STATISTICAL ANALYSIS PLAN
FOR PROTOCOL PRO 140_CD 01-EXTENSION

Sponsor:		
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Protocol Number:	PRO 140_CD 01-Extension	
Protocol Title:	An Extension of Protocol PRO 140_CD 01 to further evaluate the long-term Suppression of HIV-1 Replication following Substitution of Stable Combination Antiretroviral Therapy with a PRO 140 (Monoclonal CCR5 antibody) Monotherapy for in Adult Subjects with HIV-1 infection	
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LIST OF ABBREVIATIONS

Abbreviation	Term
ADL	Activities of Daily Living
AE	Adverse Event
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine Transaminase
ANC	Absolute Neutrophil Count
ART	Antiretroviral Therapy
AST	Aspartate Transaminase
ATC	Anatomic Therapeutic Classification
AUC	Area Under Curve
BMI	Body Mass Index
°C	Celsius
CBC	Complete Blood Count
CCR5	C-C chemokine receptor type 5
CDC	Centers for Disease Control and Prevention
CFR	Code of Federal Regulations
CHO	Chinese Hamster Ovary
cm	Centimeter
CMA	Certified Medical Assistant
CRA	Clinical Research Associate
CRF	Case Report Form
Cmax	Maximal Concentration
CRO	Contract Research Organization
CS	Clinically Significant
CTCAE	Common Terminology Criteria for Adverse Events
CV	Curriculum Vitae
DAIDS	Division of AIDS
DMC	Data Monitoring Committee
DNA	Deoxyribonucleic acid
DO	Doctor of Osteopathic Medicine
ECG	Electrocardiogram
EOT	End of Treatment
eCRF	Electronic Case Report Form
Emax	Maximum drug effect
et al	et aliae; Latin for "and others"

Abbreviation	Term
°F	Fahrenheit
FDA	U.S. Food and Drug Administration
FDP	Fixed Dose Procedure
FU	Follow-Up
GCP	Good Clinical Practice
GMP	Good Manufacturing Practices
HAART	Highly Active Antiretroviral Therapy
Hb	Hemoglobin
HCT	Hematocrit
HEENT	Head, Ears, Eyes, Nose, and Throat
HIPAA	Health Insurance Portability Accountability Act
HIV	Human Immunodeficiency Virus
IA	Interim Analysis
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization
i.e.	id est; Latin for "that is"
IEC	Independent Ethics Committee
IND	Investigational New Drug
IP	Investigational Product
IRB	Institutional Review Board
ISR	Injection Site Reactions
ITT	Intent-to-treat
IV	Intravenous
LAR	Legally Acceptable Representative
LDH	Lactate dehydrogenase
LPN	Licensed Practical Nurse
LVN	Licensed Vocational Nurse
mAb	Monoclonal Antibody
MD	Doctor of Medicine
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
mL	Milliliter
mm	Millimeter
MoCA	Montreal Cognitive Assessment
MW	Molecular Weight

Abbreviation	Term
NCS	Not Clinically Significant
NP	Nurse Practitioner
NVF	Non-Virologic Failure
PA	Physician Assistant
PI	Principal Investigator
PK	Pharmacokinetics
PP	Per Protocol
Pr	Protease
QC	Quality Control
QoL	Quality of Life
RBC	Red Blood Cells
RN	Registered Nurse
RNA	Ribonucleic acid
RT	Reverse Transcriptase
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	Standard Deviation
SOP	Standard Operating Procedure
TE	Treatment Extension
TEAE	Treatment Emergent Adverse Events
USA	United States of America
VAS	Visual Analogue Scale
VF	Virologic Failure
WBC	White Blood Cells
WHO	World Health Organization

1. INTRODUCTION

This Statistical Analysis Plan describes the planned analyses and reporting for the clinical trial protocol PRO 140_CD01-Extension, sponsored by CytoDyn Inc. The reader of this Statistical Analysis Plan (SAP) is encouraged to review the complete protocol and amendments as this plan contains only a limited overview of protocol information. The main objective of this plan is to provide details pertaining to statistical methodology, data conventions, and processes used for the analysis of data from this trial.

The format and content of this Statistical Analysis Plan are structured to provide sufficient detail to meet the requirements specified by the International Conference on Harmonization (ICH) E9: Guidance on Statistical Principles in Clinical Trials. All work planned and presented in this Statistical Analysis Plan will follow the ethical guidelines published by the American Statistical Association (ASA).

The following documents were reviewed in preparation of this Statistical Analysis Plan:

- Version 11.0, protocol 17 Feb 2020
- ASA Ethical Guidelines for Statistical Practice (2016)
- The Royal Statistical Society: Code of Conduct (2014)
- ICH Guidance on the Structure and Content of Clinical Study Reports (ICH E3, 1996)
- ICH Guidance on the Structure and Content of Clinical Study Reports (ICH E3(R1), 2013)
- ICH Guidance on the Statistical Principles for Clinical Trials (ICH E9, 1998)
- ICH Guidance on the Statistical Principles for Clinical Trials (ICH E9(R1), 2017)

2. PROTOCOL DESIGN AND OBJECTIVES

2.1 Study Objectives

The primary objective is to assess the long-term efficacy of PRO 140 monotherapy for the maintenance of viral suppression in patients who have completed 12 weeks of treatment under Protocol PRO 140_CD 01 without experiencing virologic failure.

The secondary objectives of the trial are to assess the long-term clinical safety and tolerability parameters of continued PRO 140 use in patients who have completed 12 weeks of treatment under Protocol PRO 140_CD 01 without experiencing virologic failure.

2.2 Design Overview

This study is a Phase 2b, multi-center, extension study designed to evaluate the long-term efficacy, safety, and tolerability of PRO 140 monotherapy for the maintenance of viral suppression in patients who were stable on combination antiretroviral therapy and completed 12 weeks of treatment under PRO 140_CD 01 Treatment Substitution Study without experiencing virologic failure.

Consenting patients will continue to receive PRO 140 monotherapy until IP receives marketing approval or IND is withdrawn by Sponsor. There is one week overlap of existing retroviral regimen and PRO 140 at the end of the treatment extension phase in subjects who do not experience virologic failure.

PRO 140 350 mg is administered as subcutaneous injection in the abdomen weekly. A total of 350 mg (175 mg/mL) is delivered as two 1 mL injections on opposite sides of the abdomen. Subjects who were enrolled under a previous Protocol version and are still receiving the 350 mg dose, have the option of increasing their dose to 700mg for the remainder of the Treatment Extension Phase. PRO 140 700 mg is delivered as two 2 mL injections on opposite sides of the abdomen.

Note: Alternatively, the 700 mg dose may be delivered as four 1mL doses (two SC injections on opposite sides of abdomen) for those that experience discomfort with the 2mL injections (i.e. subjects with low body fat percentages).

Study participants will be monitored for viral rebound on a weekly basis following initiation of PRO 140 monotherapy and will re-initiate their previous antiretroviral regimen if plasma HIV-1 RNA levels rise above 400 copies/ml on two consecutive blood draws at least 3 days apart. The study will have three phases: Screening Phase, Treatment Extension Phase and Follow-up Phase as shown in the study flow diagram Figure 2-1.

Screening Phase (14 ± 3 days):

This phase is designed to determine whether subjects participating in PRO 140_CD 01 Treatment

Substitution study are eligible to continue PRO 140 monotherapy in the Treatment Substitution Extension study. This phase consists of a series of screening assessments designed to determine eligibility. A written informed consent from the subject will be obtained by the Investigator or suitably qualified individual before the performance of any protocol-specific procedure.

This phase consists of two screening visits (SV1 and SV2) which correspond to Treatment Visits 12 and 13 of the PRO 140_CD 01 Treatment Substitution Study, respectively.

Subjects participating in PRO 140_CD 01 Treatment Substitution study that have not experienced virologic failure will be approached for study participation at Treatment Visit 12 (T12). A signed informed consent form will be obtained at the T12 visit which serves as Screening Visit 1 (SV1) for the PRO 140_Treatment Substitution Extension study.

In addition to assessments scheduled at T12 for the PRO 140_CD 01 Treatment Substitution study, the following assessments will also be performed to determine eligibility for the PRO 140_Treatment Substitution Extension study:

- Medical History
- Physical Examination

The lab results of blood samples collected at SV1 (or T12 of the PRO 140_CD 01 Treatment Substitution study) will be reviewed at SV2 (or T13 of the PRO 140_CD 01 Treatment Substitution study).

