NCT number NCT03018730

Statistical Analysis Plan

Protocol: PB-102-F30

An Open Label Study of the Safety and Efficacy of Pegunigalsidase alfa (aka PRX-102) in Patients with Fabry Disease Currently Treated With REPLAGAL® (Agalsidase alfa)

Protalix Ltd.
2 Snunit Street, Science Park
Carmiel 20100, Israel

Version and Date of the final Protocol:
Version 03, June 6, 2017

Prepared by: [redacted]

Table of Contents

1. ABBREVIATIONS 4
2. INTRODUCTION 6
3. OBJECTIVES AND ENDPOINTS 6
3.1. Objectives 6
3.2. Endpoints 6
3.2.1. Safety Endpoints 6
3.2.2. Efficacy Endpoints 7
4. STUDY DESIGN 7
4.1. Sample Size and Statistical Power Consideration 8
4.2. Study Flow Chart 9
5. ANALYSIS POPULATION 11
5.1. Safety Population 11
5.2. Efficacy Population 11
5.3. Per Protocol Efficacy Population 11
6. TREATMENT DESCRIPTIONS 11
7. STATISTICAL ANALYSIS METHODS AND ISSUES 11
7.1. Statistical Methods 11
7.2. Missing Data 12
7.3. Baseline Definition 12
7.4. Subgroup Analysis 12
7.5. Interim Analysis 13
8. DEMOGRAPHICS AND STUDY SUMMARY 13
8.1. Subject Disposition 13
8.2. Demographics 13
8.3. Baseline Characteristics 14
8.4. Fabry Disease Medical History 15
8.5. Other Medical History 15
8.6. Treatment Compliance 15
8.7. Overall Exposure to Study Treatment 15
8.8. Infusions 15
9. ANALYSIS OF SAFETY ENDPOINTS 16
9.1. Adverse Events 16
9.1.1. Definitions 16
9.1.2. Pre-Treatment Adverse Events 16
9.1.3. Treatment-Emergent Adverse Events (TEAE) 16
9.1.4. Time-categories of TEAE 18
9.1.5. Infusion Related Reactions (IRR) 20
9.2. Clinical Laboratory Test Results 21
9.3. Physical Examination 22
9.4. Electrocardiography (ECG) 22
9.5. Infusion Premedication 23
9.6. Treatment-emergent Anti-Pegunigalsidase alfa Antibodies 23
9.7. Vital Signs 24

9.8. Concomitant Medication 24
9.9. X-Ray 25
9.10. Pregnancies 25
10. ANALYSIS OF EFFICACY ENDPOINTS 25
10.1. Estimated Glomerular Filtration Rate (eGFRCKD-EPI) 25
10.1.1. eGFR Estimation 25
10.1.2. Annualized Change in eGFR (Slope) 26
10.1.3. eGFR and eGFR Slope Analysis 26
10.1.4. Analysis of Therapeutic Goals 27
10.2. Cardiac MRI 28
10.3. Plasma Gb3 / Lyso-Gb3 and Urine Lyso-Gb3 Concentrations 28
10.4. Urine Protein/Creatinine Ratio (UPCR) 29
10.5. Echocardiogram Report 29
10.6. Stress Test 29
10.7. Short Form Brief Pain Inventory (BPI) 30
10.8. Mainz Severity Score Index (MSSI) 30
10.9. Quality of Life EQ-5D-5L 31
10.10. Use of Pain Medications 31
10.11. Fabry Clinical Events 31
11. LIST OF TABLES, FIGURES AND DATA LISTINGS 33
11.1. Statistical Tables 33
11.2. Figures 39
11.3. Data Listings 40
12. TABLE SHELLS 41

1. ABBREVIATIONS

AE	Adverse Event
ACEi	Angiotensin-Converting Enzyme Inhibitor
ADA	Anti-Drug Antibodies
ARB	Angiotensin Receptor Blocker
BLA	Biologics License Application
BPI	Brief Pain Inventory
CKD	Chronic Kidney Disease
CRF	Case Report Form
CSR	Clinical Study Report
ECG	Electrocardiography
EDC	Electronic Data Capture
eGFR	Estimated Glomerular Filtration Rate
EP	Efficacy Population
FCE	Fabry Clinical Events
FD	Fabry Disease
Gb3	Globotriaosylceramide
HBsAg	Hepatitis B Surface Antigen
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
IRR	Infusion Related Reaction
IV	Intravenous
IRR	Infusion Related Reactions
KD	Kidney Disease
LVH	Left Ventricular Hypertrophy
LVM	Left Ventricular Mass
LVMI	Left Ventricular Mass Index
Lyso-Gb3	Globotriaosylsphingosine
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic Resonance Imaging
MSSI	Mainz Severity Score Index
NTF	Note to File
NSR	Normal Sinus Rhythm
PPEP	Per Protocol Efficacy Population
PT	Preferred Term
PrT	Prothrombin Time

PTT	Partial Thromboplastin Time
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SDTM	Study Data Tabulation Model
SOC	System Organ Class
SP	Safety Population
TEAE	Treatment-emergent adverse event
UPCR	Urine Protein to Creatinine Ratio
WHO	World Health Organization

2. INTRODUCTION

The statistical analysis plan (SAP) contains the analysis information in detail on the definition of the analysis populations, derivation of variables, convention of analysis scope, and statistical methodology for the analyses of safety and efficacy parameters of pegunigalsidase alfa (formerly known as PRX-102) administered by intravenous infusion based on the data collected per the protocol PB-102-F30, a phase 3 study sponsored by Protalix, Ltd. In case of disagreement between the SAP and the Clinical Study Protocol, the SAP prevails.

Any deviations from this SAP during the actual data analysis will be documented properly in a change request or a note-to-file document, as well as in the final Clinical Study Report (CSR).

3. OBJECTIVES AND ENDPOINTS

3.1. Objectives

The primary objective of this trial is to evaluate the safety of pegunigalsidase alfa in patients with Fabry disease currently treated with agalsidase alfa (Replagal®).
The secondary objective of this trial is to evaluate the efficacy of pegunigalsidase alfa in patients with Fabry disease currently treated with agalsidase alfa (Replagal®).

3.2. Endpoints

3.2.1. Safety Endpoints

- Change from baseline in:
  - Clinical laboratory tests
  - Physical examination
  - Electrocardiogram
- Treatment-emergent adverse events
- Assessment of the injection site and infusion-related reactions (IRR), as part of the adverse events
- Ability to taper off infusion premedication after switch to pegunigalsidase alfa
- Requirement for use of premedication overall to manage infusion reactions
- Treatment-emergent anti-pegunigalsidase alfa antibodies

3.2.2. Efficacy Endpoints

- Change in estimated glomerular filtration rate ($eGFR_{CKD-EPI}$)
- Left Ventricular Mass Index (g/m^2) by MRI
- Plasma Globotriaosylsphingosine (Lyso-Gb3)
- Plasma Globotriaosylceramide (Gb3)
- Urine Globotriaosylsphingosine (Lyso-Gb3)
- Protein to creatinine ratio (UPCR) spot urine test
- Frequency of pain medication use
- Exercise tolerance (Stress Test)
- Short Form Brief Pain Inventory (BPI)
- Mainz Severity Score Index (MSSI)
- Quality of life EQ-5D-5L
- Fabry Clinical Events (FCE)

4. STUDY DESIGN

This is an open label switch over study to assess the safety and efficacy of pegunigalsidase alfa in patients treated with agalsidase alfa (Replagal®) for at least 2 years and on a stable dose (>80% labelled dose/kg) for at least the last 6 months. Patients will be screened and evaluated over 3 months while continuing on agalsidase alfa. Following the screening period, patients will be enrolled and switched from their agalsidase alfa treatment to receive intravenous (IV) infusions of pegunigalsidase alfa 1 mg/kg every two weeks for 12 months. No more than 25% of treated patients will be female.

