[redacted]

Document Title:	Statistical Analysis Plan		
Version Number:	Final 1.0	Date:	18Oct2024
Protocol Number:	SARO.17.009	Sponsor Name:	Zydus Therapeutics INC

STATISTICAL ANALYSIS PLAN	
Protocol Title:	A Phase 2A, Double-blind, Randomized, Controlled Clinical Trial to Evaluate the Efficacy and Safety of Saroglitazar Magnesium 4 mg tablet for Treating Nonalcoholic Fatty Liver Disease (NAFLD) in Women with Polycystic Ovary Syndrome (PCOS).
Sponsor Name:	Zydus Therapeutics INC
Phase:	Phase 2A
Protocol Number:	SARO.17.009
Protocol Version No., Date	Final Version 5.0, 06 February 2020
CRF Version No., Date	Final Version 1.7, 28 April 2020
[redacted]	
SAP Version, Date:	Final Version 1.0, 18 October 2024
Scope:	Final Analysis for Clinical Study Report

[redacted]

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2 Signatures

Statistical Analysis Plan				
Protocol Number:	SARO.17.009			
Sponsor Name:	Zydus Therapeutics INC			
Version Number and Date:	Final Version 1.0, 18 Oct 2024	**Supersedes, if any:**		Not Applicable
Function Name:	Biostatistics Projects Planning And Programming			
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[redacted]				

3 Version History

Version	Date	Change to previous version
Final 1.0	18 Oct 2024	NA

4 List of Abbreviations

Abbreviation	Definition
%	Percentage
AE	Adverse Event
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
ANCOVA	Analysis of Covariance
ApoA	Apolipoprotein A
ApoB	Apolipoprotein B
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
BNP	B-Type Natriuretic Peptide
BP	Blood Pressure
BUN	Blood Urea Nitrogen
CFB	Change From Baseline Values
CI	Confidence Interval
CIOMS	Council For International Organizations of Medical Sciences
CK	Creatine Kinase
Ck-18	Cytokeratin 18
CKDEPI	Chronic Kidney Disease Epidemiology Collaboration
CK-MB	Creatine Kinase-Muscle/Brain
CRF	Case Report Form
DBL	Data Base Lock
E	Number of Events
ECG	12-Lead-Electrocardiogram
eGFR	Estimated Glomerular Filtration Rate
FSH	Follicle Stimulating Hormone
G Mean	Geometric Mean
GGT	Gamma Glutamyltransferase
H0	Null Hypothesis
H1	Alternative Hypothesis
HAV	Hepatitis A Virus
HBsAg	Anti-Hepatitis B Virus Surface Antigen
HCV	Hepatitis C Virus
HDL	High-Density Lipoprotein
HOMA	Homeostasis Model Assessment
hs-CRP	High Sensitivity C-Reactive Protein
ICH	International Conference on Harmonisation
INR	International Normalized Ratio
IP	Investigational Product
IR	Insulin Resistance

LDL	Low-Density Lipoprotein
LFTs	Liver Function Tests
LH	Luteinizing Hormone
LOCF	Last Observation Carry Forward
LS Mean	Adjusted Least Square Mean
Max	Maximum
MCHC	Mean Corpuscular Hemoglobin Concentration
MCV	Mean Corpuscular Volume
MedDRA	Medical Dictionary for Regulatory Activities
Min	Minimum
mITT	Modified Intent-To-Treat
MRI	Magnetic Resonance Imaging
n	Number of Non-Missing Participants/Observations
N	Count Corresponding to The Number of Participants for a Group
NAFLD	Nonalcoholic Fatty Liver Disease
NE	Not Evaluable
PAP	Papanicolaou
PCB	Percent Change from Baseline
PCOS	Polycystic Ovary Syndrome
PDFF	Proton-Density Fat-Fraction
PK	Pharmacokinetic
PP	Per Protocol
PT	Preferred Term
P-value	Probability Value
RBC	Red Blood Cell
RFTs	Renal Function Tests
SAE	Serious Adverse Event
SAF	Safety Population
SAP	Statistical Analysis Plan
SAS	Statistical Analysis Software
SD	Standard Deviation
sdLDL	Small Dense Low-Density Lipoprotein
SE	Standard Error
SHBG	Sex Hormone Binding Globulin
SOC	System Organ Class
TC	Total Cholesterol
TEAE	Treatment Emergent Adverse Event
TG	Triglyceride
TNF-α	Tumor Necrosis Factor-α
TSH	Thyroid Stimulating Hormone
ULN	Upper Limit of Normal
USA	United State of America
Vd/F	Apparent Volume of Distribution

VLDL	Very Low-Density Lipoprotein
WBC	White Blood Cell
WHODrug	World Health Organization Drug Dictionary