Treatment Extension Phase (weekly ± 3 days):

Treatment Extension (TE) Phase begins with an evaluation of results of laboratory samples collected during the Screening Phase. Subjects who meet all eligibility criteria, as per data gathered from Screening Phase are to be treated. All subjects who fail to meet eligibility criteria:

- will be considered screen failures,
- will not be allowed to enter the extension study,
- will re-initiate their existing anti-retroviral therapy regimen at T13 visit under the existing PRO 140_CD 01 Treatment Substitution study, and
- will proceed to enter follow-up phase after T14 visit depending on viral status.

For subject who meets the eligibility criteria, the first Treatment Extension Visit (TE1) will take

place 14 days from Screening Visit-1.

Eligible subjects will receive weekly treatments, given every week (± 3 days) or until virologic failure, whichever occurs first. Treatment Extension Phase visits will commence on TE1, i.e. the date of first treatment, with weekly visits (± 3 days) thereafter.

Efficacy assessments at each week will include assessment of viral load and CD4 cells count. Safety assessments will consist of physical exam, lab, and adverse event assessments at each Treatment Extension and Follow-Up Visits.

All study subjects will re-initiate their previous antiretroviral regimen:

- One week prior to the end of Treatment Extension Phase, or
- During the Treatment Extension Phase, if virologic failure occurs or have met any other criteria for discontinuation of study treatment as specified in the protocol.

Subjects who experience virologic failure (defined as two consecutive HIV-1 RNA levels of ≥ 400 copies/ml separated by at least 3 days) at any time during the Treatment Extension Phase will undergo the Virologic Failure (VF) Visit assessments and then exit the Treatment Extension Phase to enter the Follow-up Phase of the study.

Subjects who do not experience virologic failure will enter the Follow-up Phase of the study at the end of Treatment Extension Phase.

Follow-up Phase:

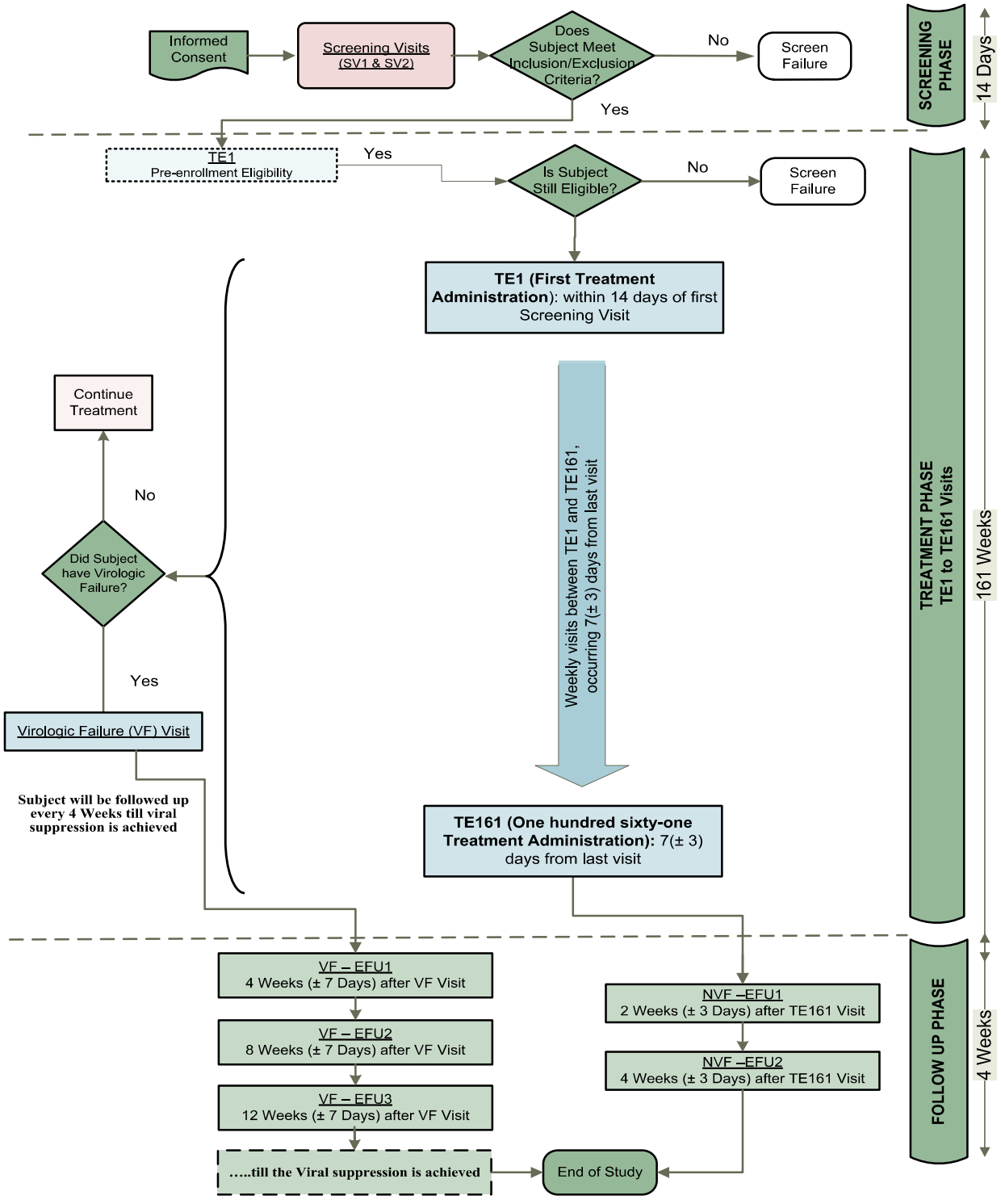
Duration of Follow-up Phase is determined based on whether or not subject has experienced Virologic Failure during the Treatment Extension Phase.

Subjects who experience virologic failure will be followed up every 4 weeks until the viral suppression is achieved (i.e., plasma HIV-1 RNA levels return to <50 copies/mL).

Subjects who do not experience Virologic Failure at the end of Treatment Extension Phase, will be followed up every 2 weeks for total of 4 weeks.

***Note**: Virologic failure subjects will have a long term safety follow up visit once a year within 2 years of completing the last VF-FU visit.*

Figure 2-1 Clinical Trial Flow Diagram



2.3 Study Duration

- **Screening Phase:** 14 ± 3 days
- **Treatment Extension Phase:** weekly ± allowed windows (±3 days).
- **Follow-up Phase:**
  - Virologic Failure: Until viral suppression is achieved
  - Non-Virologic Failure (NVF): 4 weeks

2.4 Study Treatment

2.4.1 Treatment Group

This is a single active arm study. All eligible subjects in the study will receive PRO 140 as a 350 mg subcutaneous injection weekly and have the option of increasing their dose to receive 700mg subcutaneous injections weekly.

2.4.2 Randomization and Blinding

This study is an open label study with one treatment arm with no randomization and blinding requirements.

2.5 Study Assessments/ endpoints

2.5.1 Primary Efficacy Endpoint

The primary efficacy endpoint for this study is Time to Virologic Failure after initiating PRO 140 monotherapy.

Virologic failure is defined as two consecutive HIV-1 RNA levels of ≥ 400 copies/ml separated by at least 3 days.

2.5.2 Secondary Efficacy Endpoints

- Proportion of Participants with Virologic Failure after initiating PRO 140 monotherapy.
- Mean change in Viral Load (HIV-1 RNA levels).
- Mean change in CD4 cell count.
- Change in Quality of Life metrics (up to TE107)

2.5.3 Safety Assessments

Safety measurements will include:

- Tolerability of repeated subcutaneous administration of PRO 140 as assessed by study participants (using Visual Analogue Scale) and by investigator-evaluation of injection site reactions.
- Frequency of Grade 3 or 4 adverse events as defined by the DAIDS Adverse Event scale
- Frequency of Treatment–emergent serious adverse events

3. SAMPLE SIZE DETERMINATION AND RATIONALE, STATISTICAL POWER, AND SIGNIFICANCE LEVEL

Sample size determination is not applicable as only those subjects who are currently enrolled in PRO 140_CD 01 Treatment Substitution Study are allowed to participate in this extension study.

4. INTERIM ANALYSIS

There is no planned interim analysis (IA) for this study.

5. ANALYSIS POPULATIONS

5.1 Intent-to-Treat Population

The Intent-to-Treat (ITT) population is defined as the set of subjects who have at least one dose of PRO 140 and have at least one post-treatment efficacy assessment for viral load in the extension study.

5.2 Per Protocol Population

The Per Protocol (PP) population is defined as the set of subjects who meet the ITT population requirements, and were not associated with a major protocol violation. This population will be identified before the database lock. The PP population will be the primary analysis population for the analysis of primary and secondary endpoints.