At the time of enrollment, premedication, if used for the agalsidase alfa infusions before enrollment, will be continued through the first infusion with pegunigalsidase alfa and then gradually tapered at the Investigator's discretion during the first 2 months of treatment. The first infusions of pegunigalsidase alfa will be administered under controlled conditions at the investigation site. The patient can receive pegunigalsidase alfa infusions in a home care setting once the Investigator and Sponsor Medical Director agree that it is safe to do so.

4.1. Sample Size and Statistical Power Consideration

No formal sample size calculation has been performed for this study.

The sample size of 22 patients is adequate to evaluate the safety of switching from agalsidase alfa to pegunigalsidase alfa in this orphan disease in which patient recruitment in clinical trials is difficult.

4.2. Study Flow Chart:

Activity	Screening Period		Visits Treatment Period Pegunigalsidase alfa						
	Screening Visit (-3 Month)	Visit A (-2 Month) and B (-1 Month)	Visit 1	Visits 2, 4, 6, 8, 10, 12, 13, 15, 17, 19, 21, 23, 25, 26	Visits 3, 5, 9, 11	Visits 7, 20 (Months 3 and 9)	Visit 14 (Month 6)	Visits 16, 18, 22, 24	Visit 27 (Month 12)
Sign IC	x								
Assign screening number	x								
Medical history	x								
Demographics	x								
Alpha-galactosidase activity in plasma and leucocytes	x								
Historical serum creatinine	x								
Vital signs (blood pressure, pulse, temperature and respiration)	x		x	x	x	x	x	x	x
Body weight	x		x			x	x		x
Body height	x								
Physical examination	x		x			x	x		x
Concomitant medications (including pain and premedications)	x	x	x	x	x	x	x	x	x
Hematology	x		x			x	x		x
Biochemistry	x		x			x	x		x
Serum Creatinine and Cystatin C	x	x	x		x	x	x	x	x
Urinalysis – dipstick	x		x			x	x		x
Protein/Creatinine ratio spot urine test	x	x	x			x	x		x
HbsAg, HCV & HIV	x								
Serum pregnancy test (beta HCG)	x		x						
Urine Lyso Gb3 concentration	x		x			x	x		x
Plasma Lyso Gb3	x		x			x	x		x
Plasma Gb3	x		x			x	x		x

Activity	Screening Period		Visits Treatment Period Pegunigalsidase alfa						
	Screening Visit (-3 Month)	Visit A (-2 Month) and B (-1 Month)	Visit 1	Visits 2, 4, 6, 8, 10, 12, 13, 15, 17, 19, 21, 23, 25, 26	Visits 3, 5, 9, 11	Visits 7, 20 (Months 3 and 9)	Visit 14 (Month 6)	Visits 16, 18, 22, 24	Visit 27 (Month 12)
Anti-pegunigalsidase alfa Antibodies (IgG)			x		x	x	x		x
Electrocardiography (ECG)	x		x			x	x		x
Chest X-ray	x								
Cardiac function assessment (echocardiography and stress test)	x		x				x		x
Cardiac MRI			x				x		x
Inclusion/exclusion criteria	x								
Request for subject approval	x								
Enrollment approval		x[1]							
Mutation analysis			X						
PrT, PTT	X								
C3, C4	x								
Vit D	x								
Short Form Brief Pain Inventory (BPI)			x			x	x		x
Brain MRI			x						x
Mainz Severity Score Index (MSSI)			x				x		x
EQ-ED-5L			x				x		x
Pegunigalsidase alfa infusion + clinical observation			x	x	x	x	x	x	x
Adverse event assessments		x	x	x	x	x	x	x	x

1 After Visit B

5. ANALYSIS POPULATION

5.1. Safety Population

The safety population (SP) consists of all subjects who received any dose of pegunigalsidase alfa in the study. All safety analyses will be based on this population.

5.2. Efficacy Population

The efficacy population (EP) consists of all subjects who have at least one visit with an efficacy evaluation after the first pegunigalsidase alfa infusion. All efficacy analyses will be based on this population.

5.3. Per Protocol Efficacy Population

The per protocol efficacy population (PPEP) consists of all subjects who completed the 12-month treatment period with efficacy data available and with no major protocol violations. The major protocol violations will be confirmed at the clean file meeting and prior to database lock of the final analysis. All efficacy analyses will be performed on this population as well for sensitivity purposes. In case that the Per Protocol and the Efficacy population are identical then the Per Protocol output will not be generated.

6. TREATMENT DESCRIPTIONS

Unless otherwise indicated, on the summary tables, the treatment will be identified by pegunigalsidase alfa, where applicable.

7. STATISTICAL ANALYSIS METHODS AND ISSUES

7.1. Statistical Methods

Descriptive statistics, namely sample size (n), mean and its standard error, standard deviation, median, minimum and maximum for continuous variables, and count and percentage for categorical variables, will be provided.

Statistical comparison of the efficacy endpoints, the estimated slopes of eGFR, between pre and post treatment of pegunigalsidase alfa will be performed using parametric and/or non-parametric approaches and are to be described in detail in Section 10 of this document.

7.2. Missing Data

Incomplete dates of start treatment of Fabry disease, will be imputed as follows:

- The middle of month (i.e. 15) will be imputed, if only day is missing,
- The middle of year (i.e. July 1) will be imputed if both month and day are missing.
- No imputation will be done in case the year is missing.

Imputations of missing data associated with adverse events (AE) will be specified in Section 9.1.

No other imputation will be made for missing values of safety or efficacy endpoints.

7.3. Baseline Definition

The baseline for this study is defined as the assessment made at Visit 1 prior to the first infusion of pegunigalsidase alfa. If not available, the last assessment before receiving the first treatment of pegunigalsidase alfa will be used as baseline.

7.4. Subgroup Analysis

When the following demographic and baseline characteristics are available, the subgroup analyses will be performed for safety and efficacy endpoints as specified in this plan.

1. Male vs. Female,
2. Treatment emergent Anti-Drug Antibodies (ADA) status (ADA positive vs. ADA negative):

   Treatment emergent ADA positive are patients with either:

   (1) Titer boosted: patients who were IgG positive to pegunigalsidase alfa at baseline and boosted post treatment (i.e., titer increase by at least 4-fold from baseline. See Shankar et al. 2014), or

   (2) Treatment induced: patients who were IgG negative to pegunigalsidase alfa at baseline and positive at any timepoint post treatment.

3. Baseline Fabry disease (FD) classification (classic / non-classic):

   For this analysis, FD Classic is defined as ≤ 5% mean of lab normal ranges

residual enzymatic activity in plasma or leukocytes (baseline) and at least one Fabry specific symptoms (baseline): Cornea Verticillata, Acroparesthesias, and/or Angiokeratomas.

In addition, the eGFR slopes analysis will also be analyzed according to other subgroups specified in Section 10.1.3.