5 Introduction

This document describes the statistical methods and procedures to be implemented for the analysis of data from SARO.17.009 study. The plan has been developed after review of the clinical study protocol, Version No. 5.0, Dated 06th February 2020 and Case Report Form (CRF) final Version No. 1.7, Dated 28th April 2020. This Statistical Analysis Plan is written with consideration of the recommendations outlined in the International Conference on Harmonisation (ICH) E9 guideline entitled "Guidance for Industry: Statistical Principles for Clinical Trials", ICH E9 (R1) guideline entitled "Addendum on estimand and sensitivity analysis in clinical trials" and the ICH E3 guideline entitled, "Guidance for Industry: Structure and Content of Clinical Study Reports (CSR). This Statistical Analysis Plan (SAP) was developed prior to database lock.

Any changes from the planned analysis as described in the protocol are detailed here, and any differences described here supersede the analysis as presented in the protocol. Any deviations from the planned analyses described in this SAP will be documented in the clinical study report, together with the reason for such changes.

Prior to start of any statistical analyses, the database must be authorized and all decisions regarding assignment of participants to study populations must be completed. In addition, protocol deviations must be identified prior to the start of statistical analyses.

6 Study Objectives and endpoints

6.1 Primary Objective

The primary objective of this study is to evaluate effect on hepatic fat content, measured as proton-density fat-fraction (PDFF) by magnetic resonance imaging (MRI), of once-daily Saroglitazar Magnesium 4 mg tablets for 24 weeks vs placebo.

6.2 Secondary Objectives

The secondary efficacy objectives are to assess the effect of a 24-Week treatment regimen of Saroglitazar Magnesium 4 mg tablets on the following parameters in participants of PCOS with NAFLD:

1. Liver Enzymes/LFTs
2. Insulin resistance (IR) measured by Homeostasis Model Assessment (HOMA)
3. Liver stiffness measurement obtained via transient elastography/ FibroScan®
4. Controlled attenuation parameter obtained via transient elastography/ FibroScan®
5. Body weight, body mass index (BMI) and waist circumference
6. MRI-derived total liver fat index and total liver volume
7. Serum lipid profile and lipoproteins
8. Sex hormone binding globulin (SHBG)
9. Ovarian function
10. Free androgen index
11. Pharmacokinetics of Saroglitazar following first dose and last dose.

6.3 Safety Objectives

Criteria for Safety:

1. Vitals: blood pressure (BP) (sitting BP after 05 min rest; systolic and diastolic BP), pulse rate, oral temperature and respiratory rate at Visit 1[Screening Visit] and at Visit 3 [Week 1] through Visit 8 [Week 24 (i.e. End-of-Treatment)] visits.
2. Body mass index at Screening Visit (Visit 1), at Week 12 (Visit 6) and at Week 24 (Visit 8) (i.e. End-of-Treatment) visits.
3. Waist measurements at Screening Visit (Visit 1), at Week 12 (Visit 6) and at Week 24 (Visit 8 i.e. End-of-Treatment) visits.
4. The physical examination will consist of an evaluation of the head, neck, eyes, ears, nose, throat, pelvic, breast, chest, heart, lungs, abdomen, skin, extremities, neurological systems, musculoskeletal systems and weight measurement. Investigator should also evaluate the participants for hirsutism and virilizing signs (upper lip, chin, chest, upper abdomen, lower abdomen, thighs, back, arm and buttocks). Note: Breast examination will be done as part of screening visit. Pelvic examination will be performed as part of screening visit, if not performed within 6 months of randomization.
5. Laboratory assessment:

    a. Hematology: Hematocrit, hemoglobin, mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), platelet count, mean platelet volume, red blood cell (RBC) count, white blood cell (WBC) count, differential WBC count.