5.3 Safety Population

The Safety population is defined as all subjects who received at least one dose of PRO 140. This population will be used for the analysis of safety parameters.

6. DATA CONVENTION AND RELATED DEFINITIONS

6.1 Baseline Definition

Baseline for a given parameter or endpoint is defined to be the baseline of CD01 study.

6.2 Duplicate Data

For unplanned duplicate data within a protocol-specified visit, the last measured value will be used for the analysis. If it is not possible to identify the "last measured value" the average of the duplicate values will be used.

6.3 INTERIM ANALYSIS

There is no planned interim analysis (IA) for efficacy. IA for safety will be conducted after all enrolled subjects complete extended treatment with PRO 140 or until study treatment is discontinued, whichever comes first.

6.4 Handling of Missing Data

There will be no imputation of missing data for this study.

6.5 Multicenter Clinical Trials

This is a single center clinical trial.

6.6 Multiple Comparisons and Type I Error Rate Multiplicity adjustments

This is a proof of concept study and there is no need for adjustment of Type I error rate.

6.7 Covariates and Prognostic Factors

There are no pre-planned covariates analyses of the data from this proof of concept study.

6.8 Stratification Factors

There are no stratification factors for this study.

6.9 Subgroups and Exploratory Analysis

Subgroup/ exploratory analyses may be conducted as post hoc analyses.

6.10 Standard Calculations

6.10.1 Age

Age will be calculated as the number of completed years between the date of informed consent and the subject's birth date.

Age (years) = integer of[(date of informed consent – date of birth)/ 365.25+ 0.5]

6.10.2 Body Mass Index (BMI)

BMI will be calculated using height (in cm) and weight (in kg) according to the formula noted below.

BMI (kg/m^2) = weight (kg) / [[height (cm)/100]^2]

6.10.3 *Time to Virologic failure*

This metric will only be calculated for subjects who experience virologic failure. Time to virologic failure will be used for the analysis.

Time (days) to Virologic failure = (Date of the 2nd of two consecutive HIV-1 RNA levels of ≥ 400 copies/ml – Treatment start date)+ 1

6.10.4 Change from baseline

Change from baseline will be calculated for each post baseline visit as follows:

Change From Baseline = Post baseline result at time t - Baseline result

7. STATISTICAL METHODS

All collected study data will be presented in subject data listings. Statistical analyses will be performed using SAS® for Windows, version 9.4 or later.

7.1 Summarizing and Tabulating the Collected Data

All data collected will be summarized according to the variable type:

- Continuous data summaries will include number of observations, mean, standard deviation, median, and minimum and maximum values.
- Categorical data summaries will include frequency counts and percentages.

7.1.1 Subject Disposition and Withdrawals

There will be a detailed accounting of all subjects that signed the informed consent to participate in this trial. The following will be summarized:

- The number of subjects who are screened
- Then number of subjects who are screen failures

- The number of subjects who received treatment
- The number of subjects who completed the study
- The number of subjects who discontinued during the study
- The reason for study discontinuation

In addition, there will also be a listing of all discontinued subjects, which will provide the specific reason for discontinuation.

7.1.2 Protocol Deviations

The deviations occurring during the clinical trial will be summarized descriptively according to the following categories:

- Entrance criteria deviation
- Withdrawal criteria deviation
- Received wrong treatment or incorrect dose
- Received an excluded medication
- All other deviations

Additionally a by-subject listing of all deviations will also be prepared.

7.1.3 Demographics and Baseline Characteristics

Demographic and baseline characteristics (i.e., Age, Gender, Time since HIV diagnosis, Viral load at Screening Visit, etc.) will be summarized using appropriate descriptive statistics.

Medical history of the subjects will also be provided as a by-subject listing.

7.1.4 Concomitant Medications

Concomitant medications will be summarized for the Safety population. All concomitant medications recorded in the eCRFs will be coded to generic term and all matching Anatomic Therapeutic Classification (ATC) codes using WHO Drug dictionary. Summaries will be prepared using the coded terms. All prior and concomitant medications recorded in the eCRFs will also be listed.

7.1.5 Antiretroviral Therapy

Use of concomitant antiretroviral therapy is NOT allowed during the Treatment Extension Phase of the study EXCEPT for one week overlap of oral retroviral regimen and PRO 140 at the end of the

treatment in subjects who do not experience virologic failure. Subject is allowed to re-initiate their previous antiretroviral regimen during the Treatment Extension Phase, if virologic failure occurs or if subject meets any other criteria for discontinuation of study treatment as specified in the protocol.

Data from re-initiation of anti-retroviral therapy will be summarized for the Safety Population. All such medications recorded in the eCRFs will be coded to generic term and all matching Anatomic Therapeutic Classification (ATC) codes using WHO Drug. Summaries will be prepared using the coded terms. All re-initiation of anti-retroviral therapy recorded in the eCRFs will also be listed.

In addition, Virologic failure subjects will have a long term safety follow up visit once a year within 2 years of completing the last VF-FU visit. At the time the data from long term ART will also be captured and presented as a by-subject listing.

7.1.6 Treatment Administration

PRO 140 will be administered as a 350 mg subcutaneous injection weekly during treatment extension phase. A total of 350 mg (175 mg/mL) is delivered as two 1 mL injections administered subcutaneously on opposite sides of the abdomen.

Subjects who were enrolled under a previous Protocol version and are still receiving the 350 mg dose, have the option of increasing their dose to 700mg for the remainder of the Treatment Extension Phase. PRO 140 700 mg is delivered as two 2 mL injections on opposite sides of the abdomen.

Note: Alternatively, the 700 mg dose may be delivered as four 1mL doses (two SC injections on opposite sides of abdomen) for those that experience discomfort with the 2mL injections (i.e. subjects with low body fat percentages).

All treatment PRO-140 administration data will be listed. In addition, the number and percentage of the subjects who received PRO-140 injection will be presented for the safety population for each week during the treatment period.

7.2 Analysis of Efficacy Data

The primary analysis will be conducted on the PP population. The ITT population will be used as a supportive analysis.

7.2.1 Primary Endpoint

The primary efficacy endpoint for this study is Time to Virologic Failure after initiating PRO 140 monotherapy.

Virologic Failure is defined as two consecutive HIV-1 RNA levels of ≥ 400 copies/ml separated by at least 3 days.

The time to Virologic Failure for the subjects treated with PRO 140 monotherapy will be compared to a historical data (i.e., time to HIV-1 RNA viral load > 500 copies/mL of 29 days). The statistical comparison will be conducted using Wilcoxon rank sum test and the median time to Virologic Failure for this study will be compared to 30 days.

The time to Virologic Failure for the subjects treated with PRO 140 monotherapy will be presented and summarized descriptively.

7.2.2 Secondary Endpoints

All data from the secondary endpoints will be summarized according to the variable type for the PP population.

7.2.2.1 Proportion of Participants with Virologic Failure after initiating PRO 140 monotherapy

The number and percentages of subjects with Virologic Failure after initiating PRO-140 monotherapy will be presented.

7.2.2.2 Mean change in Viral Load (HIV-1 RNA levels)

The raw and change from baseline in Viral Load (i.e.., HIV-1 RNA levels) will be summarized for each week during the treatment phase. The summary tables will include the number of observations, mean, standard deviation, median, and minimum and maximum values. For change from baseline summaries, subjects with an undefined change from baseline, because of missing data, will be excluded.

7.2.2.3 Mean change in CD4 cell count

The raw and change from baseline in CD4 cell count will be summarized for each week during the treatment phase. The summary tables will include the number of observations, mean, standard deviation, median, and minimum and maximum values. For change from baseline summaries,

subjects with an undefined change from baseline, because of missing data, will be excluded.

7.2.2.4 Change in quality of life metrics (up to TE107)

A quality of life assessment using ACTG SF-21 instrument will be performed by the Principal Investigator or Study Coordinator at Screening Visit 1 (SV1), once every four weeks from TE4 through TE107, and at EOT. Quality of life will be summarized. By-subject listing of all available data will also be provided.

7.3 Analysis of Safety Data

The Safety population will be used for the analysis of safety endpoints. No inferential statistics are planned.

7.3.1 Adverse Events

Adverse events will be classified by system organ class and preferred term (PT) according to the most recent MedDRA dictionary.

