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STATISTICAL ANALYSIS PLAN

CONFIDENTIAL

Protocol Number: ATI001-101

Phase: I/II

A Phase I/II, Open Label Study of Ad-RTS-hIL-12, an Adenovirus Vector Engineered to Express hIL-12, in Combination with an Oral Activator Ligand, in Subjects with Unresectable Stage III or IV Melanoma

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APPROVAL SIGNATURES

STUDY TITLE: A Phase I/II, Open Label Study of Ad-RTS-hIL-12, an Adenovirus Vector Engineered to Express hIL-12, in Combination with an Oral Activator Ligand, in Subjects with Unresectable Stage III or IV Melanoma.

STUDY NUMBER: ATI001-101

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Sponsor: [redacted]

[redacted]

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Abbreviations

Abbreviation	Meaning
ADV	Adenoviral vector shedding
AE	Adverse Event
ACEV	Activity Evaluable Population
ATC	Anatomical Therapeutic Chemical
bpm	Beats per minute
BMI	Body mass index
BRAF	Human gene that makes a protein called B-Raf
cm	Centimeter
CR	Complete Response
CTCAE	NCI Common Terminology Criteria for Adverse Events
CTL	Cytotoxic T Lymphocytes
DLT	Dose-limiting Toxicity
ECG	Electrocardiogram
FNA	Fine Needle Aspirate
GGT	Gamma Glutamyl Transferase
Hgb	Hemoglobin
INXN-1001	INXN-1001 (Oral Activator Ligand)
INXN-2001	INXN-2001 (Ad-RTS-hIL-12)
kg	Kilogram
KM	Kaplan-Meier
lb	Imperial pounds (weight)
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
MTD	Maximum Tolerated Dose
PB	Punch Biopsy
PBMC	Peripheral Blood Mononuclear Cells
PD	Progressive Disease
PFS	Progression-free Survival
PK	Pharmacokinetic
PR	Interval measured from the beginning of the P wave to the beginning of the QRS complex
PR	Partial Response
PT	Preferred term
PTSA	Post Treatment Safety Assessment
QRS	Complex containing Q wave, R wave and S wave
QT	Interval between start of the Q wave and the end of the T wave
RBC	Red Blood Cell Count
RECIST	Response Evaluation Criteria In Solid Tumors

Abbreviation	Meaning
SAE	Serious Adverse Event
SAF	Safety Population
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
SD	Stable Disease
SOC	System Organ Class
SRC	Safety Review Committee
TEAE	Treatment-Emergent Adverse Event
Tregs	T-regulatory cells
vp	Viral particles
WHO	World Health Organization

1.0 Version Control

This Statistical Analysis Plan (SAP) is based on the protocol ATI001-101 Amendment 7, issued 29 April 2013.

The planned enrollment for this study was approximately 30 patients (3 patients per dose level cohort) in Phase I and approximately 15 patients enrolled in Phase II at a single dose level at or below the Maximum Tolerated Dose (MTD).

Enrollment proceeded as follows:
Three patients were treated in cohort 1 at 5mg QD of INXN-1001, three patients treated in cohort 2 at 20mg QD, three patients treated in cohort 3 at 100mg QD, and 4 patients were treated at 160mg QD.

Four patients were treated in the expansion cohort (Phase II) at 160mg QD and four at 160mg QOD. A decision was then taken by the SRC to enroll into the expansion cohort at a reduced dose of INXN-1001; a further three patients were treated at 120mg QOD and two patients were treated at 80mg QOD, due to dose limiting toxicities (DLTs) occurring on the 160mg QOD and the 120mg QOD dose cohorts.

Further details of subject enrollment will be presented in the Clinical Study Report (CSR). This SAP describes the changes to the planned analysis along with the modified analysis for the amended design.

This SAP refers to the final analysis of the data. Pharmacokinetic (PK) data presentations and analysis will be performed by ZIOPHARM. No further details of PK analysis will be included in this SAP, with the exception of listing eCRF data.

2.0 Study Rationale

This study was designed to assess the safety, objective response rate and immunological and biological effects of intratumoral injections of INXN-2001 in combination with escalating dose levels of oral INXN-1001.

3.0 Objectives

3.1 *Primary Objectives*

The primary objective of this trial was to evaluate the safety and tolerability of intratumoral injections of INXN-2001 (Ad-RTS-hIL-12) in combination with INXN-1001 (activator ligand) in patients with unresectable Stage III or IV melanoma.