b. Liver enzymes/LFTs: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin (with conjugated bilirubin), gamma glutamyltransferase (GGT), serum protein and albumin.
c. Renal function tests (RFTs): blood urea nitrogen (BUN), creatinine and estimated glomerular filtration rate (eGFR). Estimated glomerular filtration rate will be calculated by using Chronic Kidney Disease Epidemiology Collaboration (CKDEPI) equation.
d. Inflammatory marker: high sensitivity C-reactive protein (hs-CRP).
e. Lipid profile and lipoproteins: triglyceride (TG), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), small dense low-density lipoprotein (sdLDL), very low-density lipoprotein (VLDL), free fatty acids, apolipoprotein A and apolipoprotein B.
f. Urine examination: physical examination (appearance, color, specific gravity and pH); microscopy (epithelial cells, red blood cells, pus cells, cast and crystals) and chemical examination (protein, glucose, bilirubin, urobilinogen, ketone bodies and nitrite).
g. T3, T4 and thyroid stimulating hormone (TSH)
h. Serum pregnancy test
i. Urine pregnancy test
j. Serology: HIV type 1 and type 2, hepatitis A virus (HAV), anti-hepatitis B virus surface antigen (HBsAg) and hepatitis C virus (HCV) (at Visit 1).
k. International normalized ratio (INR) and prothrombin time (PT)
l. Cytokeratin 18
m. Free androgen index and SHBG level
n. Total testosterone and free testosterone
o. Follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels
p. 17-hydroxyprogesterone
q. Estradiol
r. Creatine Kinase (CK)
s. Cardiac function: 12-lead-electrocardiogram (ECG)
t. Glycemic control: FPG, HbA1c and plasma insulin levels.
u. B-type natriuretic peptide (BNP) and aminoterminal fragment of BNP prohormone (NT-proBNP)
v. Papanicolaou (PAP) test
w. Cardiac troponin, creatine kinase-muscle/brain (CK-MB)
x. Lipase and amylase
y. Uric acid

6. Adverse event(s): Frequency and severity of AE /serious adverse events (SAEs), drop-outs due to AEs for all participants enrolled will be recorded. All AEs will be assessed using Council for International Organizations of Medical Sciences (CIOMS) criteria using:
   a. Causality
   b. Severity
   c. Seriousness
   d. Expectedness

Note: Efficacy assessments and laboratory assessment (liver fat content by MRI-PDFF [MRI-PDFF will be performed during screening phase, screening phase results will be used as the baseline assessment], controlled attenuation parameter, hormonal profile, fasting plasma glucose, lipid and lipoprotein profiles, MRI-derived total liver fat index and total liver volume [MRI derived total liver fat index and total liver volume assessment will be performed during screening phase, screening phase results will be used as the baseline assessment], plasma insulin levels, homeostasis model assessment -insulin resistance [HOMA-IR], liver stiffness by transient elastography/FibroScan®, ovarian function, liver enzymes/LFTs, hematology, coagulation test (PT/INR), renal function test, CK, hs-CRP, BNP , NT-proBNP, cardiac troponin, CK-MB, lipase and amylase, TNFα, uric acid, TSH, T3 and T4, serology, HIV type 1 and type 2, HAV, antiHBsAg, HCV, serum pregnancy test, urine microscopy and urine chemistry) which will be done at Visit 1 will be considered for baseline visit. PAP test, endometrial biopsy and mammography will be performed as per Time and Events Schedule (refer **Appendix 1**).

7 Study Design

7.1 Overview

This is a Phase 2A, randomized, multi-center, double-blind, placebo-controlled study to evaluate the efficacy and safety of Saroglitazar Magnesium in women with well characterized polycystic ovary syndrome (PCOS) meeting pre-specified inclusion/exclusion criteria. Female participants aged 18 to 45 years will be enrolled in this study across USA and Mexico. Approximately 90 participants who meet the inclusion and exclusion criteria will be randomized in a 1:1 ratio to have 45 Participants in each arm i.e., Saroglitazar Magnesium 4 mg tablets and placebo.

The study will be conducted over a period of up to 34 weeks. Participants will be evaluated at study sites for 8 scheduled visits: (screening (Visit 1: Day [-28], Visit 2: Day [-14 to -7]), randomization (Visit 3: Week 1, Day 1), Visit 4 (Week 2, Day 14), Visit 5 (Week 8, Day 56), Visit 6 (Week 12, Day 84), Visit 7 (Week 16, Day 112) and Visit 8 (Week 24, Day 168). After completion of the study treatment period, the participants will be followed for an additional period of 6 weeks without any study medication until Visit 9 (Week 30, Day 210).

A total of 12 completed participants (6 participants in each treatment group) are planned to be included in the pharmacokinetic assessment. Additional participants may be enrolled into the study to ensure that the pharmacokinetic assessment is performed on at least 6 completed participants in each treatment group.

Note: PK analysis details are not reported in this document, a separate pharmacokinetics analysis plan will be prepared.

7.2 Study Methodology

Pre-Screening:
An informed consent will be obtained from the potential participants before any pre-screening evaluations. The evaluation of the ALT levels during the pre-screening will be done at the local laboratory, whereas the laboratory evaluations during the screening and the treatment phase will be done at the central laboratory.

Screening Phase:
The screening phase will consist of 28 days. Unless otherwise specified, screening procedures may be completed at any time during the screening phase. Before each participant is enrolled to the study, informed consent will be obtained from the participant (or her legally authorized representative) according to the regulatory and legal requirements of the participating country. Participant eligibility criteria for participation in the study will be assessed. Participants will undergo a serum pregnancy test. During this phase participant will be seen by the investigator or designated study personnel and an AUDIT questionnaire will be administered.