7.5. Interim Analysis

An interim analysis was performed when approximately 80% of the patients completed or discontinued the study to support the Biologics License Application (BLA). The analyses were conducted based on SAP dated 24 June 2019. Additional clarification to the SAP and new analyses were described in Notes to Files (NTF). Additional analyses conducted at the interim analysis were not pre-specified. The CSR dated 6 March 2020 is based on the interim analysis provided details on the changes from the SAP and the analyses that were not pre-defined.

For the final analyses, the Sponsor plans to repeat the analyses performed in the CSR and conduct some new analyses. This SAP described all of these planned analyses. The new analyses will not have an impact on study interpretation.

8. DEMOGRAPHICS AND STUDY SUMMARY

8.1. Subject Disposition

The number and percentage of subjects who were screened, enrolled, treated, completed, and discontinued will be summarized. The documented reasons for screen failures will be tabulated. The number and percentage of subjects who discontinued will also be summarized for each reason of discontinuation, and their last completed scheduled visits. The number of subjects in each of the analysis population (Safety, efficacy and Per-Protocol) will be presented.

8.2. Demographics

The demographics (age, gender, race, and ethnicity) will be summarized using descriptive statistics by gender and overall. The analysis will be repeated for the Safety and Efficacy sets.

8.3. Baseline Characteristics

The baseline characteristics will be summarized by descriptive statistics overall and by each of the subgroups described in section 7.4. The analysis will be repeated for the Safety and Efficacy sets.

Continuous variables:

- Age started Fabry therapy
- % residual enzyme activity in leukocyte (defined as the value in leukocyte × 100/83.5, where 83.5 is the mean of reference range)
- % residual enzyme activity in plasma (defined as the value in plasma ×100/12.95, where 12.95 is the mean of reference range)
- eGFR
- pre-switch eGFR annualized slope
- Plasma Lyso-Gb3
- Plasma Gb3
- Urine Lyso Gb3

Categorical variables:

- Fabry disease (FD) classification (classic / non-classic) (See Section 7.4)
- UPCR classified into four categories (See Section 10.4)
- Presence of Proteinuria (UPCR ≥ 0.5 gr/gr / < 0.5 gr/gr)
- Treatment with ACEi or ARBs (yes/no). Status is yes if there is any concomitant medication of ACE or ARB taken before baseline visit, otherwise it will be determined based on the answer to the question 'patient is NOT treated with an ACE inhibitor or ARB'.
- Premedication use (yes / no: premedication used for agalsidase alfa infusions before enrolment)
- anti Replagal Immunogenicity status (ADA-positive or ADA- negative to agalsidase alfa (REPLAGAL). The determination of the status is based on the results of the IgG Screening for REPLAGAL.
- anti pegunigalsidase alfa Immunogenicity status (ADA-positive or ADA- negative to pegunigalsidase alfa. The determination of the status is based on the results of the IgG Screening for PRX-102.

8.4. Fabry Disease Medical History

The data collected on the three CRFs, Fabry Disease Medical History, Fabry Disease Diagnosis, and Fabry Disease Past Treatment, will be listed in a single listing.

Fabry Disease Medical history data by body system and conditions as collected on the CRF form will be tabulated. Number of patients with confirmed condition (answered Yes to the condition in specific) and the percentage based on the total number of patients in consideration will be presented, for overall and by gender.

The analysis will be repeated for the Safety and Efficacy sets.

8.5. Other Medical History

Other medical history will be listed and summarized by descriptive statistics by gender and overall. The analysis will be repeated for the Safety and Efficacy sets.

8.6. Treatment Compliance

Treatment compliance will be assessed by dividing the actual number of bi-weekly infusions, including partial infusion, over the expected number of infusions during the study in 52 weeks.

The compliance will be listed and tabulated for overall and by gender using descriptive statistics for the Safety and Efficacy sets.

8.7. Overall Exposure to Study Treatment

The overall exposure duration (in person-month) and the exposure duration by gender, in person- month will be summarized.

8.8. Infusions

The infusion duration (hours) by visit will be summarized by descriptive statistics by overall.

The number of infusions (partial or full) that a patient received will be summarized by descriptive statistics overall.

Listing of infusion should include whether the infusion was interrupted or not and whether

the complete dose was administered or not (based on data collected at the Drug Administration CRF page).

The analyses will be repeated for the Safety and Efficacy sets.

9. ANALYSIS OF SAFETY ENDPOINTS

Safety analysis will be conducted on the safety analysis set.

9.1. Adverse Events

Adverse events will be coded by the Medical Dictionary for Drug Regulatory Activities (MedDRA) version 15.0 or higher.

9.1.1. Definitions

Pre-treatment AEs include all adverse events collected during the screening and the adverse events occurred before the first pegunigalsidase alfa infusion.

Treatment-emergent adverse event (TEAE) is any AE occurring after the start of the first infusion of pegunigalsidase alfa. In case that date of onset is unknown, the AE will be classified as TEAE and not as pre-treatment AE.

9.1.2. Pre-Treatment Adverse Events

A table will be presented for the frequency of the pre-treatment adverse events by the MedDRA system organ class and preferred term for overall and by gender.

9.1.3. Treatment-Emergent Adverse Events (TEAE)

Number and percent of patients with at least one TEAE as well as the number of TEAE in the following categories will be summarized overall and by the subgroups presented in Section 7.4:

- Any TEAE
- Treatment non-related (unlikely, not-related) TEAE
- Treatment related (defined as possibly, probably or definitely related) TEAE
- Mild or moderate TEAE
- Treatment related mild or moderate TEAE
- Severe TEAE

- Treatment related severe TEAE
- Serious TEAEs
- Treatment related serious TEAE
- TEAE leading to withdrawal
- Treatment related TEAE leading to withdrawal
- TEAE leading to death
- Treatment related TEAE related to death.

These tables above will be repeated for the number and percentage of patients with at least one injection site reaction TEAE.

Summary tables will be presented for the frequency of any TEAEs by the MedDRA SOC and PT by overall and by the subgroups presented in Section 7.4; by the MedDRA SOC and PT and severity of TEAE; by MedDRA SOC and PT, and the relationship of TEAEs to study drug.

Summary tables will be presented for the frequency of serious TEAEs by the MedDRA SOC and PT for overall and by gender and by the MedDRA SOC and PT and relationship to study drug.

In the summaries of severity and relationship to study drug, the most extreme outcome (highest severity and closest relationship to study drug) will be used for those subjects who experience the same TEAE (per preferred term) on more than one occasion.

Missing values associated with TEAEs will be treated as missing except for causality, intensity, and outcome of a TEAE, at which occurrence a "worst case" approach will be taken in the analysis. Thus

- If causality is missing, the TEAE will be regarded as related to pegunigalsidase alfa
- If the intensity is missing, the intensity of the AE will be regarded as severe
- If the outcome is missing and the stop date is not provided, the outcome is regarded as "ongoing".
- If the seriousness is missing, all efforts should be made prior to database lock to make sure that this information is available, if still missing, the worst-case scenario is assumed.

If there were any TEAEs leading to withdrawal or death, these cases will be presented by patient.

Listing of TEAE will include also the TEAE onset and end date and also relative to first pegunigalsidase alfa infusion.