3.2 *Secondary Objectives*

The following secondary objectives were to be evaluated in the trial:

- To inform the selection of an INXN-1001 dose(s) and regimen for further study in combination with INXN-2001.

- To assess preliminary anti-tumor activity according to Response Evaluation Criteria In Solid Tumors (RECIST) 1.1 criteria.
- To assess anti-tumor response based on total measurable tumor burden.
- To evaluate the immunological effect of study treatment in terms of cellular and humoral immune responses, as well as other biological activities in the injected tumor(s), tumor-involved draining lymph nodes (if accessible) and in the peripheral circulation.
- To evaluate the extent of the uptake of INXN-2001 into tumor cells and tumor-infiltrating immune cells, and to assess adenoviral vector shedding in body fluids.
- To assess the pharmacokinetics (PK) of INXN-1001 in patients with unresectable stage III or IV melanoma.

4.0 Study Design

4.1 Endpoints

Safety Evaluations

Safety parameters were to include serious adverse events (SAEs), adverse events (AEs), physical examinations, electrocardiograms (ECGs), vital signs, clinical laboratory evaluations, medical history, and prior/concomitant medications.

Efficacy Evaluations

Efficacy was to be evaluated as the objective tumor response according to RECIST v1.1 guidelines. Additional assessment of anti-tumor activity was to be explored based on total measurable tumor burden.

Pharmacodynamic Evaluation

Immunological and biological markers of response were to include examinations of tumor biopsy samples, cytokine levels, peripheral blood mononuclear cells (PBMC) and antibody responses.

4.2 Overall Study Design

This was a single-arm, open label, Phase I/II dose escalation study of intratumoral injections of INXN-2001 and oral INXN-1001 in patients with unresectable Stage III or IV melanoma.

Approximately 30 patients (3 patients per dose level cohort) in Phase I and approximately 15 patients were to be enrolled in Phase II at a single dose level at or below the Maximum Tolerated Dose (MTD)).

Concurrent INXN-2001 and INXN-1001 dosing will be referred to as "study treatment" throughout this SAP.

This study is multi-center (approximately 8 to 12 centers).

Phase I

Phase I comprised of four planned sequential dose escalation cohorts of INXN-1001 in combination with a fixed dose of INXN-2001. Patient enrollment and dose escalation was to proceed according to a standard 3+3 design. Each patient was to be treated for up to 6 treatment cycles, each of 21 days in duration. In each cycle, patients were to be treated with one intratumoral injection of INXN-2001 in combination with 7 oral daily doses of INXN-1001 (Table 1).

Table 1: Study Design

Study Part	Cohorts	Dose Regimen
Phase I	Dose Escalation	INXN-2001: [redacted] INXN-1001: 5, 20, 100, 160 mg
Phase II	Group 1	INXN-2001: [redacted] INXN-1001: 160 mg daily for 7 consecutive days; 21-day cycle
	Group 2	INXN-2001: [redacted] INXN-1001: 160 mg every other day for 14 days; 28-day cycle

This study was to explore four INXN-1001 dose cohorts of 5 mg, 20 mg, 100 mg and 160 mg daily.

Phase II

Approximately 15 patients were to be enrolled in Phase II at or below the MTD. Phase II of the study was to include two groups of patients. Patients enrolled in Phase II of the study under Amendment 6 or prior were to be enrolled into Group 1; patients enrolled under Amendment 7 or later were to be enrolled into Group 2.

For Group 1, in each of six 21-day cycles, the patients were to receive one intratumoral injection of INXN-2001 in combination with oral daily doses of INXN-1001 given at 160 mg for 7 consecutive days at the beginning of the 21-day cycle.

For Group 2, in each of six 28-day cycles, the patients were to receive one intratumoral injection of INXN-2001 in combination with oral doses of INXN-1001 given at 160 mg administered every other day for 14 days at the beginning of the 28-day cycle.

Full details of the study design can be found in the protocol. Following changes to patient enrollment, the final study is shown in Table 2.

Table 2: Final Study Design

Study Part	Cohorts	Dose Regimen
Phase I	Dose Escalation	INXN-2001: [redacted] INXN-1001: 5, 20, 100, 160 mg
Phase II	Group 1	INXN-2001: [redacted] INXN-1001: 160 mg daily for 7 consecutive days; 21-day cycle
	Group 2	INXN-2001: [redacted] INXN-1001: 160 mg every other day for 14 days; 28-day cycle 120 mg every other day for 14 days; 28-day cycle 80 mg every other day for 14 days; 28-day cycle

4.3 Safety Review Committee (SRC)

A SRC comprised of the Medical Monitor, Principal Investigators, and sponsor representatives, were convened to review safety information and to decide upon dose escalation and further patient enrollment.