Randomization and Treatment Phase:
The randomization and treatment phase will include 6 outpatient visits (Visit 3 to Visit 8) over a period of 24 weeks including the randomization visit. All the eligible participants will be randomly assigned into either of the two treatment arms: Saroglitazar Magnesium 4 mg tablets and matching placebo tablets in a 1:1 ratio. Efficacy assessments will be conducted at Visit 6 Week 12 and Visit 8 Week 24 visits. In addition,

participants will be monitored during the study and at every visit for development of any adverse events including drug induced liver injury. In addition to physical examination, laboratory data and ECGs done during the study period will be monitored to detect any treatment emergent adverse events.

Safety Follow-up Visit:
A final post-treatment visit will occur 6 weeks (±3 days) [i.e. Visit 9 Week 30] after the end-of-treatment visit (i.e. Visit 8 Week 24) for safety monitoring. A telephonic follow-up visit will be performed to assess any AE or SAE after the end-of-treatment visit for safety monitoring. As far as possible, all assessments scheduled for end-of-treatment must be performed on all participants who receive the study drug but do not complete the study according to protocol.

7.3 Study Population

Participants of PCOS with NAFLD will be recruited for this study.

Number of Participants Planned:
A total 90 participants (including 20% dropouts) was planned to enrolled across USA and Mexico in a ratio of 1:1 to have 45 participants in each treatment arm i.e., Saroglitazar Magnesium 4 mg and placebo.

Six participants in each group are planned for pharmacokinetic assessment therefore a total of 12 participants will be included for pharmacokinetic assessment.

In view of the difficulty and challenges observed in recruitment of study population, it is decided to close recruitment at 60 participants.

7.4 Randomization

An independent statistician will generate the randomization schedule(s) for study treatment assignment. Eligible participants will be randomized in a 1:1 ratio to receive Saroglitazar Magnesium 4 mg or placebo respectively. Block randomization will be performed. The block randomization schedule will be generated to ensure the treatment balance by using SAS® software (Version: 9.4 or higher; SAS Institute Inc., USA).

7.5 Blinding and Unblinding

The study will be performed in a double-blind manner. All study drug will be supplied in identical packages and study drug kits. The study drug tablets will be similar in color, smell, taste, and appearance, thereby maintaining double-blind conditions.

The study blind should not be broken except in a medical emergency where knowledge of the study drug received would affect the treatment of the emergency.

The blind must only be broken following a discussion on a case-by-case basis, at the discretion of the Sponsor/Medical Expert. If an emergency unblinding becomes necessary, the PI should notify the Sponsor/Medical Expert, if possible, before unblinding. If it is determined that unblinding is necessary, a scratch card will be decoded to reveal the treatment received by the participant. All cases resulting in an unblinding event will be documented and reported to the Medical Expert and the Sponsor. If the blind is

broken, the date, time and reason must be recorded in the participant's eCRF/source document and any associated AE report completed.

The overall randomization code will be broken only for reporting purposes. This will occur once all final clinical data have been entered into the database, all data queries have been resolved, and the assignment of participants to the analysis sets has been completed.

Emergency code break (Unblinding):
An emergency code break will be available to the investigator and / or pharmacist. This code break must only be opened in emergency situations when the identity of the study drug must be known by the investigator in order to provide appropriate medical treatment. If the code break for a Participant is opened, Sponsor must be informed immediately. The reason for opening the code break must be documented along with the date and the initials of the person who broke the code. Participants whose treatment assignment becomes unblinded inadvertently, need not complete the scheduled evaluations and participant will be withdrawn from the trial from that visit.

7.6 Investigational Products

The Investigational products that will be used in this study are outlined in the following table:

Study drug	Formulation	Strength	Route	Manufacturer
Saroglitazar Magnesium	Tablet	4 mg	Oral	[redacted]