Since this is an extension of the PRO 140_CD 01 study, all adverse events (AE) that captured in this study will be considered as Treatment Emergent Adverse Events (TEAEs). The following TEAE summaries will be provided, using frequency counts and percentages:

- Overall (*i.e.,* regardless of severity or relationship to treatment)
- By severity grade (mild, moderate, severe, life threatening or death)
- By relationship to study treatment

In addition, separate summaries of SAEs, and AEs resulting in discontinuation of study treatment will be presented.

Unless otherwise specified, at each level of subject summarization, a subject will be counted only once. If there is more than one occurrence of an event, the event of the worst severity or the worst-case relationship category will be summarized.

7.3.2 Tolerability Assessment

7.3.2.1 Injection Site Reaction

At each visit during the Treatment Extension Phase, an injection site reaction assessment will be made for the current and previous injection sites. Injection site reaction assessments are recorded by the Investigator starting after the first injection is given. Injection site reaction assessments will not

be completed when subjects perform self-administration.

All data from the injection site reaction assessments of the repeated subcutaneous administration of PRO 140 will be presented and descriptively summarized.

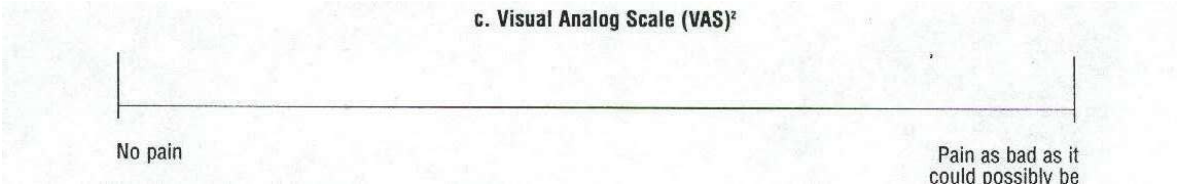
7.3.2.2 Injection Site Pain Assessment

Tolerability of repeated subcutaneous administration of PRO 140 is evaluated based on assessment of subject-perceived injection site pain using the Pain Visual Analog Scale (VAS).

Beginning at Screening Visit 1, subjects will be asked to mark the point that best represents the pain intensity at the time of injection administration on a horizontal line (100 mm in length) anchored by the following word descriptors at each end, “no pain" on the left side and "pain as bad as it could possibly be" on the right side of the line. The subject marks on the line or by pointing to a position on the line the point that they feel represents their perception of their pain state. The VAS score is determined by measuring in millimeters from the left-hand end of the line to the point that the patient marks.

All data from the VAS assessment of the repeated subcutaneous administration of PRO 140 will be presented and descriptively summarized.

Figure 7-1 Visual Analog Scale



7.3.3 Clinical Laboratory Evaluations

All available results of the clinical laboratory evaluations will be listed and summarized. Laboratory evaluations include hematology (routine CBC), biochemistry, etc.

7.3.3.1 Laboratory Values over Time

Summary statistics of raw data and change from baseline values for each laboratory parameter will be presented. Data will be summarized as appropriate to the variable type.

For change from baseline summaries, subjects with an undefined change from baseline, because of missing data, will be excluded.

7.3.3.2 Individual Subject Changes (Shift Tables)

Individual subject changes will be identified through shift tables. Shift tables will be presented for each laboratory parameter with counts and percentages of subjects, for shift (change) from baseline.

7.3.4 Physical Examination

All physical examination findings will be listed and/or summarized.

7.3.5 Vital Signs

Tabulations of raw data and change from baseline values will be presented by time point for each vital sign parameter [*i.e.,* Heart Rate (beats/min), temperature (^{0}C / ^{0}F), systolic BP (mmHg), diastolic BP (mmHg), and Respiration Rate].

Tabulations will include the number of observations, mean, standard deviation, median, and minimum and maximum values. For change from baseline summaries, subjects with an undefined change from baseline, because of missing data, will be excluded.

7.3.6 Additional Data listings and tabulations

7.3.6.1 Neurological Assessment

All neurological assessment results will be listed and any abnormality will be summarized.

7.3.6.2 Pregnancy Test

All the results from serum and urine pregnancy will be presented as a by-subject listing.

7.3.6.3 *Notification and Outcome Pregnancy*

All the results for Notification and Outcome Pregnancy will be presented as a by-subject listing.

7.3.6.4 PK sample for PRO140

Data for PK concentration of PRO 140 will be provided by external vendor *QPS*. All data will be presented as by-subject listings.

7.3.6.5 HIV-1 Trofile® DNA/RNA Assay and Drug Resistance, Genotypic and Phenotypic data

Data for HIV-1 trofile® DNA/RNA assay as well us Drug Resistance, Genotypic and Phenotypic data will be provided by external vendor Monogram Biosciences. All data will be presented as by-subject listings.

7.3.6.6 TruCount Assay (including CD4 Counts)

Data for TruCount assay will be provided by external vendor Covance. All data will be presented as by-subject listings.

7.3.6.7 Anti-idiotypic antibodies to PRO 140

Data for Anti-idiotypic antibodies to PRO 140 will be provided by external vendor *QPS*. All data will be presented as by-subject listings.

7.3.6.8 HIV-1 Co-Receptor Tropism (exploratory assay)

Data for HIV-1 co-receptor tropism will be provided by external vendor Quest Diagnostics. All data will be presented as a by-subject listing.

7.3.6.9 Serum Concentration of ART Drugs

All serum concentration of ART drugs will be provided from the external vendor CLS. All data will be presented as a by-subject listing.

8. APPENDIX 1: SCHEDULE OF ASSESSMENTS

TABLE 1: SCHEDULE OF ASSESSMENTS – SCREENING AND TREATMENT EXTENSION PHASE (1 OF 8)

Procedure/Assessments	**Screening Visit 1** (coincide with T12 under the PRO 140_CD 01 protocol)	**Screening Visit 2** (coincide with T13 under the PRO 140_CD 01 protocol)	**Treatment Extension Visit 1** (Week-1)	**Treatment Extension Visit 2** (Week-2)	**Treatment Extension Visit 3** (Week-3)	**Treatment Extension Visit 4** (Week-4)	**Treatment Extension Visit 5** (Week-5)	**Treatment Extension Visit 6** (Week-6)	**Treatment Extension Visit 7** (Week-7)	**Treatment Extension Visit 8** (Week-8)	**Treatment Extension Visit 9** (Week-9)	**Treatment Extension Visit 10** (Week-10)	**Treatment Extension Visit 11** (Week-11)	**Treatment Extension Visit 12** (Week-12)	**Treatment Extension Visit 13** (Week-13)	**In case of Virologic Failure**
Visit	**SV1**	**SV2**	**TE1**	**TE2**	**TE3**	**TE4**	**TE5**	**TE6**	**TE 7**	**TE8**	**TE9**	**TE10**	**TE11**	**TE12**	**TE13**	**VF**
Window Period	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	
Informed Consent[1]	X															
Eligibility Evaluation[2]	X	X														
Pre-enrollment Eligibility[3]			X													
Medical History[4]			-													
Physical Examination	X	-X-[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X	X
Neurological Assessment[6]	-X-					X				X				X		X
Quality of Life Assessment[7]	-X-					X				X				X		X
Vital Signs[8]	-X-	-X-	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Complete Blood Count (CBC)[9]																X
Biochemistry[10]																X
Serum Pregnancy Test[11]	X															
Urine Pregnancy Test[11]		X														
Plasma HIV-1 RNA level	-X-	-X-		X		X		X		X		X		X		X
TruCount T assay[12]	-X-	-X-		X		X		X		X		X		X		X
PK sample for PRO 140[13]	-X-					X				X				X		X
Serum concentration for	-X-					X				X				X		

Procedure/Assessments	Screening Visit 1 (coincide with T12 under the PRO 140_CD 01 protocol)	Screening Visit 2 (coincide with T13 under the PRO 140_CD 01 protocol)	Treatment Extension Visit 1 (Week-1)	Treatment Extension Visit 2 (Week-2)	Treatment Extension Visit 3 (Week-3)	Treatment Extension Visit 4 (Week-4)	Treatment Extension Visit 5 (Week-5)	Treatment Extension Visit 6 (Week-6)	Treatment Extension Visit 7 (Week-7)	Treatment Extension Visit 8 (Week-8)	Treatment Extension Visit 9 (Week-9)	Treatment Extension Visit 10 (Week-10)	Treatment Extension Visit 11 (Week-11)	Treatment Extension Visit 12 (Week-12)	Treatment Extension Visit 13 (Week-13)	In case of Virologic Failure
Visit	SV1	SV2	TE1	TE2	TE3	TE4	TE5	TE6	TE 7	TE8	TE9	TE10	TE11	TE12	TE13	VF
Window Period	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	
ART drugs[14]																
HIV Genotyping Assay																X
Trofile® RNA and PhenoSense Assay																X
Anti-idiotypic antibodies to PRO 140	-X-					X				X				X		X
Blood sample collection for Exploratory/Confirmatory analysis[15]		X														X
PRO 140 Administration	-X-	-X-	X	X	X	X	X	X	X	X	X	X	X	X	X	
PRO 140 Administration by subject[16]					X		X		X		X		X		X	
Subject drug dispensing/accountability[17]				X		X		X		X		X		X		
Re-initiate Antiretroviral Regimen[18]																X
Injection Site Reaction Assessment[19]	-X-	-X-	X	X	X	X	X	X	X	X	X	X	X	X	X	
Injection Site Pain Assessment (VAS)[20]	-X-	-X-	X	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse Events	-X-	-X-	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications	-X-	-X-	X	X	X	X	X	X	X	X	X	X	X	X	X	X