In Phase I, following a cohort review, the SRC could recommend proceeding with enrollment in the next dose cohort, enrolling additional patients in the current cohort, dropping back to a lower cohort, exploring an alternate dose level, or not enrolling any additional patients. The dose escalation and enrollment guidelines and study stopping rules outlined in the protocol (Sections 6.2.6 and 6.2.7) were to be used as the basis for these assessments.

In Phase II, Group 2, the DLT definitions in the protocol (Section 6.2.4) were to be utilized along with the criteria for de-escalation. The SRC could recommend a dose reduction for patients in Group 2 if one or more DLTs are observed.

4.4 Design Post Safety Review Committee Decision

Dose escalations in Phase I occurred as detailed in the protocol. For Phase II of the study, four patients were enrolled on 160mg QD and four patients on 160mg QOD; the decision was then taken to enroll patients on a reduced dose of 120mg QOD. The dose was then further reduced to 80mg QOD. The decision to reduce the dosing was due to DLTs occurring on the 160mg QOD and the 120mg QOD dose cohorts respectively.

5.0 Study Procedures

Various procedures will be performed during the study. The schedule of assessments is detailed in the protocol.

6.0 Patient Disposition

6.1 *Sample Size*

No formal sample-size estimation was performed.

Thirteen patients were treated in Phase I and 13 patients were treated in Phase II.

7.0 Protocol Deviations

Protocol deviations are defined as those deviations from the study protocol that may have the ability to impact the results.

No patient will be removed from any analysis population because of a protocol deviation. Protocol deviations were partially collected on the CRF. A further review of the data will be conducted to identify any of the following:

- Deviation from inclusion/exclusion criteria
- Withdrawal criteria met during the study but patient was not withdrawn
- Use of prohibited concomitant medications.

Where possible the first two items will be checked programmatically. For prohibited medications, a spreadsheet of the coded terms will be provided for the sponsor to review.

All protocol deviations including those not databased will be listed.

8.0 Analysis Populations

The target population for this study is adult patients with unresectable Stage III or IV melanoma for which there is no alternative curative therapy.

For the analysis, two populations will be used: a Safety population (SAF) and an Activity Evaluable population (ACEV).

8.1 *Safety Population (SAF)*

The Safety population is defined as all patients who receive at least one INXN-1001 capsule or, in the event an injection of INXN-2001 is administered before an INXN-1001 capsule is taken, at least one injection of INXN-2001.

The safety population will be used for the analysis of safety data based on the actual initial dose of INXN-1001 received.

8.2 *Activity Evaluable Population (ACEV)*

The Activity Evaluable population is defined as all SAF patients who receive at least one dose of INXN-2001 and INXN-1001 and have at least one post-screening response evaluation. The ACEV population is the primary population for the analysis of efficacy data.

9.0 Data Reporting Conventions

All listings will be ordered by phase, group (for Phase II only) and INXN-1001 actual initial dose (5mg QD, 20mg QD, 100mg QD, 160mg QD in Phase I; 160mg QD, 160mg QOD, 120mg QOD, 80mg QOD in Phase II) and patient number. Listings will present all available data.

Unless otherwise stated, data will be summarized by phase and dose cohort based on the actual dose of INXN-1001 received on Cycle 1 Day 1. For Phase II, data will be summarized based on group; additionally for Group 2, data will be presented by dose cohort. The combined data for each phase will also be summarized as an 'Overall' column.

No inferential statistics will be performed.

9.1 *Descriptive Statistics*

Unless otherwise stated, all continuous parameters will be summarized using standard summary statistics as appropriate (n, mean, standard deviation, minimum, median and maximum). Summary statistics for categorical variables will include frequency counts and percentages.

In the presentation of descriptive summary statistics, the minimum and maximum will be presented to the same number of decimal places as the variable being reported. The mean and median will be reported to one extra decimal place; the standard deviation (SD) to two extra decimal places.