9.1.4. Time-categories of TEAE

TEAE will be classified by time of occurrence in relationship to the infusion into one of the following 3 categories:

- Occurring during the infusion or within 2 hours after the completion of the infusion
- Occurring between 2 hours after the completion of the infusion and 24 hours after the completion of the infusion
- Occurring at least 24 hours after the completion of the infusion

A summary of TEAE (number and percentage of subjects with TEAE and number of TEAEs) by the MedDRA SOC and PT and by the three time-categories will be presented

The following rules, including imputation convention when there is missing date/time of TEAE onset and/or infusion, will be applied:

Category #1. TEAE occurring during the infusion or within 2 hours after the completion of infusion.

A TEAE will be classified into this category if date and time are available for both the TEAE and the last infusion and the TEAE onset during the infusion or the time from the stop of infusion to time of TEAE onset < 2 hours.

Category #2. TEAE occurring between 2 hours and 24 hours after the completion of infusion.

A TEAE will be classified into this category if

(1) date and time available for both TEAE and the last infusion and the time from the stop of infusion to time of TEAE onset ≥ 2 hours but < 24 hours, or

(2) the time of TEAE onset is not available, but the date of TEAE onset is the same day of the last infusion.

Category #3. TEAE occurring at least 24 hours after the completion of infusion.

A TEAE will be classified into this category if

(1) the date and time available for both TEAE and the last infusion and the time from the stop of infusion to time of TEAE onset ≥ 24 hours, or

(2) the time of TEAE onset is not available, but the onset date is after the date of last infusion, or

(3) TEAE onset date is incomplete, or

(4) the date and time of last infusion cannot be determined.

Per the Drug Administration CRF, there are three options: (1). "During the infusion", (2). "Within 2 hours after the infusion", and (3). "Up to 24 hours after the infusion" to be selected if the answer is Yes to the question "Did the patient experience an Adverse Event

during or after the infusion?". The specific adverse event and a date and/or time (not specified, but in the context, the date/time should be the onset date/time of the adverse event) were collected in a text field.

The information will be used to derive the variables necessary to associate with the adverse events entered in the Adverse Events CRF. The record with a selection of the three options but without specific adverse event or date of onset, or vice versa, will not be considered in determination of the time category.

For those adverse events reported on the Drug Administration CRF, matched by the original term of adverse event and onset date/time on the Adverse Events CRF, the time category will be assigned as follows, which overrides the category assigned by the above rules.

Category #1. TEAE occurring during the infusion or within 2 hours after the completion of infusion.

The TEAE will be classified into this category if the selection of the three options is either (1). During the infusion, or (2). Within 2 hours after the infusion.

Category #2. TEAE occurring between 2 hours and 24 hours after the completion of infusion.

The TEAE will be classified into this category if the selection of the three options is (3). Up to 24 hours after the infusion.

Category #3. TEAE occurring at least 24 hours after the completion of infusion.

Not applicable.

9.1.5. Infusion Related Reactions (IRR)

The IRRs are those treatment emergent adverse events (TEAE) which occurred during the infusion or within 2 hours after the completion of the infusion and the causality of the adverse events are determined to be definitely, probably, or possibly related, based on the the site reports in the eCRF.

Injection site reactions which are not considered IRR are excluded from the summary of IRRs, and will be identified based on their SOC and PT, as listed in the following table:

MedDRA SOC	MedDRA Preferred Term
General disorders and administration site conditions	Infusion site discomfort
	Injection site discomfort
	Infusion site pain
	Injection site pain
	Infusion site hematoma
	Injection site hematoma
Injury poisoning and procedural complications	Contusion
	Procedural site reaction
	Procedural pain
Vascular disorders	Vein rupture

The number and percentage of IRRs in the following categories will be summarized for overall, and by gender, FD Classification, and Treatment Emergent pegunigalsidase alfa ADA. The percentage will be based on the total number of IRRs of the population or subset. In addition, the number and percentage of IRR will be summarized by administration location (Home/Site). The summary will include the

following categories:

- Overall number of IRR (used to calculate the percentage),
- Mild or Moderate IRR,
- Severe IRRs,
- Very Severe IRRs,
- Serious IRR.
- IRR that lead to study discontinuation
- IRR that lead to death

Number and percentage of patients with IRRs by MedDRA SOC and PT will be summarized for overall, and by gender, FD Classification, and Treatment Emergent ADA. The number and percentage of patients with IRRs by MedDRA SOC and PT and severity will be summarized for overall.

Number of IRRs by MedDRA SOC and PT will be summarized for overall, and by gender, FD Classification, and Treatment Emergent pegunigalsidase alfa ADA. The number of IRRs by MedDRA SOC and PT and severity will be summarized as well for overall.

9.2. Clinical Laboratory Test Results

The laboratory test results will be summarized, for overall and by gender, by descriptive statistics at the scheduled visits, including the change from baseline and percent change from baseline for continuous results. For the continuous test results being classified into the three categories (low, normal, high) according to the normal ranges, the shift table from baseline to each post-baseline visit will be presented as well. When available, all the test results in the following table will be summarized.

Hematology:	**Biochemistry:**
Hemoglobin	Alanine transaminase
Platelets	Albumin
Total white blood cell count	Alkaline phosphatase
	Aspartate transaminase
Coagulation Profile:	Bilirubin (total)
Partial thromboplastin time (PTT)	Blood urea nitrogen
Prothrombin time (PrT)	Calcium

	Creatinine
Vitamin D	Creatine phosphokinase
	Cystatin c
Urinalysis:	Gamma-glutamyl transferase
Dipstick for presence of Blood	Glucose
Dipstick for presence of Glucose	Lactate dehydrogenase
Dipstick for presence of Ketones	Phosphate (inorganic)
Dipstick for presence of Protein	Potassium
	Sodium
	Total protein
	Uric acid

Note to programmers:

- Values in urinalysis (e.g. protein), spot urine test (protein to creatinine ratio UPCR), and chemistry (e.g. bilirubin) started with a '<' sign will be excluded from the analysis, but will be presented in listings with the '<' sign.
- Serum creatinine can be recorded in two units, µmol/L and mg/dL. In calculation of eGFR or summary of creatinine, the value in µmol/L needs to be converted to mg/dL using the following conversion formula: 1 mg/dL = 88.4 µmol/L.
- Serum creatinine can be entered in two fields in the SDTM (CHEMISTRY and ENZYMATE). When the results from same sample is entered at both fields, then the value is identical. In such cases, only one of them will be taken in the analysis.

9.3. Physical Examination

The physical examination results (normal / abnormal / not done) will be summarized by body system. Shift table by body system from baseline to each post-baseline visit will be presented as well. The tables will be presented for overall and by gender.

9.4. Electrocardiography (ECG)

Descriptive statistics of ECG parameters (quantitative) and assessments (qualitative) will be summarized for overall and by gender. The change and percent change from baseline will be summarized as well for ECG quantitative parameters. The shift from baseline will be presented for ECG qualitative assessments.

ECG parameters (quantitative)	ECG assessments (qualitative)
Mean Heart Rate	Rhythm – Normal Sinus Rhythm (NSR)
PR Interval, Aggregate	Conduction abnormalities
QRS Duration, Aggregate	Left ventricular hypertrophy
QT Interval, Aggregate	Supraventricular tachycardia
	Premature atrial contraction
	Atrial flutter
	Atrial fibrillation
	Premature ventricular contraction
	Ventricular tachycardia
	Any clinically abnormal findings (i.e. any abnormal condition as listed above)

9.5. Infusion Premedication

Premedication administered before infusion or during infusion or not used (collected in Drug Administration CRF) will be tabulated in a data listing to present longitudinally for all scheduled visits (every two weeks).