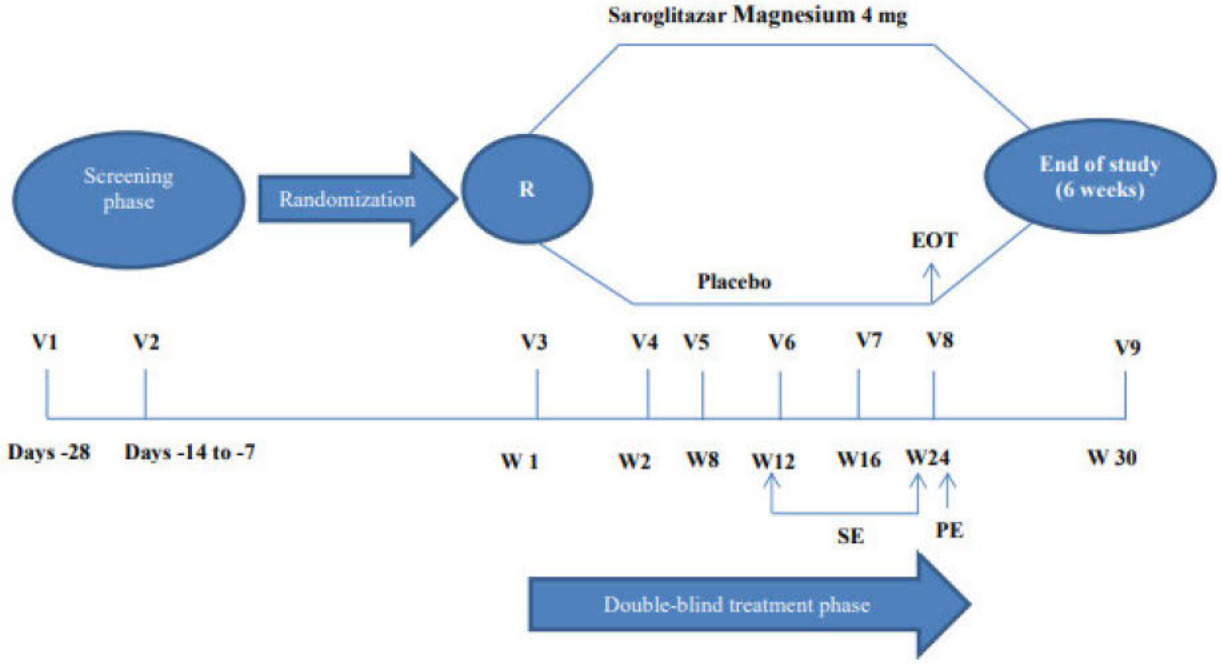
Dosage and Treatment Schedule:
Participants will receive either 4 mg Saroglitazar Magnesium or placebo orally once each morning before breakfast without food, for 24 weeks during the double-blinded treatment period. However, on scheduled visits participants will have the IP administered on site after the blood sample collection. The drug dose during the treatment phase will be checked and verified with study medication compliance by using drug accountability form.

7.7 Schedule of Assessment

Schedule of Assessment table is provided in Appendix 1

7.8 Study Flow Chart

The study plan is as follow:


Saroglitazar Magnesium 4 mg
Screening phase
Randomization
R
End of study (6 weeks)
EOT
Placebo
V1
V2
V3
V4
V5
V6
V7
V8
V9
Days -28
Days -14 to -7
W 1
W2
W8
W12
W16
W24
W 30
SE
PE
Double-blind treatment phase

8 General Statistical Considerations

8.1 Descriptive Statistics

The following descriptive statistics will be calculated for continuous data as well as for categorical data:

The summary statistics will be displayed with the following digits:

Description	Characteristic	Number of Decimal Places
Number of non-missing participants/observations	n	0
Number of events	E	0
Count corresponding to the number of participants for a group	N	0
Percentage#	%	1 decimal
Number of missing observations*	Missing	0
Mean	Mean	As in source + 1
Adjusted Least Square Mean	LS Mean	As in source +1
Standard Deviation	SD	As in source + 2
Standard Error	SE	As in source + 2
Minimum	Min	As in source
Median	Median	As in source + 1
Maximum	Max	As in source
Probability value	p-value	4 decimals
Confidence Interval	CI	2 decimals
Change From Baseline values	CFB	As in source
Percent Change from Baseline	PCB	2 decimals

*: If no observation is missing then "nmiss" row will not be printed.
#: Number of decimal places can be more than one, if necessary. All table percentages should be rounded to one decimal place if not stated otherwise.

Data will be summarized by the treatment groups (i.e. Saroglitazar Magnesium 4 mg or Placebo) wherever appropriate. The total number of participants in the treatment groups (N) under the stated population will be displayed in the header of summary tables as required.

Data will be summarized using descriptive statistics for continuous variables. Unless otherwise stated, descriptive statistics will include total number of participants with non-missing value of a variable/parameter (n), mean (Mean), Standard Deviation (SD), minimum (Min), median (Median), and maximum (Max).

In case of n=1, (where 'n' indicates the number of evaluable participants at the particular time point) then "SD" will be presented as 'NE' i.e. 'Not Evaluable'.

In case of n<1, (where 'n' indicates the number of evaluable participants at the particular time point) then "Mean, SD, Median, Minimum, Maximum" will be presented as 'NE' i.e. 'Not Evaluable'.