Frequency counts will be provided for categorical variables (e.g., gender). Unless otherwise stated, this will consist of the number of patients in a particular category and the percentage of total patients for the treatment (Phase I)/treatment regimen (Phase II only) in each, presented to one decimal place. Categorical data will be summarized using counts and percentages based on non-missing values.

Zero counts will be presented as '0' lined up on the decimal place.

Tables will have a footnote of the form "Table XX is supported by Listing XX".

Analyses will be undertaken using the validated statistical software Statistical Analysis System (SAS) version 9.3 or later.

9.2 *Baseline*

Unless otherwise specified, baseline is the last observation before the first study drug administration.

9.3 *Missing Data*

If there are partial dates which require imputation, the day and/or month and/or year will be imputed in a conservative manner i.e. for the start dates, if only the day is missing, it will be imputed with the first day of the month. If the month is also missing, it will be imputed with the 1st January. For the end dates, if only the day is missing, it will be imputed with the last day of the month and if the month is also missing, it will be imputed with the 31st December. In addition, imputed dates for data that is

expected to occur on study will be modified to be consistent with appropriate known study visit dates.

Missing values for safety measures at Baseline such as laboratory data, vital signs and electrocardiogram (ECG) data will be substituted by values from the screening visit, where available.

No further imputations for missing data will be made.

10.0 Patient Disposition and Baseline Information

10.1 *Patient Disposition*

Study completion/discontinuation details, time to discontinuation, date of first dose of study treatment, informed consent, inclusion/exclusion criteria including protocol amendment recruited under, eligibility, protocol deviations and population allocation will be listed.

Time to discontinuation (days) = (date of last contact) - (date of first dose of INXN-1001 or INXN-2001, whichever is earliest) +1 day

The number of patients screened and treated, prematurely discontinued/completed the study and primary reason for study treatment completion/discontinuation will be tabulated.

The number and percentage of patients in each analysis population (i.e. SAF, ACEV) will be tabulated.

10.2 *Demographic Characteristics*

Demographic parameters (including date of birth, age, sex, ethnicity, race, height (cm), weight (kg) and BMI (kg/m^2)), BRAF status and mutation type will be listed. Demographics will be tabulated using frequency counts and descriptive statistics as appropriate.

Age will be derived as follows:

```
Age=floor ((intck('month',birth,screen) - (day(screen) <
day(birth))) / 12)
```

Conversions for height and weight are as follows:

Height (cm) = Height (inches) x 2.54
Weight (kg) = Weight (lb) x 0.4536

10.3 *Medical History*

Details of medical/surgical history will be listed including start and stop dates, and whether medication currently used.

Medical histories will be coded according to the MedDRA dictionary version 10. A summary of medical histories and number of patients with a medical history will be presented by System Organ Class and Preferred Term.

Tables will be presented by phase only.

10.4 *Oncology History and Prior Cancer Therapy*

Details of oncology history will be listed including tumor type, diagnosis date, current disease status, staging (TNM, Tumor – Tis, Ta, Tx; Node – N0, N1, N2; Metastasis - M0, M1, M2) and staging.

Time from first diagnosis to date of screening, current disease status and staging (TNM, T – Tis, Ta, Tx; N – N0, N1, N2; M - M0, M1, M2) will be tabulated.

Time from first diagnosis will be derived as follows:

Time from first diagnosis = Date of screening – Date of first diagnosis + 1 day.

Oncology histories will be coded according to the MedDRA dictionary version 10. A summary of oncology histories and number of patients with an oncology history will be presented by System Organ Class and Preferred Term.

Prior cancer treatment information will be tabulated. This will include the number of previous treatments received and therapy type.

Tables will be presented by phase only.

10.5 *Prior and Concomitant Medication*

Medications will be classified according to whether they were being taken pre-study (prior) and/or during the study (concomitant). Prior medications are any that were being taken prior to the first dose of study medication (medication stop date prior to the first dose of study medication). Concomitant medications are any that were being taken on or after the first dose of study medication. If the start and stop dates of the medications do not clearly define the period(s) during which a medication was taken, it will be assumed to be a concomitant medication.

Prior and concomitant medications recorded during the study will be coded using World Health Organization (WHO)-Drug dictionary Q3 2009. Details of prior and concomitant medication will be listed separately.

Prior and concomitant medications will be summarized by preferred term and Anatomical Therapeutic Chemical (ATC) level 2 term.

Tables will be presented by phase only.

