month.

B. Stop Dates

1) If the year is unknown, then the date will not be imputed and will be assigned a missing value.

2) If the month is unknown, then assign 'December.'

3) If the day is unknown, then assign the last day of the month.

Imputation

Missing data will not be imputed.

7.4.9 Pooling of Investigator Centers

The data from all study centers will be pooled together for analysis.

7.4.10 Baseline Values

Baseline values are the values obtained prior to the first vaccination on Day 1. If the baseline value is missing, the value at Screening will be treated as the baseline.

8 Summary of Study Data

8.1 Subject Disposition and Dosing Summary

The tabulation of number of subjects in each dosage group and overall will be displayed for all subjects who are screened, in the Safety Population and in the Immunologic Population, respectively.

The number and percent of subjects who completed or discontinued the study will be displayed for each dosage group and overall together with reasons for early termination, where the percent is with respect to the total number of treated subjects in that dosage group. Similarly, the number and percent of subjects who completed or discontinued treatment will be displayed for each dosage group and overall together with reasons for treatment discontinuation.

The number of study treatments administered will be summarized by dosage group for the Safety Population.

8.2 Demographics and Baseline Characteristics

Subject demographic data and baseline characteristics will be summarized descriptively by dosage group and overall. The demographic data and baseline characteristics will be summarized for the Safety and Immunologic Populations.

Medical/oncology history and tumor burden evaluation data will be listed.

8.3 Protocol Deviations

All protocol deviations will be presented in a data listing.

8.4 Prior and Concomitant Medications

Prior and concomitant medications are defined in Section 7.4.5. The number and percentages of all concomitant medications will be summarized by dosage group, Anatomical Therapeutic Chemical (ATC) level 4 and PT. Subjects will be summarized through Day 43 using the assigned dose level as the treatment group. For additional treatment visits, follow up visits, and end of study, subjects will be summarized by cohort and by the dose level the subject took at the start date of the concomitant medication—this allows for subjects who changed their dose level to be summarized at the new dose level. The total number of concomitant medications and the number and percentages of subjects with at least 1 concomitant medication will be summarized by dosage group for the Safety Population.

Prior medications that are not concomitant will be listed but not tabulated.

8.5 Clinical Analysis

PSA will be summarized descriptively for each dosage group by visit for the observed value as well as for the change from baseline value (Day 1). Subjects will be summarized through Day 43 using the assigned dose level as the treatment group. For additional treatment visits, follow up visits, and end of study, subjects will be summarized by cohort and by the dose level the subject took at the visit immediately prior to the current visit—this allows for subjects who changed their dose level to be summarized at the new dose level.

PSA velocity (ng/mL/year) will be estimated by the slope of the least-square regression line fit to PSA versus time in years [1]. PSA velocity will be calculated using PSA values between Day 1 and Day 43, and subjects will be summarized using the assigned dose level as the treatment group. Also, to account for additional treatment visits, PSA velocity will be calculated using PSA values between Day 1 and the end of treatment phase visit, and subjects will be summarized by cohort and by the dose level the subject took at the last additional treatment visit. Finally, to account for follow up visits, PSA velocity will be calculated using PSA values between Day 1 and the end of study visit, and subjects will be summarized by cohort and by the dose level the subject took at the last treatment visit prior to the end of study.

PSA doubling time (months) will be estimated as follows for each visit range [1]:

1) Calculate the natural log-transform of all PSA observations [log(PSA)] in the visit range
2) Determine the slope of the least-square regression line of log(PSA) versus time in months of PSA measurement; convert the slope from years to months by multiplying the slope in years by the factor 12.
3) Divide the natural log of 2 [log(2)] by the slope calculated in step 2.

PSA doubling time will be estimated for 3 visit ranges: 1) up to and including Day 1 (baseline); 2) Day 1 through Day 43; 3) Day 1 through end of treatment phase visit; and 4) Day 1 through end of study. The baseline value will use all PSA values collected in the Medical History eCRF as well as any screening or Day 1 values in the safety laboratory data extract. For each post-baseline date range, each subject's PSA doubling time will be compared to their baseline value, and the number of subjects who have improved in the parameter (longer or negative doubling time) will be summarized, as well as the number of subjects who have not improved or who are worse (no change or shorter doubling time). For the summary from Day 1 through Day 43, subjects will be summarized using the assigned dose level as the treatment group. For Day 1 through end of treatment phase visit, subjects will be summarized by cohort and by the dose level the subject took at the last additional treatment visit and for Day 1 through end of study, subjects will be summarized by cohort and by the dose level the subject took at the last treatment visit prior to the end of study.