For categorical variables, data will be summarized using numbers of frequency count and percentages. The number [n] indicates the actual number of participants with a particular value of a variable or event, which should always be less than or equal to the total number of participants in the respective treatment group [N], unless participant is counted under multiple categories. The number and percentage of participants with missing values for a variable/category/event will also be presented for the resulting visits under the "Missing" category.

All data will be presented in the participant data listings. If either table or listing does not include any observation, then the following placeholder will be used: "No Participant Meets the Reporting Criteria".

8.2 Analysis Populations

Participant evaluability and their impact on analysis populations will be determined prior to locking the database.

Analysis Population	Definition
Safety (SAF)	The Safety (SAF) analysis population will consist of all participants who: - Were Randomized, - Had administered at least one dose of investigational product.
Modified Intention to Treat (mITT)	Modified Intention to Treat analysis population will consist of all participants who: - Were randomized, - Had administered at least one dose of investigational product - Have at least 1 post-baseline efficacy data of primary outcome.
Per Protocol (PP)	The Per Protocol (PP) analysis population will consist of all participants who: - Were in mITT analysis population, - Completed the treatment phase (i.e., Had both baseline and end-of-treatment primary efficacy outcome & has taken ≥80% and ≤120% of the study drug) - Have no protocol deviations that could affect primary efficacy outcome.

8.3 Definitions

In the following table, the required definitions and calculation for derivation during the analysis are summarized.

Term	Definition / Way of Calculation
Baseline	Baseline is defined as the last non-missing observation (including scheduled and unscheduled assessments within the pre-treatment period) prior to the first dose administration of study drug.
Change from Baseline	Post Baseline Value - Baseline value.
Percentage Change From Baseline	$\frac{(\text{Post Baseline} - \text{Baseline})}{\text{Baseline}} \times 100$
Treatment Start Date/time	Date/time of first dose administration in the study.
Treatment End Date/time	Date/time of last dose administration in the study.
Treatment Emergent Adverse Event (TEAE)	Treatment-emergent AEs are defined as any AE that started after the first dose of study drug or started before the first dose but increased in severity or frequency after administration of the initial dose of study drug.
Duration of Treatment (Days)	Treatment End Date – Treatment Start Date + 1.
Duration of Study (Days)	Last Visit Date – Informed Consent Date + 1.

8.4 Handling of Dropouts and Missing data

Clarifications, wherever possible, will be obtained from the respective Investigator or data management team for any missing data or for any illegible entry, unused or unauthenticated data and this will be recorded in the data handling report (If required) before the final database lock.

Dropouts and missing values, considering missing values as missing at random (MAR) will be imputed by using multiple imputation method for primary efficacy variable, for mITT population only, and will be considered as supportive to the analysis.

Dropouts and missing values will not be imputed for safety and secondary endpoints.

Imputed data should be flagged and properly footnoted as "imputed". Title should indicate that imputed data is used for summary.

Adverse events with unknown end date/time will be counted as an ongoing AEs, if ongoing is ticked on the CRF. Medications with unknown end date/time will be considered as concomitant. Adverse events and medications with partially missing start or end dates will be considered ongoing and concomitant respectively unless the non-missing portion of the dates definitively proves otherwise.

Partial dates for Adverse events and medications will be imputed as follows for derivation of treatment emergent and Prior/Concomitant flags respectively:

- Missing day in start date of a time period is imputed by the first day of the month.
- Missing day in end date of a time period is imputed by the last day of the month.
- Missing month in start date of a time period is imputed by January of the year.
- Missing month in end date of a time period is imputed by December of the year.
- Missing year is not imputed.
- After above imputation if start or end date is after Participant's end of study date then start or end date is set to Participant's end of study date.

If required, time will be imputed in the following way:
Times should be printed in the format "HH:MM". "HH" represents the 2-digit hour portion of the time. "MM" represents the 2-digit minute portion of the time. Both hour and minute portions of time are zero padded integer values. Missing time portions should be represented on Participant listings as dashes ("10: --" and "--:--").

Missing or partial dates for medical history findings will not be completed by imputation, for example, if only a month and year are available as --FEB2019, the day will not be imputed. If "Stop Date" information is not available, it will be assumed that the finding is "Ongoing" at the time of enrollment in the study.

8.5 Sample Size Calculation

The primary efficacy endpoint of this study is "change from baseline in hepatic fat content at Week 24 as measured by MRI-PDFF".

Sample Size at the Study Initiation:

The sample size was estimated assuming change of 0.8 unit from baseline (treatment difference), standard deviations of 0.3 and 0.4 units, at one-sided 2.5% level of significance (α) and with β level of 0.20 (i.e., 80% power). Using these assumptions, at least 23 completed subjects in each arm (Saroglitazar Magnesium 4 mg and placebo) was required for PP analysis. Considering ~20% dropout rate, around 60 subjects should be enrolled in this proof-of-concept study, with 1:1 treatment allocation ratio i.e. Saroglitazar Magnesium 4 mg (30): placebo (30).