11.0 Efficacy

Patients with measurable disease will have tumor dimensions measured according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 at Screening

and at the each cycle up to cycle 6 during the study and 8-10 weeks after follow-up if the patient is without objective evidence of disease progression at the Follow-Up Tumor Assessment visit. The investigator will evaluate each patient for response to therapy according to RECIST v1.1 guidelines. For each patient, disease sites are to be assessed throughout the study using the same method(s) of assessment used at screening.

Additional assessment of anti-tumor activity will be explored based on total measurable burden.

Immunological and biological markers of response will include examinations of tumor biopsy samples, cytokine levels, peripheral blood mononuclear cells (PBMC) and antibody responses.

All summaries will be performed on the ACEV population and based on the dose of INXN-1001 received.

11.1 *Efficacy Endpoints*

Details of target lesions, non-target lesions and new lesions will be listed.

11.1.1 Objective Response Rate

Individual overall tumor responses (Complete Response (CR), Partial Response (PR), Stable Disease (SD), Progressive Disease (PD) and Unevaluable) as measured by RECIST v1.1 guidelines will be listed. The objective response is defined as a complete response or a partial response. Non-responders are those either with stable or progressive disease. Those subjects that cannot be assessed will be treated as non-responders. Objective response will be listed as a Yes/No response for each subject. The objective response rate will not be tabulated.

The best overall response (BOR) will be listed for each subject and tabulated.

11.1.2 Progression-free Survival

Progression free survival is the time in days from the first dose of INXN-1001 to the first assessment on which the overall response is reported as disease progression or death due to any cause (whichever is first) + 1 day. Patients withdrawing from the study will be censored at their last non-progressive disease response assessment. If a patient does not have a disease response assessment, the patient will be censored on the date of the first treatment as described above.

Progression-free survival and censoring information will be listed.

PFS times will be summarized using Kaplan-Meier methods. The median, 25^{th} and 75^{th} percentiles will be calculated. Kaplan-Meier plots will not be presented.

11.1.3 Duration of Response

Duration of response will not be calculated.

11.1.4 Immune-Related Response Criteria

Immune-related responses will not be determined.

For ease of use the derived efficacy information will be presented as follows: date of first dose, date of progression, date of death, date of discontinuation, PFS, objective response (yes or no) and best overall response (PD, SD, PR, CR, Unevaluable).

11.2 *Pharmacodynamic Endpoints*

11.2.1 Immunologic and Biological Response Markers

Immunologic and biological response marker data will be listed only.

11.3 *Pharmacokinetic Assessment*

PK sample timings will be listed by patient. ZIOPHARM will perform the PK analysis.

12.0 Safety Endpoints

Safety will be assessed from records of AEs, laboratory values (clinical chemistry, hematology and urinalysis), vital signs, 12-Lead electrocardiogram (ECG) and results of physical examination. Severity of adverse events as determined by NCI Common Terminology Criteria for Adverse Events (CTCAE) v4.03.

All safety analyses will be conducted on the SAF population.

12.1 *Treatment Exposure*

Details of study drug administration including injection of INXN-2001 on Day 1 of each cycle and oral doses of INXN-1001 throughout the study including time on treatment (days) will be listed. Details of planned and actual dosing at each cycle and overall will be listed.

Actual dose of INXN-2001 at each cycle will be calculated as follows:

((Number of capsules dispensed - Number of capsules returned) x Strength of capsules) + Day 1 dose

The strength of capsule prescribed at each dose cohort is as follows in Table 3.

Table 3: Capsule Strength per Dose Cohort

Dose Cohort	Strength of Capsule
5mg	5mg
20mg	10mg
80mg	20mg
120mg	20mg
160mg	20mg

Compliance with the planned dosing regimen will be measured as follows:

Percentage compliance = (Actual dose of INXN-2001 taken)*100
(Scheduled dose of INXN-2001 to be received)

For scheduled dose regimens of QOD, the dose is administered over a 14 day period, therefore all subjects are scheduled to receive 7 doses within a cycle of treatment.

In instances where subjects receive multiple cycles within a dose group, percentage compliance will be calculated for the entire duration of treatment.

The number of cycles started, total time on treatment, total dose of INXN-2001 taken and percentage compliance will be summarized.

Time on treatment (days) = Last dose date – first dose date +1

Percentage compliance will be presented in the categories: ≤ 80%, 81 – 90%, and 91 – 100%.