The number of patients with or without premedication use will be summarized by visit for overall and by gender.

Note to programmer: this analysis is based on data captured in the CM dataset where CMSCAT = 'Premedication'.

9.6. Treatment-emergent Anti-Pegunigalsidase alfa Antibodies

Treatment emergent anti-pegunigalsidase alfa antibodies (ADA+ vs. ADA-) is defined in Section 7.4.

The number and percentage of patients who are Treatment emergent ADA will be summarized by visit

An overall anti-pegunigalsidase alfa antibodies status per patient during the study ("positive" if positive at any visit, negative if negative at all visits), will be summarized as well.

Analyses will be repeated by gender and by Fabry disease classification (classic/non-classic).

Note to programmer: The treatment-emergent anti-pegunigalsidase alfa antibodies (ADA) including the three test results:

a. IgG = negative if 'IgG Screening (Presumptive Pos/Neg)'(LBTEST) for LBSCAT = for PRX-102 is Negative; otherwise the status will be determined based on the result of 'IgG Immunodepletion (Pos/Neg)': Positive or Negative,
b. Neutralizing Antibody = the result of 'Neutralizing Antibody (Pos/Neg)' (LBTEST): Positive or Negative,
c. IgE = the result of 'IgE Screening (Presumptive Pos/Neg)' (LBTEST): Positive or Negative.

9.7. Vital Signs

The vital signs (systolic and diastolic blood pressure, pulse rate, temperature, and respiratory rate) will be summarized overall and by gender, by visit for pre-dose, 30, 60, and every hour after infusion. The change and percent change from pre-dose to each post-dose (30, 60 minutes etc. after infusion) will be summarized as well for each visit.

9.8. Concomitant Medication

The summary table for all concomitant medications reported during the study, and coded by World Health Organization (WHO) Drug Dictionary 2018, will be summarized for overall and be gender

The medication used for pain will be identified based on the classification on the eCRF. These pain medications will be summarized for overall and by gender, by descriptive statistics, i.e. the count and percentage of the subjects with each medication by standardized medication name within medication class.

Additionally, the number of patients treated with ACEi and/or ARBs while on pegunigalsidase alfa will be summarized by descriptive statistics for overall and by gender.

Listing of medication will include start and end date and whether the drug was taken prior to 1st infusion of pegunigalsidase alfa.

9.9. X-Ray

Results of x-ray will be listed.

9.10. Pregnancies

Results of pregnancy tests will be listed.

10. ANALYSIS OF EFFICACY ENDPOINTS

10.1. Estimated Glomerular Filtration Rate ($eGFR_{CKD-EPI}$)

The change in eGFR will be examined by comparing the change in annualized slope of eGFR while on Replagal® ("Pre-switch") to the slope in eGFR after switch to pegunigalsidase alfa treatment ("Post-switch"). Due to the nature of the prevalence of this rare disease and the variability of disease state between patients, using patients as their own control provides a rational method for clinical and statistical analysis of this patient population.

10.1.1. eGFR Estimation

eGFR will be calculated based on the value of the serum creatinine values according to the CKD-EPI formula:

$$eGFR\ (mL/min/1.73\ m^2) = 141 \times \min(Scr/\kappa,1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018\ [\text{if female}] \times 1.159\ [\text{if black / African American}]$$

where Scr is serum creatinine (mg/dL), κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1. (Note to programmer: serum creatinine can be found in two categories (CHEMISTRY and ENZYMATE) in the SDTM. Both will be used to estimate eGFR)

The age should be the actual age when the subject's serum creatinine is collected, the calendar age at each timepoint should be used in the formula to be consistent with that in the Electronic Data Capture (EDC) system.

The eGFR will not be calculated again if its value is available from the CRF system (all eGFR values are calculated for the screening assessments).

10.1.2. Annualized Change in eGFR (Slope)

The annualized change in eGFR per subject will be estimated using a linear regression:

eGFR = $\alpha + \beta \times$ [time in year], based on all visits where eGFR is available.

The slope β (mL/min/1.73 m^2 / year) will be an estimate of the subject's annualized change in eGFR. The "[time in year]" in the formula is the time, in year, from "baseline" to the respective visit, and will be estimated by (date of the visit – date of baseline)/365.25.

The eGFR obtained in Visit 1 pre-infusion of pegunigalsidase alfa will be included in the calculation of both slopes, as the last data point to be used in the pre-switch annualized slope calculation, and the first data point to be used in the post-switch annualized slope calculation.

Any eGFR data obtained more than 730 days (approximately 24 months) prior to Screening visit will not be used in estimating the pre-switch annualized slope. The exact exclusion rule

is: data will not be used if the time in days from the date of evaluation to the date of screening is greater than 730 days. The "pre" switch slope calculation will include all eGFR values with less than 730 days before Screening, eGFR values during screening period (about 3 months), and pre-infusion eGFR at visit 1.

10.1.3. eGFR and eGFR Slope Analysis

The eGFR values at all visits, and the pre- and post-switch eGFR slopes, along with the difference between the pre- and post-switch eGFR slopes will be presented per individual subject.

The change in eGFR from baseline up to 12 months will be summarized by descriptive statistics.

The eGFR slopes pre- and post-switch, and the change in eGFR slopes from pre- to post-switch, will be summarized by descriptive statistics. The comparison of eGFR slopes between pre- and post-switch will be made by using a paired t-test. A 95% Confidence Interval (CI) will be presented as well.

The analyses in this section will be repeated for the subgroups described in Section 7.4 and the following additional subgroups:

1. Annualized slope of eGFR ≤ and > -3 mL/min/1.73 m^2/year at baseline (i.e. pre-switch eGFR slope),
2. Baseline eGFR ≤ and > 60 mL/min/1.73 m^2 (Visit 1 or, when not available, the last measurement before receiving the first treatment with pegunigalsidase alfa),
3. Baseline UPCR based on the categories defined in Section 10.4,
4. Usage of ACEi or ARBs treatment pre-switch (Yes/No).

10.1.4. Analysis of Therapeutic Goals

According to *Wanner et al.* 2018: "*European Expert Consensus Statement on Therapeutic Goals in Fabry Disease*", eGFR slope can be used to assess renal function in patients with Fabry disease. Based on patients' pre- switch eGFR slope, the patients will be classified into three kidney disease (KD) severity groups, and the therapeutic goals proposed by the *Wanner et al.* 2018 will be assessed respectively based on the pre- and post-switch eGFR slopes as indicated in the table below.

Patients KD Severity Groups	**Therapeutic Goals**
Stable KD: if pre-switch eGFR slope ≥ -3 mL/min/1.73 m^2/year	Achieved if eGFR slope remain in the range of stable KD (i.e. post-switch eGFR slope ≥ -3 mL/min/1.73 m^2/year)
Progressing KD: if pre-switch eGFR slope between ≥ -5 and < -3 mL/min/1.73 m^2/year	Achieved if response to the treatment (i.e. post-switch eGFR slope become ≥ -3 mL/min/1.73 m2/year)
Fast progressing KD: if pre-switch eGFR slope < -5 mL/min/1.73 m^2/year	Achieved if progression slowdown (i.e. post-switch eGFR slope become ≥ -5 mL/min/1.73m^2/year), OR more than 50% decrease in progression (i.e., (pre-switch eGFR slope – post-switch eGFR slope) / pre-switch eGFR slope > 50%)

The number and percentage of patients achieving therapeutic goals (yes / no) for each patient KD group, as well as for all patient groups combined, will be presented.