TABLE 1: SCHEDULE OF ASSESSMENTS – SCREENING AND TREATMENT EXTENSION PHASE (2 OF 8)

Procedure/Assessments	**Treatment Extension Visit 14** (Week-14)	**Treatment Extension Visit 15** (Week-15)	**Treatment Extension Visit 16** (Week-16)	**Treatment Extension Visit 17** (Week-17)	**Treatment Extension Visit 18** (Week-18)	**Treatment Extension Visit 19** (Week-19)	**Treatment Extension Visit 20** (Week-20)	**Treatment Extension Visit 21** (Week-21)	**Treatment Extension Visit 22** (Week-22)	**Treatment Extension Visit 23** (Week-23)	**Treatment Extension Visit 24** (Week-24)	**Treatment Extension Visit 25** (Week-25)	**In case of Virologic Failure**
Visit	**TE14**	**TE15**	**TE16**	**TE17**	**TE18**	**TE19**	**TE20**	**TE21**	**TE22**	**TE23**	**TE24**	**TE25**	**VF**
Window Period	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	
Informed Consent[1]													
Eligibility Evaluation[2]													
Pre-enrollment Eligibility[3]													
Medical History[4]													
Physical Examination	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X
Neurological Assessment[6]			X				X				X		X
Quality of Life Assessment[7]			X				X				X		X
Vital Signs[8]	X	X	X	X	X	X	X	X	X	X	X	X	X
Complete Blood Count (CBC)[9]													X
Biochemistry[10]													X
Serum Pregnancy Test[11]													
Urine Pregnancy Test[11]													
Plasma HIV-1 RNA level	X		X		X		X		X		X		X
TruCount T assay[12]	X		X		X		X		X		X		X
PK sample for PRO 140[13]			X				X				X		X
Serum concentration for ART drugs[14]			X				X				X		
HIV Genotyping Assay													X

Procedure/Assessments	**Treatment Extension Visit 14** (Week-14)	**Treatment Extension Visit 15** (Week-15)	**Treatment Extension Visit 16** (Week-16)	**Treatment Extension Visit 17** (Week-17)	**Treatment Extension Visit 18** (Week-18)	**Treatment Extension Visit 19** (Week-19)	**Treatment Extension Visit 20** (Week-20)	**Treatment Extension Visit 21** (Week-21)	**Treatment Extension Visit 22** (Week-22)	**Treatment Extension Visit 23** (Week-23)	**Treatment Extension Visit 24** (Week-24)	**Treatment Extension Visit 25** (Week-25)	**In case of Virologic Failure**
Visit	**TE14**	**TE15**	**TE16**	**TE17**	**TE18**	**TE19**	**TE20**	**TE21**	**TE22**	**TE23**	**TE24**	**TE25**	**VF**
Window Period	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	
Trofile® RNA and PhenoSense Entry Assay													X
Anti-idiotypic antibodies to PRO 140			X				X				X		X
Blood sample collection for Exploratory/Confirmatory analysis[15]													X
PRO 140 Administration	X	X	X	X	X	X	X	X	X	X	X	X	
PRO 140 Administration by subjects[16]		X		X		X		X		X		X	
Subject drug dispensing/accountability[17]	X		X		X		X		X		X		
Re-initiate Antiretroviral Regimen[18]													X
Injection Site Reaction Assessment[19]	X	X	X	X	X	X	X	X	X	X	X	X	
Injection Site Pain Assessment (VAS)[20]	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X

TABLE 1: SCHEDULE OF ASSESSMENTS – SCREENING AND TREATMENT EXTENSION PHASE (3 OF 8)

Procedure/Assessments	**Treatment Extension Visit 26** (Week-26)	**Treatment Extension Visit 27** (Week-27)	**Treatment Extension Visit 28** (Week-28)	**Treatment Extension Visit 29** (Week-29)	**Treatment Extension Visit 30** (Week-30)	**Treatment Extension Visit 31** (Week-31)	**Treatment Extension Visit 32** (Week-32)	**Treatment Extension Visit 33** (Week-33)	**Treatment Extension Visit 34** (Week-34)	**Treatment Extension Visit 35** (Week-35)	**Treatment Extension Visit 36** (Week-36)	**Treatment Extension Visit 37** (Week-37)	**In case of Virologic Failure**
Visit	**TE26**	**TE27**	**TE28**	**TE29**	**TE30**	**TE31**	**TE32**	**TE33**	**TE34**	**TE35**	**TE36**	**TE37**	**VF**
Window Period	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	
Informed Consent[1]													
Eligibility Evaluation[2]													
Pre-enrollment Eligibility[3]													
Medical History[4]													
Physical Examination	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X
Neurological Assessment[6]			X				X				X		X
Quality of Life Assessment[7]			X				X				X		X
Vital Signs[8]	X	X	X	X	X	X	X	X	X	X	X	X	X
Complete Blood Count (CBC)[9]													X
Biochemistry[10]													X
Serum Pregnancy Test[11]													
Urine Pregnancy Test[11]													
Plasma HIV-1 RNA level	X		X		X		X		X		X	X	X
TruCount T assay[12]	X		X		X		X		X		X	X	X
PK sample for PRO 140[13]			X				X				X		X
Serum concentration for ART drugs[14]			X				X				X		
HIV Genotyping Assay													X

Procedure/Assessments	**Treatment Extension Visit 26** (Week-26)	**Treatment Extension Visit 27** (Week-27)	**Treatment Extension Visit 28** (Week-28)	**Treatment Extension Visit 29** (Week-29)	**Treatment Extension Visit 30** (Week-30)	**Treatment Extension Visit 31** (Week-31)	**Treatment Extension Visit 32** (Week-32)	**Treatment Extension Visit 33** (Week-33)	**Treatment Extension Visit 34** (Week-34)	**Treatment Extension Visit 35** (Week-35)	**Treatment Extension Visit 36** (Week-36)	**Treatment Extension Visit 37** (Week-37)	**In case of Virologic Failure**
Visit	**TE26**	**TE27**	**TE28**	**TE29**	**TE30**	**TE31**	**TE32**	**TE33**	**TE34**	**TE35**	**TE36**	**TE37**	**VF**
Window Period	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	
Trofile® RNA and PhenoSense Entry Assay													X
Anti-idiotypic antibodies to PRO 140			X				X				X		X
Blood sample collection for Exploratory/Confirmatory analysis[15]													X
PRO 140 Administration	X	X	X	X	X	X	X	X	X	X	X	X	
PRO 140 Administration by subjects[16]		X		X		X		X		X		X	
Subject drug dispensing/accountability[17]	X		X		X		X		X		X		
Re-initiate Antiretroviral Regimen[18]													X
Injection Site Reaction Assessment[19]	X	X	X	X	X	X	X	X	X	X	X	X	
Injection Site Pain Assessment (VAS)[20]	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X

TABLE 1: SCHEDULE OF ASSESSMENTS – SCREENING AND TREATMENT EXTENSION PHASE (4 OF 8)