The following treatment exposure details will also be listed: date of first dose, number of cycles started, number of cycles completed, total dose of INXN-2001 taken, percentage compliance, reason for discontinuation or ongoing, time on treatment, whether the subject experienced a DLT.

12.2 *Adverse Events*

Adverse events will be coded according to MedDRA dictionary version 10.

Symptoms and signs of exacerbation or worsening of the patient's primary disease will be captured as AEs.

A treatment emergent adverse event (TEAE) is defined as an AE occurring during or after administration of first dose of study drug, or any event after the first dose of study drug considered study drug-related regardless of event start date, or any worsening in intensity or event considered drug related by the investigator of a pre-existing medical condition/AE with onset after the start of study drug, and until Post-Treatment Safety Assessment visit (28 days after the last INXN-1001 dose per patient). AEs with unknown start date/time will be assumed to be treatment-emergent

unless the end date/time is known to be before start of study drug. AEs with onset after the completion of screening but prior to the start of study drug will be considered non-treatment emergent.

An overall AE summary will be presented for all AEs and the pre-defined subsets of events below:

- Any AEs
- Any TEAE events
- Any drug-related AEs
- Any CTC Grade 3 or greater AEs
- Any CTC Grade 3 or greater drug-related AEs
- Any AEs leading to death
- Any drug-related AEs leading to death
- Any serious AEs (SAEs)
- Any drug-related serious AEs
- Any AEs leading to discontinuation
- Any drug-related AEs leading to discontinuation
- Any dose limiting toxicities

Related is defined as 'possibly related' or 'related' to treatment in the opinion of the investigator.

Both number of events and number of patients will be tabulated. For patients, percentages will be calculated from the total number of patients per INXN-1001 dose cohort in each phase and group (for phase II only).

Summaries of TEAEs, drug-related adverse events, SAEs, drug-related SAEs, AEs with CTC grade ≥ 3, drug-related AEs with CTC grade ≥ 3 and AEs leading to discontinuation will be tabulated by MedDRA System Organ Class (SOC) and specific AE preferred Term (PT) sorted by decreasing frequency within SOC. Both number of events and number of patients will be tabulated. For patients, percentages will be calculated from the total number of patients per INXN-1001 dose group.

All AEs, TEAEs, SAEs, drug-related adverse events, adverse events leading to discontinuation of study medication and adverse events leading to death will be listed.

Details of injection reactions including injection site reaction, start/stop date/time, outcome, severity, relation to study drug, treatment required details, injection lesion, whether or not a DLT and seriousness will be listed.

Summaries of injection reactions will be tabulated by type, type by severity and type by relationship to study drug and will be presented by phase only. Relationship to study drug refers to either drug.

12.3 *Laboratory Evaluations*

Laboratory data for blood chemistry, hematology, and urinalysis will be collected throughout the study.

The following laboratory tests are to be performed as indicated by the schedule of assessments:

Blood Chemistry	*Hematology*	*Urinalysis*
Albumin	Basophils	Appearance
Alanine aminotransferase		pH
Alkaline phosphate	Eosinophils	Specific gravity
Aspartate aminotransferase	Platelets	Glucose
Bicarbonate	Red blood cell (RBC)	Protein/Albumin
Total bilirubin	Hepatitis C Virus	RBC Hgb
Blood urea nitrogen	Hemoglobin (Hgb)	Ketones
Calcium	Hematocrit	Bilirubin
Chloride	International Normalized Ratio	Nitrates
Creatinine	Mean corpuscular volume	Leukocyte esterase
Gamma glutamyl transferase	Mean corpuscular hemoglobin	
Glucose	Neutrophils	
Lactic dehydrogenase	Partial thromboplastin time	
Potassium	Reticulocytes	
Phosphorus	White blood cell	
Sodium		
Total protein		

Shift tables will be constructed for the clinical chemistry and hematology data showing the shift from the baseline value to the worst (minimum or maximum value) post baseline.

The absolute value and the change from baseline will be tabulated for each scheduled time-point during the study for all continuous urinalysis parameters. Baseline is defined as the Screening value.

Details of clinical chemistry and hematology data will be listed including converted values and showing reference ranges and flagging of abnormal findings and their clinical significance. Out of reference range values will be flagged as high (H) or low (L) in the listing. Laboratory reference ranges will be presented by site.

Pregnancy test details at Screening (serum) and Day 1 of each cycle (urine) will be listed.