All PSA analyses will be conducted on the Safety Population.

8.6 Safety Analysis

All safety analyses will be conducted on the Safety Population.

Unless otherwise specified, subjects will be summarized through Day 43 using the assigned dose level as the dosage group. For additional treatment visits and end of treatment phase visit, subjects will be summarized by cohort and by the dose level the subject took at the visit immediately prior to the current visit—this allows for subjects who changed their dose level to be summarized at the new (elevated) dose level.

8.6.1 Administration Site Reactions

Administration Site reactions include local (injection site) reactions, such as pain, tenderness, erythema/redness, and swelling. Events are collected via the Physician Administration Site Assessment eCRF page and are graded using a severity rating of 0 (none), and 1, 2, 3, 4 (mild, moderate, severe, potentially life threatening).

A summary of the number and percentage of subjects experiencing at least one administration site reaction anytime after the first study treatment administration will be tabulated by reaction type, maximum severity, and dosage group through Day 43, and separately, for additional treatment visits after Day 43. A separate summary will be tabulated for each visit that an assessment is scheduled.

8.6.2 Adverse Events

The number and percent of subjects with any TEAEs will be displayed by SOC and PT for each dosage group. For additional treatment visits and end of study, the level used as the dosage group will be determined by the dose level the subject took at the start of the TEAE. Within each PT, subjects will be counted only once if they had more than one event reported during the treatment period.

For MedDRA SOC, the number and percentage of subjects experiencing at least one TEAE overall and at least one TEAE for a system will be tabulated by severity grade (Grades 1-5) and dosage group. For MedDRA PT, the number and percentage of subjects reporting at least one TEAE within a PT category will be tabulated by relationship to study products and dosage group. For the calculations in these tables, each subject's TEAEs will be counted once under the maximum severity or the strongest recorded causal relationship to study product.

Summaries will be generated for all serious TEAEs and all TEAEs causing permanent dose discontinuation by SOC and PT for each dosage group.

A listing will be produced for all subjects who reported serious TEAEs. The listing will provide details of the events including severity, relationship to study product, time between onset and last study treatment administration, and a summary of the event.

All TEAEs and non-treatment emergent AEs will be listed individually by subject.

8.6.3 Laboratory Parameters

Laboratory results will be summarized descriptively for each parameter and dosage group by visit for the observed value as well as for the change from baseline value. Laboratory abnormalities (grade 1 and greater that are listed in the NCI-CTCAE V4.03) will be recorded on the AE page regardless of their causality.

Test analytes are provided in the table below.

Hematology	**Serum chemistry**
Full and differential blood count Hematocrit (Hct) Hemoglobin (Hgb) Platelet count Red blood cell (RBC) count White blood cell (WBC) count with differential	Albumin Alanine aminotransferase (ALT) Aspartate aminotransferase (AST) Alkaline phosphatase (ALP) Blood Urea Nitrogen (BUN) or Urea Carbon dioxide (CO2) Creatinine Electrolytes (Na, K, Cl, Ca, P) Glucose (either fasting or non-fasting) Lactate dehydrogenase (LDH) Total bilirubin Direct bilirubin Total cholesterol Triglycerides
Coagulation, CH50	
Prothrombin time (PT)/INR Activated partial thromboplastin time (PTT)	

8.6.4 Vital Signs

Vital sign data, including systolic blood pressure (mmHg), diastolic blood pressure (mmHg), temperature (℃), and heart rate (bpm), will be summarized descriptively for each dosage group by time point for the observed value as well as for the change from baseline value.

8.6.5 ECOG Performance Score

The health, activity and well-being of the patient is measured by the ECOG performance status and is assessed on a scale of 0 to 5, with 0 being fully active and 5 being dead. The ECOG performance score will be summarized categorically by dosage group and visit. In addition, a shift table will be provided comparing the baseline ECOG

performance score and the worst (highest) post-baseline score that was recorded through Day 43.

8.6.6 ECG

ECG results will be summarized descriptively for each parameter and dosage group by visit for the observed value as well as for the change from baseline value. In addition, a shift table will be provided comparing the baseline overall interpretation (normal, abnormal, not clinically significant, abnormal, clinically significant) to the post-baseline value by visit through Day 43.

8.6.7 Other Safety Variables

Other safety variables, such as physical examination, will be listed.

8.7 Immunological Analysis

All immunological analyses will be conducted on the Immunologic Population.

As for the safety variables, subjects will be summarized through Day 43 using the assigned dose level as the dosage group. For additional treatment visits and end of treatment phase visit, subjects will be summarized by cohort and by the dose level the subject took at the visit immediately prior to the current visit—this allows for subjects who changed their dose level to be summarized at the new (elevated) dose level.