Procedure/Assessments	**Treatment Extension Visit 38** (Week-38)	**Treatment Extension Visit 39** (Week-39)	**Treatment Extension Visit 40** (Week-40)	**Treatment Extension Visit 41** (Week-41)	**Treatment Extension Visit 42** (Week-42)	**Treatment Extension Visit 43** (Week-43)	**Treatment Extension Visit 44** (Week-44)	**Treatment Extension Visit 45** (Week-45)	**Treatment Extension Visit 46** (Week-46)	**Treatment Extension Visit 47** (Week-47)	**Treatment Extension Visit 48** (Week-48)	**Treatment Extension Visit 49** (Week-49)	**In case of Virologic Failure**
Visit	**TE38**	**TE39**	**TE40**	**TE41**	**TE42**	**TE43**	**TE44**	**TE45**	**TE46**	**TE47**	**TE48**	**TE49**	**VF**
Window Period	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	
Informed Consent[1]													
Eligibility Evaluation[2]													
Pre-enrollment Eligibility[3]													
Medical History[4]													
Physical Examination	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X
Neurological Assessment[6]			X				X				X		X
Quality of Life Assessment[7]			X				X				X		X
Vital Signs[8]	X	X	X	X	X	X	X	X	X	X	X	X	X
Complete Blood Count (CBC)[9]													X
Biochemistry[10]													X
Serum Pregnancy Test[11]													
Urine Pregnancy Test[11]													
Plasma HIV-1 RNA level	X		X		X		X		X		X		X
TruCount T assay[12]	X		X		X		X		X		X		X
PK sample for PRO 140[13]			X				X				X		X
Serum concentration for ART drugs[14]			X				X				X		
HIV Genotyping Assay													X

Procedure/Assessments	**Treatment Extension Visit 38** (Week-38)	**Treatment Extension Visit 39** (Week-39)	**Treatment Extension Visit 40** (Week-40)	**Treatment Extension Visit 41** (Week-41)	**Treatment Extension Visit 42** (Week-42)	**Treatment Extension Visit 43** (Week-43)	**Treatment Extension Visit 44** (Week-44)	**Treatment Extension Visit 45** (Week-45)	**Treatment Extension Visit 46** (Week-46)	**Treatment Extension Visit 47** (Week-47)	**Treatment Extension Visit 48** (Week-48)	**Treatment Extension Visit 49** (Week-49)	**In case of Virologic Failure**
Visit	**TE38**	**TE39**	**TE40**	**TE41**	**TE42**	**TE43**	**TE44**	**TE45**	**TE46**	**TE47**	**TE48**	**TE49**	**VF**
Window Period	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	
Trofile® RNA and PhenoSense Entry Assay													X
Anti-idiotypic antibodies to PRO 140			X				X				X		X
Blood sample collection for Exploratory/Confirmatory analysis[15]													X
PRO 140 Administration	X	X	X	X	X	X	X	X	X	X	X	X	
PRO 140 Administration by subjects[16]		X		X		X		X		X		X	
Subject drug dispensing/accountability[17]	X		X		X		X		X		X		
Re-initiate Antiretroviral Regimen[18]													X
Injection Site Reaction Assessment[19]	X	X	X	X	X	X	X	X	X	X	X	X	
Injection Site Pain Assessment (VAS)[20]	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X

TABLE 1: SCHEDULE OF ASSESSMENTS – SCREENING AND TREATMENT EXTENSION PHASE (5 OF 8)

Procedure/Assessments	**Treatment Extension Visit 50** (Week-50)	**Treatment Extension Visit 51** (Week-52)	**Treatment Extension Visit 52** (Week-52)	**Treatment Extension Visit 53** (Week-53)	**Treatment Extension Visit 54** (Week-54)	**Treatment Extension Visit 55** (Week-55)	**Treatment Extension Visit 56** (Week-56)	**Treatment Extension Visit 57** (Week-57)	**Treatment Extension Visit 58** (Week-58)	**Treatment Extension Visit 59** (Week-59)	**In case of Virologic Failure**
Visit	**TE50**	**TE51**	**TE52**	**TE53**	**TE54**	**TE55**	**TE56**	**TE57**	**TE58**	**TE59**	**VF**
Window Period	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	
Informed Consent[1]											
Eligibility Evaluation[2]											
Pre-enrollment Eligibility[3]											
Medical History[4]											
Physical Examination	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X
Neurological Assessment[6]			X				X				X
Quality of Life Assessment[7]			X				X				X
Vital Signs[8]	X	X	X	X	X	X	X	X	X	X	X
Complete Blood Count (CBC)[9]											X
Biochemistry[10]											X
Serum Pregnancy Test[11]											
Urine Pregnancy Test[11]											
Plasma HIV-1 RNA level	X		X		X		X		X		X
TruCount T assay[12]	X		X		X		X		X		X
PK sample for PRO 140[13]			X				X				X
Serum concentration for ART drugs[14]			X				X				
HIV Genotyping Assay											X

Procedure/Assessments	**Treatment Extension Visit 50** (Week-50)	**Treatment Extension Visit 51** (Week-52)	**Treatment Extension Visit 52** (Week-52)	**Treatment Extension Visit 53** (Week-53)	**Treatment Extension Visit 54** (Week-54)	**Treatment Extension Visit 55** (Week-55)	**Treatment Extension Visit 56** (Week-56)	**Treatment Extension Visit 57** (Week-57)	**Treatment Extension Visit 58** (Week-58)	**Treatment Extension Visit 59** (Week-59)	**In case of Virologic Failure**
Visit	**TE50**	**TE51**	**TE52**	**TE53**	**TE54**	**TE55**	**TE56**	**TE57**	**TE58**	**TE59**	**VF**
Window Period	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	±3 days since last treatment	
Trofile® RNA and PhenoSense Entry Assay											X
Anti-idiotypic antibodies to PRO 140			X				X				X
Blood sample collection for Exploratory/Confirmatory analysis[15]											X
PRO 140 Administration	X	X	X	X	X	X	X	X	X	X	
PRO 140 Administration by subjects[16]		X		X		X		X		X	
Subject drug dispensing/accountability[17]	X		X		X		X		X		
Re-initiate Antiretroviral Regimen[18]											X
Injection Site Reaction Assessment[19]	X	X	X	X	X	X	X	X	X	X	
Injection Site Pain Assessment (VAS)[20]	X	X	X	X	X	X	X	X	X	X	
Adverse Events	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X

X (red bold)**:** Activities performed under Extension study protocol
-X- : Activities performed under PRO 140_CD 01 protocol

[1] Informed consent must be obtained at the Screening Visit 1 (SV1) coincides with the T12 clinic visit under the PRO 140_CD 01 protocol.

[2] Initial evaluation of patient eligibility will be performed by Investigator.

[3] Based on results of lab samples collected at the Screening Visit 1 under Extension protocol / T12 clinic visit under the PRO 140_CD 01 protocol

[4] Medical history collected at the time of screening for PRO 140_CD 01 protocol will be carried forward. Medical history will not be collected for the PRO 140_CD 01-Extension protocol.

[5] Symptom-directed physical examination

[6] Performed by Principal Investigator or designated study personnel. The neurological assessment tool is based on the three question survey used by Simioni et al. (Simioni S, 2010). Additional neurological assessment modalities may be used as per Investigator's discretion.

[7] Performed by Principal Investigator or Study Coordinator

[8] Blood pressure, heart rate, respiration rate, temperature assessed before and 15 minutes after study treatment administered at clinic

[9] Hemoglobin, Hematocrit (HCT), Red Blood Cells (RBC), White Blood Cells (WBC) with total and differential count, Absolute Neutrophil Count (ANC) and platelets.

[10] Serum Biochemistry

Hepatic function indicators: total and direct bilirubin, alkaline phosphatase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein, Lactate dehydrogenase (LDH)

Renal function indicators: BUN, creatinine

Electrolytes: sodium, potassium, chloride, calcium and bicarbonate

Other: glucose (random), cholesterol (total)

[11] ONLY performed on women of childbearing potential.

[12] Includes: Absolute Lymphocytes, CD3 cell count, CD4 cell count, CD8 cell count, CD3 %, CD4 %, and CD8 %

[13] PK samples for PRO 140 may be collected at during Treatment Extension Phase and at virologic failure

[14] To assess subject compliance in abstaining from previous ART regimen after SV1 visit;

[15] Blood sample collection prior to first treatment administration at SV2 and at the time of early breakthrough/virologic failure will be used for exploratory or confirmatory purposes.

[16] ONLY for subjects trained to perform self-administration of study treatment on weeks when clinic visit optional, i.e., no lab samples are required

[17] Study treatment for self-administration will be provided to subjects during treatment visits at clinic; used vials from prior self-administration must be collected and accounted for (see Section 4.2.2)

[18] All study subjects will re-initiate their previous antiretroviral regimen: (1) One week prior to the end of 161-week Treatment Extension Phase, or (2) Anytime during the Treatment Extension Phase, if virologic failure occurs or have met any other criteria for discontinuation of study treatment as specified in the protocol.

[19] As assessed by Investigator when study treatment administered at the clinic.