12.4 *Vital Signs*

Vitals signs will be collected throughout the study as detailed below. Details of vital signs including oral temperature (°C), respiratory rate (breaths/min), heart rate (bpm) and blood pressure (systolic and diastolic) (mmHg) will be listed and the number and percentage of patients will be tabulated by scheduled timepoint.

The absolute and change from baseline in vital signs will be summarized descriptively for the SAF. Baseline is defined as the last observation before the first study dose of INXN-1001.

Vitals signs will be listed.

12.5 *ECG Data*

ECG data will be collected by using a digital 12-lead ECG machine throughout the study.

The absolute value and change from baseline in 12-Lead ECG parameters (PR, QRS, QT) will be summarized descriptively for the SAF.

The number and percentage of patients with any clinically significant findings reported by the investigator will be tabulated by scheduled time-point. The absolute 12-Lead ECG parameters will be listed by patient and visit along with ECG findings.

12.6 *ECOG Status*

ECOG status will be collected throughout the study.

ECOG status will be listed.

12.7 *Physical Examination*

Physical examinations will be performed throughout the study. Details of physical examinations will be listed.

13.0 Interim Analysis

There is no planned interim analysis.

14.0 Changes to Planned Methodology

The following changes will be made to the planned analysis based on the final number of enrolled subjects:

Section 10.3.3 of the Protocol states that following completion of the study, best response will be determined for each subject in accordance with RECIST v.1.1 guidelines and the objective response rate presented for each dose cohort. Progression-free survival and durability of response will be determined using Kaplan-Meier methodology.

Objective response, BOR and PFS will be determined and listed for each individual subject. Additionally BOR and PFS will be tabulated. Objective response rate and duration of response will not be calculated.

Section 10.3.3 of the Protocol also states that as a supplement to the standard RECIST v1.1 guidelines established to evaluate anti-tumor responses to chemotherapeutic agents, the sponsor will be analyzing anti-tumor response by assessing total tumor burden over time. Tumor burden activity was not collected and as such no summaries will be included for this data.

Section 10.3.3 of the Protocol also states that at each time point, the change in immunologic response (CTL and Treg frequency in blood) from baseline and from the preceding time point will be correlated with the INXN-1001 dosage level. In addition, tumor punch biopsies or FNAs will be examined for genomic changes due to IL-12 expression, presence of injected adenovirus and CTL frequency, Treg and MDSC frequency, and other immunological markers. The change in each measure from baseline and from the preceding biopsy will be correlated with the INXN-1001 dose used in the each cohort.

Immunologic and biological response marker data will be listed only.

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15.0 Tables, Figures and Listings

Tables and listings will be presented landscape. A font size of 8 and a font of courier new will be used throughout for tables and listings. Tables and listings will be provided as a bookmarked pdf.

The patient subset being utilized in the table will be indicated in the table title. Page numbers and dates of production will be included in an appropriate place at the bottom of the output. Listings which support the table will also be detailed in an appropriate place at the bottom of the output.

Tables will only be generated where there is sufficient data to warrant the inclusion of the table.

15.1 *List of Tables*

Table Number	Table Title	Population
Table 14.1.1	Patient Disposition	Safety Population
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Table 14.2.1	Best Overall Response	Activity Evaluable Population
Table 14.2.2	Progression-free Survival (Kaplan-Meier Analysis)	Activity Evaluable Population
Table 14.3.1	Exposure	Safety Population
Table 14.3.2.1	Overall Adverse Event Summary	Safety Population
Table 14.3.2.2	Adverse Events by System Organ Class and Preferred Term	Safety Population
Table 14.3.2.3	Treatment Emergent Adverse Events by System Organ Class and Preferred Term	Safety Population