The variables that will be analyzed are listed in Table 8-1:

Table 8-1. Variables Included in Immunological Analysis

Type	Name	Unit
Antigen-specific anti-HAAH antibody titers	HAAH-1λ	Antibody Units / mL
	H460 (HAAH)	Antibody Units / mL
Cellular Immune Response	CD4+ T Cells IFN-γ	% of CD4+ T cells
	CD8+ T Cells IFN-γ	% of CD8+ T cells
	HAAH-Specific B Cells	% of B cells
Immunophenotyping	B Cells	% of Leukocytes
	T Cells	% of Leukocytes
	CD4+ T Cells	% of T cells
	CD8+ T Cells	% of T cells
	CD3+, CD56+ Cells	% of Leukocytes
	NK Cells	% of Leukocytes
	Neutrophils	% of Leukocytes
	Eosinophils	% of Leukocytes
	Monocytes	% of Leukocytes

Assay data will be tabulated by time point, An appropriate data transformation (e.g., $\log_{10}$ transformation) may be applied to better satisfy assumptions of symmetry and homoscedasticity (constant variance). Graphical representations of the longitudinal immune responses will also be given.

All data related to immunologic collection and analysis will be listed.

9 References

1. Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC. Natural History of Progression After PSA Elevation Following Radical Prostatectomy. *JAMA* 1999;281:1591-1597.

10 Appendices

10.1 List of Tables, Figures, and Listings

Table No.	Description of Table	Population
14.1.1	Subject Disposition	All Subjects
14.1.2.1	Demographics and Baseline Characteristics	Safety
14.1.2.2	Demographics and Baseline Characteristics	Immunologic
14.2.1.1	Study Treatment Administration Through Day 43	Safety
14.2.1.2	Study Treatment Administration by Additional Treatment Visit	Safety
14.2.2.1	Concomitant Medications Through Day 43	Safety
14.2.2.2	Concomitant Medications For Additional Treatment Visits	Safety
14.2.3.1.1	Change from Baseline in PSA by Visit Through Day 43	Safety
14.2.3.1.2	Change from Baseline in PSA by Additional Treatment Visit	Safety
14.2.3.2.1	Summary of PSA Velocity and PSA Doubling Time Through Day 43	Safety
14.2.3.2.2	Summary of PSA Velocity and PSA Doubling Time Through End of Treatment	Safety
14.2.3.2.3	Summary of PSA Velocity and PSA Doubling Time Through End of Study	Safety
14.3.1.1.1	Summary of Worst Administration Site Reactions Through Day 43 by Grade	Safety
14.3.1.1.2	Summary of Worst Administration Site Reactions For Additional Treatment Visits by Grade	Safety
14.3.1.2.1	Summary of Administration Site Reactions by Visit Through Day 43 and Grade	Safety
14.3.1.2.2	Summary of Administration Site Reactions by Additional Treatment Visit and Grade	Safety
14.3.2.1.1	Overall Summary of Adverse Events Through Day 43	Safety
14.3.2.1.2	Overall Summary of Adverse Events For Additional Treatment Visits	Safety
14.3.2.2.1	Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term Through Day 43	Safety
14.3.2.2.2	Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term For Additional Treatment Visits	Safety
14.3.2.3.1	Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Severity Through Day 43	Safety
14.3.2.3.2	Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Severity For Additional Treatment Visits	Safety
14.3.2.4.1	Treatment-Emergent Adverse Events (TEAE) by Preferred Term and Relationship to Study Treatment Through Day 43	Safety
14.3.2.4.2	Treatment-Emergent Adverse Events (TEAE) by Preferred Term and Relationship to Study Treatment For Additional Treatment Visits	Safety
14.3.2.5.1	Serious Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term Through Day 43	Safety
14.3.2.5.2	Serious Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term For Additional Treatment Visits	Safety
14.3.2.6.1	Treatment-Emergent Adverse Events (TEAE) Leading to Permanent Dose Discontinuation by System Organ Class and Preferred Term Through Day 43	Safety