In addition to examine the therapeutic goals, we'll also examine the KD status by using the same criteria to classify the patients into the three KD groups based on the post-switch

eGFR slopes, and a shift table will be provided to show the number and percentage of patients from pre-switch to post-switch in their KD status. The percentage will be based on the number of patients in the respective pre-switch KD status.

The number and percentage of patients in each of the KD groups of pre-switch and post-switch will be presented in this shift table as well. The percentage will be based on the total number of patients with KD status determined in the analysis population.

10.2. Cardiac MRI

The left ventricular mass (LVM), and left ventricular ejection fraction (%EF) from cardiac MRI, and the calculated left ventricular mass index (LVMI) indexed to patient's body surface area (g/m^2), will be summarized by descriptive statistics at baseline (prior to infusion in Visit 1), and 12-month visits. The change and percent change from baseline will be summarized as well. The table will be presented overall and by gender.
The left ventricular fibrosis segments will be presented by a shift table from baseline to 12-month visit.

10.3. Plasma Gb3 / Lyso-Gb3 and Urine Lyso-Gb3 Concentrations

Descriptive statistics of plasma Lyso-Gb3 concentration (nM) will be summarized at each visit. The change and percent change from baseline will be summarized as well. The summaries will be presented for the three subgroups in Section 7.4.

The plasma Lyso-Gb3 levels at all visits and the corresponding change and percent change from baseline will be presented in a per subject table. The plasma Lyso-Gb3 levels over time will be presented graphically by a spaghetti plot, for all individual subjects, and for by gender.

In addition, the number and percentage of patients with a reduction from baseline with thresholds of 20%, 30%, 40% and 50% will be summarized at each visit.

Descriptive statistics of plasma Gb3 concentration (nM) will be summarized at each visit and the change and percent change from baseline will be summarized for overall and by the three subgroups in Section 7.4. The change and percent change from baseline will also be presented in the data listing as well.

Descriptive statistics of urine Lyso-Gb3 concentration (pM/mM Creatinine) will be summarized at each visit for overall and the three subgroups in Section 7.4. The change and percent change from baseline will be summarized as well.

10.4. Urine Protein/Creatinine Ratio (UPCR)

UPCR will be classified into four categories. The 1st three are based on the Kidney Disease Improving Global Outcomes (KDIGO) guidelines:

- Normal to mildly increased: if UPCR < 0.15 gr/gr,
- Moderately increased: if UPCR ≥ 0.15 gr/gr and ≤ 0.5 gr/gr, and
- Severely increased: if UPCR > 0.5 gr/gr
- PU (Protein Undetectable): in any case that UPCR is reported with a < sign. This happens in any case that the protein level is below the level of detection.

Urine protein/creatinine ratio (UPCR), by spot urine test, will be summarized at each visit based on the above 4 categories (Normal to mild increased; Moderately increased; Severely increased; PU) for overall population and by gender.

The shift of UPCR category from baseline to each of the post-treatment visit will be presented including number and percentage of patients. The percentage will be based on the number of patients in the respective baseline UPCR category.

10.5. Echocardiogram Report

The echocardiography reports were performed by local laboratories, and the evaluations with substantial variations, therefore only data listing will be provided.

Qualitative assessments (normal / other) regarding Aortic, Mitral, Tricuspid, and Pulmonic will be presented by a shift from baseline table will be presented for overall and by gender.

10.6. Stress Test

The quantitative evaluation (yes / no) of symptoms (chest pain, shortness of breath, Dizziness, palpitations, and other) and the overall impression: normal stress test (yes / no) from stress tests will be summarized by descriptive statistics at each visit for overall and be gender.

The shift from baseline will be presented for overall impression: normal stress test (yes / no).

10.7. Short Form Brief Pain Inventory (BPI)

Descriptive statistics of the qualitative assessments regarding pain severity and pain interference will be summarized at each visit. The change of the assessments will be examined using a shift table from baseline for individual qualitative items and change and percent change from baseline for individual scores and composite scores.

This will be done according to the Brief Pain Inventory User Guide. (Charles S. Cleeland, PhD). The details are as follows.

Pain severity will be analyzed by each of the four pain severity items (worst, least, average, and right now) respectively and a composite of the four pain severity items (a mean severity score) will be analyzed as well.

Pain interference will be analyzed by each of the seven pain interference items (general activity, mood, walking ability, normal work, relations with others, sleep, and enjoyment of life) respectively, and a composite of the seven pain interference items (a mean interference score) will be analyzed as well. When at least four out of seven interference items for a subject at a visit are available, the mean interference score will be calculated. Otherwise, it will be considered not available (i.e., missing).

BPI summary tables will be presented overall and by the three subgroups in section 7.4.

10.8. Mainz Severity Score Index (MSSI)

Descriptive statistics of the scores, including the change and percent change from baseline, regarding the sign/symptom in general, neurological, cardiovascular, renal dysfunction, and overall score (sum of these four scores) will be summarized at each visit for overall and by gender.

The change of the assessments (scores) will also be examined using a shift table from baseline. Theoretically the range of the scores in general, neurological, and renal dysfunction are from 0 to 18 respectively, 0 to 20 for total cardiovascular score, and 0 to 74 for the overall score. However, majority of the subjects should have the scores in the

middle of the range, especially for the overall score. Therefore, the scores will be categorized in the shift tables, would be < 4, 4-6, 7-9, 10-12, 13-15, and > 15 in six (6) categories for individual scores, and < 11, 11-15, 16-20, 21-25, 26-30, 31-35, 36-40, and > 40 in eight (8) categories for the overall score. Adjustment of the categories might be needed if there were more patients with extreme scores.

10.9. Quality of Life EQ-5D-5L

Descriptive statistics of the qualitative assessments regarding mobility, self-care, usual activities, pain/discomfort, and anxiety/depression will be summarized at each visit for overall and by gender. The change of the assessments will be examined using a shift table from baseline.

The overall health score (from 0 to 100) will be summarized by descriptive statistics at each visit. The change and percent change from baseline will be summarized for overall and by gender.

10.10. Use of Pain Medications

The number of patients used pain medication, and the number of patients used several pain medications (0, 1, 2, up to the maximum, where the medications with identical standard name is counted once), will be summarized by count and percentage as well.

The change from baseline in pain medication use will be examined by shift table to identify how many patients changed their pain medication use from baseline to the last visit (Visit 27 (Month 12) or the last assessment before discontinuation). This analysis will be based on the pain medication use on the day of the baseline visit, and the day of last visit.
Two shift tables will be generated, one for whether pain medication used (Yes / No), the other for number of pain medication used in three categories (0, 1, and 2+).
The tables will be presented by overall and by gender.

10.11. Fabry Clinical Events

Based on the reported adverse events, the adjudicated decisions will be made by the Sponsor medical monitor.

Fabry clinical events are classified into four categories: renal, cardiac, cerebrovascular and non-cardiac death:

1. Renal events:
    - First occurrence of either initiation or chronic dialysis (>40 days),
    - Renal transplantation.
2. Cardiac events:
    - Cardiac related death,
    - Myocardial infarction,
    - First time congestive heart failure,
    - Atrial fibrillation,
    - Ventricular tachycardia,
    - Evidence of progressive heart disease severe enough to require pacemaker,
    - Implantation of pacemaker,
    - Bypass surgery,
    - Coronary artery dilatation,
    - Implantation of defibrillator.
3. Cerebrovascular events:
    - Hemorrhagic or ischemic stroke,
    - Transient Ischemic Attack.
4. Non-cardiac related Death

Number and percentage of patients with specific Fabry clinical events will be presented for overall and by the subgroups presented in Section 7.4.