Table Number	Table Title	Population
Table 14.3.2.4	Drug-Related Treatment Emergent Adverse Events by System Organ Class and Preferred Term	Safety Population
Table 14.3.2.5	Serious Adverse Events by System Organ Class and Preferred Term	Safety Population
Table 14.3.2.6	Drug-Related Serious Adverse Events by System Organ Class, Preferred Term	Safety Population
Table 14.3.2.7	CTC Grade 3 or greater Adverse Events by System Organ Class, Preferred Term	Safety Population
Table 14.3.2.8	Drug-Related CTC Grade 3 or Greater Adverse Events by System Organ Class and Preferred Term	Safety Population
Table 14.3.2.9	Adverse Events Leading to Discontinuation by System Organ Class and Preferred Term	Safety Population
Table 14.3.2.10	Summary of Injection Site Reactions	Safety Population
Table 14.3.2.11	Summary of Injection Site Reactions by Type and Severity	Safety Population
Table 14.3.2.12	Summary of Injection Site Reactions by Type and Relationship	Safety Population
Table 14.3.3.1	Shift from Baseline to Worst Post-Baseline Value (Low/High) for Clinical Chemistry Parameters	Safety Population
Table 14.3.3.2	Shift from Baseline to Worst Post-Baseline Value (Low/High) for Hematology Parameters	Safety Population
Table 14.3.3.3	Summary of Absolute and Change from Baseline Value for Urinalysis Results	Safety Population
Table 14.3.4	Summary of Absolute and Change from Baseline Value for Vital Sign Parameters	Safety Population
Table 14.3.5.1	Summary of Absolute and Change from Baseline Value for ECG Parameters	Safety Population
Table 14.3.5.2	Summary of ECG Findings	Safety Population

15.2 *List of Figures*

No Figures are required for this study.

15.3 *List of Listings*

Listings will sorted by patient number within Phase, group (for Phase II patients) and dose cohort.

Listing Number	Listing Title	Population
Listing 16.2.1.1	Patient Disposition	Safety Population
Listing 16.2.1.2	Inclusion and Exclusion Criteria	
Listing 16.2.1.3	Eligibility	Safety Population
Listing 16.2.2	Protocol Deviations	Safety Population
Listing 16.2.3	Population Allocation	Safety Population
Listing 16.2.4.1	Demography and Baseline Characteristics	Safety Population
Listing 16.2.4.2	Medical History	Safety Population
Listing 16.2.4.3	Oncology History	Safety Population
Listing 16.2.4.4	Prior Cancer Therapy	Safety Population
Listing 16.2.4.5	Prior Medications	Safety Population
Listing 16.2.4.6	Concomitant Medications	Safety Population
Listing 16.2.5.1	Study Drug Administration	Safety Population
Listing 16.2.5.2	Drug Dosing Schedule	Safety Population
Listing 16.2.5.3	Overall Study Drug Exposure	Safety Population
Listing 16.2.5.4	Pharmacokinetic Sampling	Safety Population
Listing 16.2.6.1	Tumor Assessments	Safety Population
Listing 16.2.6.2	Overall Tumor Assessments	Safety Population
Listing 16.2.6.3	Best Overall Response and Progression-free Survival	Safety Population
Listing 16.2.6.4	PBMC	Safety Population
Listing 16.2.6.5	Serum Antibody Responses	Safety Population
Listing 16.2.6.6	Cytokine Profiling Responses	Safety Population
Listing 16.2.6.7	Serum Tryptase Responses	Safety Population
Listing 16.2.6.8	T cells	Safety Population
Listing 16.2.6.9	NK cells	Safety Population
Listing 16.2.6.10	T-regulatory (Tregs)	Safety Population
Listing 16.2.6.11	Adenoviral Vector Shedding	Safety Population
Listing 16.2.7.1	Adverse Events	Safety Population
Listing 16.2.7.2	Treatment Emergent Adverse Events	Safety Population

Listing Number	Listing Title	Population
Listing 16.2.7.3	Treatment Emergent Serious Adverse Events	Safety Population
Listing 16.2.7.4	Treatment Emergent Adverse Events Related to Study Drug	Safety Population
Listing 16.2.7.5	Treatment Emergent Adverse Events Leading to Withdrawal	Safety Population
Listing 16.2.7.6	Treatment Emergent Adverse Events Leading to Death	Safety Population
Listing 16.2.7.8	Injection Reaction	Safety Population
Listing 16.2.8.1	Laboratory Reference Ranges	
Listing 16.2.8.2	Clinical Chemistry	Safety Population
Listing 16.2.8.3	Hematology	Safety Population
Listing 16.2.8.4	Urinalysis Data	Safety Population
Listing 16.2.8.5	Pregnancy Test	Safety Population
Listing 16.2.9	Vital Signs	Safety Population
Listing 16.2.10	ECG Data	Safety Population
Listing 16.2.11	ECOG Status	Safety Population
Listing 16.2.12	Physical Examination	Safety Population
Listing 16.2.13	Visit Dates	Safety Population
Listing 16.2.14	Photo Catalog	Safety Population
Listing 16.2.15	Waiver	Safety Population
Listing 16.2.16	Adenoviral Vector Shedding	Safety Population