[20] Subject-perceived injection site pain (average pain since last treatment) will be assessed using the Pain Visual Analog Scale (VAS) prior to each study treatment administration for subject's randomized to PRO 140

TABLE 1: SCHEDULE OF ASSESSMENTS – SCREENING AND TREATMENT EXTENSION PHASE (6 OF 8)

Procedure/Assessments	Treatment Extension Visit 60 - 63	Treatment Extension Visit 64-67	Treatment Extension Visit 68-71	Treatment Extension Visit 72-75	Treatment Extension Visit 76-79	Treatment Extension Visit80-83	Treatment Extension Visit 84-87	Treatment Extension Visit 88-91	Treatment Extension Visit 92-95	Treatment Extension Visit 96-99	Treatment Extension Visit100-103	Treatment Extension Visit104-107	In case of Virologic Failure
Visit	TE60-63	TE64-67	TE68-71	TE72-75	TE76-79	TE80-83	TE84-87	TE88-91	TE92-95	TE96-99	TE100-103	TE104-107	VF
Window Period	±3 days since last treatment												
Symptom-directed physical examination	X	X	X	X	X	X	X	X	X	X	X	X	
Physical Examination													X
Neurological Assessment[21]	X	X	X	X	X	X	X	X	X	X	X	X	X
Quality of Life Assessment[21]	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs[22]	X	X	X	X	X	X	X	X	X	X	X	X	X
Complete Blood Count (CBC)[23]													X
Biochemistry[24]													X
Plasma HIV-1 RNA level[21]	X	X	X	X	X	X	X	X	X	X	X	X	X
TruCount T assay[21]	X	X	X	X	X	X	X	X	X	X	X	X	X
PK sample for PRO 140[21]	X	X	X	X	X	X	X	X	X	X	X	X	X
Serum concentration for ART drugs[21]	X	X	X	X	X	X	X	X	X	X	X	X	
Anti-idiotypic antibodies to PRO 140[21]	X	X	X	X	X	X	X	X	X	X	X	X	X

Procedure/Assessments	Treatment Extension Visit 60 - 63	Treatment Extension Visit 64-67	Treatment Extension Visit 68-71	Treatment Extension Visit 72-75	Treatment Extension Visit 76-79	Treatment Extension Visit80-83	Treatment Extension Visit 84-87	Treatment Extension Visit 88-91	Treatment Extension Visit 92-95	Treatment Extension Visit 96-99	Treatment Extension Visit100-103	Treatment Extension Visit104-107	In case of Virologic Failure
Visit	TE60-63	TE64-67	TE68-71	TE72-75	TE76-79	TE80-83	TE84-87	TE88-91	TE92-95	TE96-99	TE100-103	TE104-107	VF
Window Period	±3 days since last treatment												
HIV Genotyping Assay													X
Trofile® DNA/RNA and PhenoSense Entry Assay													X
Blood sample collection for Exploratory/Confirmatory analysis[25]													X
PRO 140 Administration[26]	X	X	X	X	X	X	X	X	X	X	X	X	
Subject drug dispensing/accountability[28]	X	X	X	X	X	X	X	X	X	X	X	X	
Antiretroviral Regimen[29]													X
Injection Site Reaction Assessment[30]	X	X	X	X	X	X	X	X	X	X	X	X	
Injection Site Pain Assessment (VAS)[31]	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X

[21] Performed when subject comes to clinic by Principal Investigator or designated study personnel. ***NOTE:*** *The neurological assessment tool is based on the three question survey used by Simioni et al. (Simioni S, 2010). Additional neurological assessment modalities may be used as per Investigator's discretion.*.

[22] Blood pressure, heart rate, respiration rate, temperature assessed before and 15 minutes after study treatment administered at clinic

[23] Hemoglobin, Hematocrit (HCT), Red Blood Cells (RBC), White Blood Cells (WBC) with total and differential count, Absolute Neutrophil Count (ANC) and platelets.

[24] Serum Biochemistry:

Hepatic function indicators: total and direct bilirubin, alkaline phosphatase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein, Lactate dehydrogenase (LDH)

Renal function indicators: BUN, creatinine

Electrolytes: sodium, potassium, chloride, calcium and bicarbonate

Other: glucose (random), cholesterol (total)

[25] Sample collected on adhoc basis, as per discretion of Sponsor/Investigator during the treatment phase.

[26] ONLY for subjects trained to perform self-administration of study treatment on weeks when clinic visit optional, i.e., no lab samples are required

[27] Study treatment should be administered at clinic.

[28] Study treatment for self-administration will be provided to subjects during treatment visits at clinic; used vials from prior self-administration must be collected and accounted for (see Section 4.2.2).

[29] All study subjects will re-initiate their previous antiretroviral regimen: (1) One week prior to the end of 161-week Treatment Extension Phase, or (2) Anytime during the Treatment Extension Phase, if virologic failure occurs or have met any other criteria for discontinuation of study treatment as specified in the protocol.

[30] As assessed by Investigator when study treatment administered at the clinic.

[31] Subject-perceived injection site pain (average pain since last treatment) will be assessed using the Pain Visual Analog Scale (VAS) prior to each study treatment administration for subjects randomized to PRO 140.

TABLE 1: SCHEDULE OF ASSESSMENTS – SCREENING AND TREATMENT EXTENSION PHASE (7 OF 8)

Procedure/Assessments	Subsequent Weekly TE Visits (TE108-TE159)	Treatment Extension Visit	Treatment Extension Visit	In case of Virologic Failure
Visit[32]		TE160	TE161	VF
Window Period	±3 days since last treatment			
Symptom-directed physical examination	X[32]	X		
Physical Examination			X	X
Neurological Assessment[34]	X[32]	X		X
Quality of Life Assessment[34]		X		X
Vital Signs[35]	X[32]	X	X	X
Complete Blood Count (CBC)[36]			X	X
Biochemistry[37]			X	X
Plasma HIV-1 RNA level	X[32]	X	X	X
TruCount T assay	X[32]	X	X	X
PK sample for PRO 140	X[32]	X		X
Serum concentration for ART drugs[38]	X[32]	X		
Anti-idiotypic antibodies to PRO 140	X[32]	X		X
HIV Genotyping Assay				X
Trofile® DNA/RNA and PhenoSense Entry Assay			X	X
Blood sample collection for Exploratory/Confirmatory analysis[38]			X	X
PRO 140 Administration	X[39]	X[40]	X[40]	
Subject drug dispensing/accountability[41]	X	X		
Antiretroviral Regimen[42]		X	X	X
Injection Site Reaction Assessment[43]	X[32]	X	X	

Procedure/Assessments	Subsequent Weekly TE Visits (TE108-TE159)	Treatment Extension Visit	Treatment Extension Visit	In case of Virologic Failure
Visit[32]		TE160	TE161	VF
Window Period	±3 days since last treatment			
Injection Site Pain Assessment (VAS)[44]	X[32]	X	X	
Adverse Events[33]	X	X	X	X
Concomitant Medications	X	X	X	X

[32] In-clinic assessment(s) should be performed at least once every 4 weeks from TE108-TE159.

[33] Subjects should be instructed to report any new AEs that occur between clinic visits to site promptly

[34] Performed by Principal Investigator (or designee) when subject comes to clinic. NOTE: The neurological assessment tool is based on the three question survey used by Simioni et al. (Simioni S, 2010). Additional neurological assessment modalities may be used as per Investigator's discretion.

[35] Blood pressure, heart rate, respiration rate, temperature assessed before and 15 minutes after study treatment administered at clinic

[36] Hemoglobin, Hematocrit (HCT), Red Blood Cells (RBC), White Blood Cells (WBC) with total and differential count, Absolute Neutrophil Count (ANC) and platelets.

[37] Serum Biochemistry:

Hepatic function indicators: total and direct bilirubin, alkaline phosphatase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein, lactate dehydrogenase (LDH)

Renal function indicators: BUN, creatinine

Electrolytes: sodium, potassium, chloride, calcium and bicarbonate

Other: glucose (random), cholesterol (total)

[38] Sample may be collected on ad hoc basis, as per discretion of Sponsor/Investigator during the Treatment Phase

[39] ONLY for subjects trained to perform self-administration of study treatment on weeks when clinic visit optional, i.e., no lab samples are required

[40] Study treatment for self-administration will be provided to subjects during treatment visits at clinic; used vials from prior self-administration must be collected and accounted for (see Section 4.2.2).

[41] Study treatment should be administered at clinic.

[42] All study subjects will re-initiate their previous antiretroviral regimen: (1) One week prior to the end of 61109-week Treatment Extension Phase, or (2) Anytime during the Treatment Extension Phase, if virologic failure occurs or have met any other criteria for discontinuation of study treatment as specified in the protocol.