The listings of Fabry clinical events will show the categories by SOC and PT and the time to event measured from Visit 1.

11. LIST OF TABLES, FIGURES AND DATA LISTINGS

11.1. Statistical Tables

The statistical tables will be generated using SAS version 9.4. In general, the sample size (n), minimum, and maximum will be presented by whole number. The mean and its standard error, standard deviation, and median will be rounded and presented to one decimal place. For some values with meaningful decimal digits, their mean, standard error of mean, standard deviation, and median will be rounded to more than one decimal place when necessary. The count will be the whole number. The percentage will be rounded and presented to one decimal place. The p-value will be rounded to three decimal places. While the p-value is less than 0.001, it will be presented as <0.001.

Tables for the Per Protocol population will be generated only in case that the Per Protocol and the Efficacy population are different. In such cases, “PP” will be added to the table number to distinguish it from the efficacy population.

Disposition of Subjects, Baseline Characteristics, Exposure and Compliance:

Number	Title	Population
14.1.1	Disposition of Subjects for Overall	All
14.1.2.1	Demographics for Overall and by Gender	Safety
14.1.2.2	Demographics for Overall and by Gender	EP, PP
14.1.3.1	Treatment Compliance for Overall and by Gender	Safety
14.1.3.2	Treatment Compliance for Overall and by Gender	EP, PP
14.1.4.1.1	Baseline Characteristics by Overall and by Gender	Safety
14.1.4.2.1	Baseline Characteristics by Baseline FD Classification and Treatment Emergent ADA	Safety
14.1.4.1.2	Baseline Characteristics for Overall and by Gender	EP, PP
14.1.4.2.2	Baseline Characteristics by Baseline FD Classification and Treatment Emergent ADA	EP, PP
14.1.5.1.1	Fabry Disease Medical History for Overall and by Gender	Safety
14.1.5.1.2	Fabry Disease Medical History for Overall and by Gender	EP, PP
14.1.5.2.1	Other Medical History for Overall and by Gender	Safety
14.1.5.2.2	Other Medical History for Overall and by Gender	EP, PP
14.1.6.1.1	Exposure Overall and by Gender	Safety
14.1.6.1.2	Exposure Overall and by Gender	EP, PP
14.1.7.1.1	Number of Infusions and Duration Overall	Safety
14.1.7.1.2	Number of Infusions and Duration for Overall	EP, PP

Efficacy:

Number	Title	Population
14.2.1.1.1	Kidney Functions (eGFR and eGFR Slope) for Overall and by Gender	EP, PP
14.2.1.1.2	Kidney Functions (eGFR and eGFR Slope) by Baseline FD Classification and Treatment Emergent ADA	EP, PP
14.2.1.2	Kidney Functions (eGFR and Slope) Per Patient Listing	EP, PP
14.2.1.3.1	Kidney Functions (eGFR Slope) by Baseline eGFR Slope and Baseline eGFR Categories	EP, PP
14.2.1.3.2	Kidney Functions (eGFR Slope) by Baseline UPCR Categories	EP, PP
14.2.1.3.3	Kidney Functions (eGFR Slope) with/without ACEi or ARBs treatment pre-switch	EP, PP
14.2.1.4	Kidney Functions (eGFR Slope) Therapeutic Goal Analysis	EP, PP
14.2.1.5	Kidney Functions (eGFR Slope) by kidney disease Severity Shift from Pre-Switch to Post-Switch	EP, PP
14.2.2.1.1.1	Plasma Lyso-Gb3 Concentrations for Overall and by Gender	EP, PP
14.2.2.1.1.2	Plasma Lyso-Gb3 Concentrations by Baseline FD Classification and Treatment Emergent ADA	EP, PP
14.2.2.1.2	Plasma Lyso-Gb3 Concentrations including Change from Baseline Per Patient Listing	EP, PP
14.2.2.1.3	Number of Subjects with 20%, 30%, 40% and 50% Reduction from Baseline in Plasma Lyso-Gb3 Concentrations for Overall	EP, PP
14.2.2.2.1	Plasma Gb3 Concentrations for Overall and by Gender	EP, PP
14.2.2.2.2	Plasma Gb3 Concentrations by Baseline FD Classification and Treatment Emergent ADA	EP, PP
14.2.2.3.1	Urine Lyso-Gb3 Concentrations for Overall and by Gender	EP, PP
14.2.2.3.2	Urine Lyso-Gb3 Concentrations by Baseline FD Classification and Treatment Emergent ADA	EP, PP
14.2.2.4.1.1	Short Form Brief Pain Inventory (BPI) for Overall and by Gender	EP, PP
14.2.2.4.1.2	Short Form Brief Pain Inventory (BPI) by Baseline FD Classification and Treatment Emergent ADA	EP, PP

Number	Title	Population
14.2.2.4.2	Short Form Brief Pain Inventory (BPI) - Shift from Baseline for Overall	EP, PP
14.2.2.5.1	Cardiac MRI (LVM, LVMi, and %EF) for Overall and by Gender	EP, PP
14.2.2.5.2	Cardiac MRI (Left Ventricular Fibrosis Segments) – Shift from Baseline for Overall	EP, PP
14.2.2.6	Echocardiogram Report – Shift from Baseline for Overall and by Gender	EP, PP
14.2.2.7.1	Stress Test for Overall and by Gender	EP, PP
14.2.2.7.2	Stress Test - Shift from Baseline for Overall and by Gender	EP, PP
14.2.2.8.1	Quality of Life EQ-5D-5L (Overall Health Score) for Overall and by Gender	EP, PP
14.2.2.8.2	Quality of Life EQ-5D-5L (Qualitative Assessments) for Overall and by Gender	EP, PP
14.2.2.8.3	Quality of Life EQ-5D-5L (Qualitative Assessments) - Shift from Baseline for Overall	EP, PP
14.2.2.9.1	Urine Protein/Creatinine Ratio (UPCR) for Overall and by Gender	EP, PP
14.2.2.9.2	Urine Protein/Creatinine Ratio (UPCR) - Shift from Baseline for Overall	EP, PP
14.2.2.10.1	Mainz Severity Score Index (MSSI) for Overall and by Gender	EP, PP
14.2.2.10.2	Mainz Severity Score Index (MSSI) - Shift from Baseline for Overall	EP, PP
14.2.2.11.1	Usage of Pain Medications for Overall and by Gender	EP, PP
14.2.2.11.2	Usage of Various Pain Medications for Overall and by Gender	EP, PP
14.2.2.11.3	Pain Medication Use – Shift from Baseline to Last Visit for Overall and by Gender	EP, PP
14.2.2.11.4	Number of Pain Medication Use – Shift from Baseline to Last Visit for Overall and by Gender	EP, PP
14.2.2.12.1	Number of Subjects with Fabry Clinical Events for Overall and by Gender	EP, PP
14.2.2.12	Number of Subjects with Fabry Clinical Events by Baseline FD Classification and Treatment Emergent ADA	EP, PP

Safety – Adverse Events:

Number	Title	Population
14.3.1.1.1	Number of Subjects with Treatment-Emergent Adverse Events for Overall and by Gender	Safety
14.3.1.1.2	Number of Subjects with Treatment-Emergent Adverse Events by Baseline FD Classification and Treatment Emergent ADA	Safety
14.3.1.2.1	Number of Treatment-Emergent Adverse Events for Overall and by Gender	Safety
14.3.1.2.2	Number of Treatment-Emergent Adverse Events by Baseline FD Classification and Treatment Emergent ADA	Safety
14.3.1.3.1	Number of Subjects with TEAE by MedDRA System Organ Class / Preferred Term for Overall and by Gender	Safety
14.3.1.3.2	Number of Subjects with TEAE by MedDRA System Organ Class / Preferred Term by Baseline FD Classification and Treatment Emergent ADA	Safety
14.3.1.4	Number of Subjects with TEAE by MedDRA System Organ Class / Preferred Term and Severity for Overall	Safety
14.3.1.5	Number of Subjects with TEAE by MedDRA System Organ Class / Preferred Term and Relationship to Study Drug for Overall	Safety
14.3.1.6	Number of Subjects with Pre-Treatment AE by MedDRA System Organ Class / Preferred Term for Overall and by Gender	Safety
14.3.1.7	Number of Subjects with TEAE by MedDRA System Organ Class / Preferred Term by Time Categories for Overall	Safety
14.3.1.8	Number of TEAEs by MedDRA System Organ Class / Preferred Term by Time Categories for Overall	Safety
14.3.1.9.1	Number of IRRs for Overall, by Gender and Location of Administration	Safety
14.3.1.9.2	Number of IRRs by Baseline FD Classification and Treatment Emergent ADA	Safety
14.3.1.10.1	Number of IRRs by MedDRA System Organ Class / Preferred Term for Overall and by Gender	Safety
14.3.1.10.2	Number of IRRs by MedDRA System Organ Class / Preferred Term by Baseline FD Classification and Treatment Emergent ADA	Safety
14.3.1.11	Number of IRRs by MedDRA System Organ Class / Preferred Term and Severity for Overall	Safety
14.3.1.12.1	Number of Subjects with IRRs by MedDRA System Organ Class / Preferred Term for Overall and by Gender	Safety

Number	Title	Population
14.3.1.12.2	Number of Subjects with IRRs by MedDRA System Organ Class / Preferred Term by Baseline FD Classification and	Safety
14.3.1.13	Number of Subjects with IRRs by MedDRA System Organ Class / Preferred Term and Severity for Overall	Safety
14.3.1.14	Treatment-Emergent Adverse Events Leading to Withdrawal or Death	Safety
14.3.1.15.1	Number of Subjects with Injection Site Reaction TEAE for Overall and by Gender	Safety
14.3.1.15.2	Number of Subjects with Injection Site Reaction TEAE by Baseline FD Classification and Treatment Emergent ADA	Safety
14.3.1.16.1	Number of Injection Site Reactions TEAE for Overall and by Gender	Safety
14.3.1.16.2	Number of Injection Site Reactions TEAE by Baseline FD Classification and Treatment Emergent ADA	Safety
14.3.1.17	Number of Subjects with Serious TEAE by MedDRA System Organ Class / Preferred Term for Overall and by Gender	Safety
14.3.1.18	Number of Subjects with Serious TEAE by MedDRA System Organ Class / Preferred Term and Relationship to Study Drug for Overall	Safety

Safety – Laboratory Test Results:

Number	Title	Population
14.3.4.1.1	Laboratory Test Results – Biochemistry for Overall and by Gender	Safety
14.3.4.1.2	Laboratory Test Results Shift from Baseline – Biochemistry for Overall and by Gender	Safety
14.3.4.2.1	Laboratory Test Results – Hematology for Overall and by Gender	Safety
14.3.4.2.2	Laboratory Test Results Shift from Baseline – Hematology for Overall and by Gender	Safety
14.3.4.3	Laboratory Test Results – Urinalysis for Overall and by Gender	Safety
14.3.4.4	Laboratory Test Results – Coagulation Profile at Screening for Overall and by Gender	Safety
14.3.4.5	Laboratory Test Results – Vitamin D at Screening for Overall and by Gender	Safety
14.3.4.6	Anti-PRX-102 Antibodies for Overall and by Gender and Baseline FD Classification	Safety

Safety – Other:

Number	Title	Population
14.3.5.1	Vital Signs for Overall and by Gender	Safety
14.3.5.2.1	Physical Examinations for Overall and by Gender	Safety
14.3.5.2.2	Physical Examinations – Shift from Baseline for Overall and by Gender	Safety
14.3.5.3.1	Electrocardiography (ECG) for Overall and by Gender	Safety
14.3.5.3.2	Electrocardiography (ECG) – Shift from Baseline for Overall and by Gender	Safety
14.3.5.4.1	Number of Subjects Used Concomitant Medications for Overall and by Gender	Safety
14.3.5.4.2	Number of Subjects Used Pain Medications for Overall and by Gender	Safety
14.3.5.4.3.1	Number of Subjects Treated with ACEi and/or ARBs for Overall and by Gender	Safety
14.3.5.5.1	Infusion Premedication for Overall and by Gender	Safety

11.2. Figures

Number	Title	Population
14.2.2.1.1.1	Spaghetti Plot of Plasma Lyso-Gb3 Concentrations over Time	EP
14.2.2.1.1.2	Spaghetti Plot of Plasma Lyso-Gb3 Concentrations over Time (Male Subjects)	EP
14.2.2.1.1.3	Spaghetti Plot of Plasma Lyso-Gb3 Concentrations over Time (Female Subjects)	EP

11.3. Data Listings

The following data listings would not be provided if the data listings of the raw data are already provided and suffice per sponsor's perspective. Data listings will be sorted by the subject ID.

Number	Title
1	Subject Disposition
2	Demographics
3	Concomitant Medications
4.1	Fabry Disease Medical History
4.2	Other Medical History
5	Vital Signs
6	Physical Examination
7.1	Laboratory Test Results – Biochemistry
7.2	Laboratory Test Results – Hematology
7.3	Laboratory Test Results – Anti-PRX-102 Antibodies (IgG)
7.4	Laboratory Test Results – Gb3 Concentration (Plasma GB3 and Plasma Lyso-Gb3)
7.5	Laboratory Test Results – Spot Urine
7.6	Laboratory Test Results – Urinalysis (Dipstick)
7.7	Laboratory Test Results – Coagulation Profile
7.8	Laboratory Test Results – Vitamin D
7.9	Laboratory Test Results – GB3 Concentration (including Urine Lyso-GB3
8	Electrocardiography (ECG)
9.1	Pre-treatment Adverse Events
9.2	Treatment Emergent Adverse Events
9.3	Fabry Clinical Events
9.4	Infusion Related Events
10	Exposure - Treatment
11.	Findings About - Brain MRI
11.	Findings About - Cardiac MRI
11.	Findings About – Stress Test
11.	Findings About - Echocardiogram
12.	Questionnaires - Brief Pain Inventory (BPI)
12.	Questionnaires – Mainz Severity Score Index (MSSI)
12.	Questionnaires – Quality of Life EQ-5D-5L
13	Protocol Deviations
14	Infusion Premedication
15	Treatment Compliance
16	X-rays
17	Pregnancies

12. TABLE SHELLS

The table shells are to be provided in a separate document.