14.3.2.6.2	Treatment-Emergent Adverse Events (TEAE) Leading to Permanent Dose Discontinuation by System Organ Class and Preferred Term For Additional Treatment Visits	Safety
14.3.2.7	Listing of Serious Treatment Emergent Adverse Events	Safety
14.3.3.1.1	Change from Baseline in Hematology Parameters by Visit Through Day 43	Safety
14.3.3.1.2	Change from Baseline in Hematology Parameters by Additional Treatment Visit	Safety
14.3.3.2.1	Change from Baseline in Chemistry Parameters by Visit Through Day 43	Safety
14.3.3.2.2	Change from Baseline in Chemistry Parameters by Additional Treatment Visit	Safety
14.3.3.3.1	Change from Baseline in Coagulation and CH50 Parameters by Visit Through Day 43	Safety
14.3.3.3.2	Change from Baseline in Coagulation and CH50 Parameters by Additional Treatment Visit	Safety
14.3.4.1	Change from Baseline in Vital Sign Parameters by Visit Through Day 43	Safety
14.3.4.2	Change from Baseline in Vital Sign Parameters by Additional Treatment Visit	Safety
14.3.5.1.1	ECOG Performance Score by Visit Through Day 43	Safety
14.3.5.1.2	ECOG Performance Score by Additional Treatment Visit	Safety
14.3.5.2	Shift from Baseline in ECOG Performance Score (Worst Case) Through Day 43	Safety
14.3.6.1.1	Change from Baseline in ECG Parameters by Visit Through Day 43	Safety
14.3.6.1.2	Change from Baseline in ECG Parameters by Additional Treatment Visit	Safety
14.3.6.2	Shift from Baseline in ECG Overall Interpretation by Visit	Safety
14.4.1.1	Summary of Antigen-Specific anti-HAAH Antibody Titers by Visit Through Day 43	Immmunologic
14.4.1.2	Summary of Antigen-Specific anti-HAAH Antibody Titers by Additional Treatment Visit	Immmunologic
14.4.2.1	Summary of Cellular Immune Response by Visit Through Day 43	Immmunologic
14.4.2.2	Summary of Cellular Immune Response by Additional Treatment Visit	Immmunologic
14.4.3.1	Summary of Immunophenotyping by Visit Through Day 43	Immmunologic
14.4.3.2	Summary of Immunophenotyping by Additional Treatment Visit	Immmunologic

Figure No.	**Description of Figure**	**Population**
14.4.1.1	Mean (SD) of H460 (HAAH) by Treatment	Immmunologic
14.4.1.2	Mean (SD) of HAAH-1λ by Treatment	Immmunologic
14.4.2.1	Mean (SD) of CD4+ T Cells IFN-γ by Treatment	Immmunologic
14.4.2.2	Mean (SD) of CD8+ T Cells IFN-γ by Treatment	Immmunologic
14.4.2.3	Mean (SD) of HAAH-Specific B Cells by Treatment	Immmunologic
14.4.3.1	Mean (SD) of B Cells by Treatment	Immmunologic
14.4.3.2	Mean (SD) of T Cells by Treatment	Immmunologic
14.4.3.3	Mean (SD) of CD4+ T Cells by Treatment	Immmunologic
14.4.3.4	Mean (SD) of CD8+ T Cells by Treatment	Immmunologic
14.4.3.5	Mean (SD) of CD3+, CD56+ Cells by Treatment	Immmunologic
14.4.3.6	Mean (SD) of NK Cells by Treatment	Immmunologic
14.4.3.7	Mean (SD) of Neutrophils by Treatment	Immmunologic
14.4.3.8	Mean (SD) of Eosinophils by Treatment	Immmunologic

14.4.3.9	Mean (SD) of Monocytes by Treatment	Immmunologic

Listing No.	Description of Listing
16.2.1.1	Subject Disposition
16.2.1.2	End of Treatment
16.2.1.2	Treatment Assignment and Analysis Populations
16.2.1.3	Elgibility
16.2.2.1	Protocol Deviations
16.2.2.2	Demographics
16.2.2.3	Oncology History
16.2.2.4	General Medical History
16.2.2.5	Tumor Burden Evaluation
16.2.3	Study Treatment Administration
16.2.4	Prior and Concomitant Medications
16.2.5	Immunological Results
16.2.6	Physician Administration Site Assessment
16.2.7	Adverse Events
16.2.8.1	Laboratory Results – Hematology and Coagulation
16.2.8.2	Laboratory Results – Chemistry and PSA
16.2.8.3	Laboratory Results – CH50
16.2.8.4.1	PSA Velocity and PSA Doubling Time Through Day 43
16.2.8.4.2	PSA Velocity and PSA Doubling Time Through End of Study
16.2.9	ECOG Performance Score
16.2.10.1	ECG Parameters
16.2.10.2	ECG Overall Interpretation
16.2.11	Vital Signs
16.2.12	Physical Examination

10.2 Mock Tables, Figures, and Listings

Please refer to the separate document of table, figure, and listing shells and programming notes.