[43] As assessed by Investigator when study treatment administered at the clinic.

[44] Subject-perceived injection site pain (average pain since last treatment) will be assessed using the Pain Visual Analog Scale (VAS) prior to each study treatment administration for subjects randomized to PRO 140.

TABLE 1: SCHEDULE OF ASSESSMENTS – SCREENING AND TREATMENT EXTENSION PHASE (8 OF 8)

Procedure/Assessments	Subsequent Weekly TE Visits (TE160 onwards)	Treatment Extension Visit	In case of Virologic Failure
Visit[32]		EOT	VF
Window Period	±3 days since last treatment		
Symptom-directed physical examination	X[32]	X	
Physical Examination			X
Neurological Assessment[34]	X[32]	X	X
Vital Signs[35]	X[32]	X	X
Complete Blood Count (CBC)[36]	X[45]	X	X
Biochemistry[37]	X[45]	X	X
Plasma HIV-1 RNA level	X[32]	X	X
TruCount T assay	X[32]	X	X
PK sample for PRO 140	X[32]	X	X
Serum concentration for ART drugs[38]	X[32]	X	
Anti-idiotypic antibodies to PRO 140	X[32]	X	X
HIV Genotyping Assay			X
Trofile® DNA/RNA and PhenoSense Entry Assay		X	X
Blood sample collection for Exploratory/Confirmatory analysis[38]		X	X
PRO 140 Administration	X[39]	X[40]	
Subject drug dispensing/accountability[41]	X	X	
Antiretroviral Regimen[42]		X	X
Injection Site Reaction Assessment[43]	X[32]	X	
Injection Site Pain Assessment (VAS)[44]	X[32]	X	

Procedure/Assessments	**Subsequent Weekly TE Visits (TE160 onwards)**	**Treatment Extension Visit**	**In case of Virologic Failure**
Visit[32]		**EOT**	**VF**
Window Period	±3 days since last treatment		
Adverse Events[33]	X	X	X
Concomitant Medications	X	X	X

[32] In-clinic assessment(s) should be performed at least once every 4 weeks from TE108-TE159.

[33] Subjects should be instructed to report any new AEs that occur between clinic visits to site promptly

[34] Performed by Principal Investigator (or designee) when subject comes to clinic. NOTE: The neurological assessment tool is based on the three question survey used by Simioni et al. (Simioni S, 2010). Additional neurological assessment modalities may be used as per Investigator's discretion.

[35] Blood pressure, heart rate, respiration rate, temperature assessed before and 15 minutes after study treatment administered at clinic

[36] Hemoglobin, Hematocrit (HCT), Red Blood Cells (RBC), White Blood Cells (WBC) with total and differential count, Absolute Neutrophil Count (ANC) and platelets.

[37] Serum Biochemistry:

Hepatic function indicators: total and direct bilirubin, alkaline phosphatase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein, lactate dehydrogenase (LDH)

Renal function indicators: BUN, creatinine

Electrolytes: sodium, potassium, chloride, calcium and bicarbonate

Other: glucose (random), cholesterol (total)

[38] Sample may be collected on ad hoc basis, as per discretion of Sponsor/Investigator during the Treatment Phase

[39] ONLY for subjects trained to perform self-administration of study treatment on weeks when clinic visit optional, i.e., no lab samples are required

[40] Study treatment for self-administration will be provided to subjects during treatment visits at clinic; used vials from prior self-administration must be collected and accounted for (see Section 4.2.2).

[41] Study treatment should be administered at clinic.

[42] All study subjects will re-initiate their previous antiretroviral regimen: (1) One week prior to the end of 61109-week Treatment Extension Phase, or (2) Anytime during the Treatment Extension Phase, if virologic failure occurs or have met any other criteria for discontinuation of study treatment as specified in the protocol.

[43] As assessed by Investigator when study treatment administered at the clinic.

[44] Subject-perceived injection site pain (average pain since last treatment) will be assessed using the Pain Visual Analog Scale (VAS) prior to each study treatment administration for subjects randomized to PRO 140.

[45] Should be performed at least once every 12 weeks from TE160 onwards.

TABLE 2: SCHEDULE OF ASSESSMENTS – FOLLOW-UP PHASE

(a) Subjects who do NOT experience virologic failure

Procedure/Assessments	Follow-Up Visit -1	Follow-Up Visit -2
	NVF-EFU1	NVF-EFU2
Window Period	2 weeks (±3 days) after TE161	4 weeks (±3 days) after TE161
Physical Examination	X[1]	X[1]
Vital Signs	X	X
Plasma HIV-1 RNA level	X	X
TruCount T assay	X	X
Previously used Antiretroviral Regimen	X	X
Adverse Events	X	X
Concomitant Medications	X	X
Anti-idiotypic Antibodies to PRO 140		X

[1] Symptom-directed physical examination

(b) Subjects who experience virologic failure

- Short term follow up visits

Procedure/Assessments	Follow-Up Visit -1	Follow-Up Visit -2	Follow-Up Visit -3[1]
	VF-EFU1	VF-EFU2	VF-EFU3
Window Period	4 weeks (±7 days) after VF	8 weeks (±7 days) after VF	12 weeks (±7 days) after VF
Physical Examination	X[2]	X[2]	X[2]
Vital Signs	X	X	X
Plasma HIV-1 RNA level	X	X	X
TruCount T assay	X	X	X
Previously used Antiretroviral Regimen	X	X	X
Adverse Events	X	X	X
Concomitant Medications	X	X	X
Anti-idiotypic Antibodies to PRO 140	X		

[1] Subject will be followed up every 4 weeks until viral suppression is achieved (i.e., plasma HIV-1 RNA levels to return back to <50 copies/mL). Subject will undergo additional follow-up visits every 4 weeks beyond VF-EFU3 visit, if viral suppression is not achieved at the end of VF-EFU3 visit.

[2] Symptom-directed physical examination

(c) Subjects who experience virologic failure

- Long term follow up visits

Procedure/Assessments	Long-Term Follow-Up Visit -1	Long-Term Follow-Up Visit -2
	VF-12mFU	**VF-24mFU**
Window Period	**12 months (±1 month)** after VF visit	**24 months (±1 month)** after VF visit
Assessment of cART changes[1]	X	X
Plasma HIV-1 RNA level	X	X
TruCount T assay	X	X
Trofile® DNA or RNA Assay[3]	X*	X*
PhenoSense® Entry Assay[4]	X*	X*
HIV-1 Drug Resistance Assay[5]	X*	X*

[1] Any changes to the combination antiretroviral regimen since the viral re-suppression is achieved.

[2] Monogram Biosciences Trofile® DNA or RNA (or both) assay will be performed depending on last known HIV-1 RNA levels.

[3] Monogram Biosciences HIV-1 PhenoSense® Entry assay with AMD3100 (X4 inhibitor drug), Maraviroc and PRO 140 (R5 inhibitor drugs).

[4] Monogram Biosciences GenoSure Archive Assay or PhenoSense® GT (and PhenoSense Integrase and GeneSeq Integrase testing, if applicable), will be performed depending on last known HIV-RNA levels.

*As per discretion if the investigator

9. APPENDIX 2 – PLANNED TLG

9.1 Planned by-subject listings

DISPOSITION/WITHDRAWALS

ELIGIBILTY AND PROTOCOL DEVIATIONS

EXCLUDED SUBJECTS

DEMOGRAPHICS, POPULATION, AND BASELINE CHARACTERISTICS

TREATMENT ADMINISTRATION LISTINGS

EFFICACY RESPONSE DATA

ADVERSE EVENT DATA

SAFETY DATA

9.2 Planned Summary Tables

POPULATION DISPOSITION AND PROTOCOL DEVIATIONS

POPULATION DEMOGRAPHICS AND BASELINE CHARACTERISTICS

CONCOMITANT MEDICATION USAGE

EFFICACY SUMMARIES

SAFETY SUMMARIES

- ADVERSE EVENT SUMMARIES
- SERIOUS ADVERSE EVENTS
- LABORATORY
- VITAL SIGNS AND PE
- OTHER SAFETY

10. VERSION HISTORY

This is the first version of the document.

11. REFERENCES

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2. The Royal Statistical Society: Code of Conduct (2014).
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4. E9(R1) Statistical Principles for Clinical Trials, ICH Guideline, Federal Register, 2017
5. Guideline for the Format and Content of the Clinical and Statistical Section of an Application, 1988.
6. Guideline for Industry: Structure and Content of Clinical Study Reports (ICH E3(R1)), July 2013.