There was no available data with this type of study. In order to understand the disease prevalence and enhance our knowledge of correlation of PCOS and NAFLD, determination of sample size section has been revised.

Revised Sample Size based on current protocol version 5.0:

A sample size of 74 completed participants (37 participants in each treatment arm) will provide 80% power to detect a 4% treatment difference in change from baseline in hepatic fat content at Week 24 between Saroglitazar 4 mg and Placebo using a two-sided 5% level of significance based on a two-sample t-test, assuming change from baseline in hepatic fat content of 9% at Week 24 in Saroglitazar 4 mg treatment arm with a common standard deviation of 0.6.

Assuming a 20% dropout rate at week 24, approximately 90 participants will be randomized in a 1:1 ratio to receive either Saroglitazar 4 mg (45 Participants) or placebo (45 Participants). The sample size estimation was performed using PASS 14 software.

A total of 12 Participants, 6 Participants in each treatment arm will be included in the pharmacokinetic assessment.

In view of the difficulty and challenges observed in recruitment of study population, it was decided to close recruitment at 60 participants.

8.6 Interim Analysis

No Interim Analysis has been planned for this study.

8.7 Statistical Software

All statistical analyses will be performed using SAS® Version 9.4 or higher [SAS Institute Inc., USA]. The sample size estimation was performed using PASS 14 software.

9 Statistical Analyses

9.1 Participant Disposition

Participant disposition table will be presented by treatment group and by overall. The following summaries will be included in the disposition table: total number of participants screened in the study, number of participants who failed screening, number of participants discontinued before randomization (apart from screen failure), number of participants randomized, number of participants treated (i.e., administered with treatment), number of participants who completed the study (Week 24 treatment assessment), and number of participants who discontinued from the study with primary reason for discontinuation. Percentages of participants will be calculated based on the number of participants who are randomized. All screened participants (i.e., who have provided informed consent) will be used for participants disposition summary table.

Summary of participants for each investigational site will also be provided by treatment using frequency count and percentage (%) for safety population.

Participants who are consented to participate in the study, by-participants data listing for all available data information will be provided for participant disposition.

9.2 Analysis Populations

The analysis population will be defined and the assignment of participants to each of the analysis population will be finalized before data base lock (DBL). The complete list of participants excluded from any of the analysis populations as well as the reason(s) for exclusion will be presented. Analysis population, that is number (n) and percentage (%) of participants included in each analysis population, will be presented by treatment group and by overall, for all centers/countries combined as appropriate for the study design. A participant may have more than one reason for exclusion from a given analysis population and all percentages will be calculated relative to the number of participants randomized. All randomized participants will be used for analysis populations summary table.

9.3 Protocol Deviation

The number (n) and percentage (%) of participants presenting with at least one protocol deviation, as determined by sponsor before DBL, will be presented by treatment groups and overall, for all investigational sites combined as appropriate for the study design. An additional summary of participants per major protocol deviation category as well as minor protocol deviation will also be presented. Safety analysis population will be used for participants protocol deviation summary table. Participants may have more than one protocol deviation, which will be counted only once with respect to deviation and deviation category.

The by-participants data listing will be prepared for all protocol deviations.

9.4 Baseline Characteristics

9.4.1 Demographic Data and Other Baseline Characteristics

Demographic and baseline characteristics will be summarized descriptively by the treatment group and by overall for the Safety, mITT and PP populations.

Descriptive summaries will be provided for the demographic and baseline characteristics. Demographic characteristics such as age, gender, race, ethnicity, baseline height, baseline weight, baseline waist circumference, baseline Body Mass Index (BMI), reproductive status, history of significant emotional problems, history of ovarian dysfunction, history of alcohol intake and hirsutism score will be summarized and tabulated for all the analysis populations. All the continuous variables (i.e., age, height etc.) will be summarized by n, mean, standard deviation, minimum, median and maximum values. All the categorical variables (i.e., gender, race etc.) will be summarized as frequency count (n) and percentage (%).

A by-participants data listing for all demographic and baseline characteristics data for randomized participants will be provided. Safety analysis population will be used for by participants data listing.

9.4.2 Medical History

Medical history findings will be coded using the latest version of the Medical Dictionary for Regulatory Activities (MedDRA), and will be presented by Primary System Organ Class (SOC), and by Preferred Term (PT) within SOC.

The number (n) and percentage (%) of unique participants with at least one medical history finding will be presented by default summary statistics. In addition, the number (n) and percentage (%) of participants with at least one medical history finding within each primary SOC, and PT, will be presented by treatment group for all centers combined. Safety analysis population will be used for Medical History summary table. Participants may have more than one medical history, will be counted only once with respect to Primary System Organ Class, and by Preferred Term within SOC.

A by-participant listing of medical history information will be provided for safety population.

9.5 Prior and Concomitant Medications

Medications are classified according to active drug using substances latest version of the World Health Organization Drug Dictionary WHODrug (Global).

Prior medications are defined as medications that started and ended prior to the first administration of study drug. Concomitant medications are defined as medications started on or after first administration of study drug and include medications started prior to the first administration of study drug but continued during the study.

A summary for the frequency and percentage of participants who had previous therapies/medications and a separate summary of participants who had concomitant therapy/medications according to the WHODrug Global primary ATC level 3 subgroup, Preferred Name will be provided treatment group for safety

population. If a medication codes to the ATC level 2 only, the ATC level 2 will be presented in the table in place of the ATC level 3 subgroup.

A by-participant data listing of all prior and concomitant medications including the reported term, Preferred Name, ATC level 3 term (ATC level 2 term, if ATC level 3 is missing), start dates, stop dates and other relevant data will be provided for safety population. Each medication included in the data listing, will be flagged to indicate whether it was a prior or concomitant medication.

9.6 Extent of Exposure and Compliance

Study duration is defined as the date of last visit minus date of informed consent date plus one. Treatment duration is defined as the date of last dose administration minus the date of the first dose administration plus one. If the date of last dose is not available, the date of the last visit will be used in the calculation. If the date of first dose is not available, the date of first study drug dispensation will be used in the calculation. Study duration and the treatment duration will be summarized descriptively by treatment groups for overall study.

Total IP compliance as collected on CRF, will be summarized descriptively by treatment groups. In addition, a categorical summary of compliance will also be presented using the following categories: < 80%, 80% to 120% and >120%. A participant is considered to be compliant if participant takes ≥ 80% but ≤120% of the study drug during the study treatment period. Safety analysis population will be used for extent of exposure and compliance summary table.

A by-participant data listing of all information related to exposure and compliance relevant data will be provided for safety population.

9.7 Efficacy Analysis

9.7.1 Primary Efficacy Analysis

9.7.1.1 Endpoint

The primary efficacy endpoint is the change from baseline in hepatic fat content at Visit 8 (Week 24) measured by MRI-PDFF.

9.7.1.2 Estimand

The attributes for the primary estimand related to the first primary endpoint are described below:

1. Treatment: The study compares the efficacy of the Investigational Product (i.e., Saroglitazar Magnesium 4mg) versus the Placebo as randomized in 1:1 ratio.

2. Population: The target population is female participants of PCOS with NAFLD, 18 to 45 years of age. Primarily, analysis will be based on the PP population.

3. Variable: The primary endpoint is the "Change in hepatic fat content from baseline to Week 24" measured by MRI-PDFF.

4. Intercurrent Events:

- Missing Data: Participants may discontinue the study treatment before completing the Visit 8 (Week 24) period, might miss the Week 24 MRI-PDFF measurement, will be considered as missing. The missing data values may be imputed for primary endpoint analysis to consider the analysis treatment effect assuming all participants completed treatment as planned.

- Rescue/Concomitant medication: Participants might require additional treatments (rescue medication or concomitant medications) during the treatment period. The effect of the study treatment will be evaluated regardless of the rescue or concomitant medication.

- Change in ALT inclusion criteria: Participants recruited before the amendment may not fulfill the ALT inclusion criteria due to absence of inclusion criterion. A selection bias will be handled by conducting sensitive analysis, for analyzing subgroup treatment difference (within stratum) based on the ALT score, which will lead to assess whether the change in inclusion criteria has influenced the treatment effect. OR adjustment of the covariates for ALT levels can be performed.

5. Population Level Summary:

The primary efficacy endpoint, the change from baseline in hepatic fat content at Visit 8 (Week 24) will be analyzed using an analysis of covariance (ANCOVA) model. The effectiveness of the investigational product (Saroglitazar magnesium 4 mg) will be achieved using the lower bound of the 95% confidence interval of the LS Mean difference between the treatment groups.

9.7.1.3 Analysis Strategy

Primary analysis will be primarily based on the PP population and analysis, based on mITT population with missing value imputation for primary endpoint will be considered as supportive analyses.

The primary efficacy endpoint in this study is the change in hepatic fat content from baseline following 24 weeks of treatment measured by MRI-PDFF. The change from baseline of hepatic fat will be determined as (Visit 8 [Week 24] value – Baseline value).

The actual values observed and change from baseline values of hepatic fat content will be summarized using the number of non-missing observations (n), mean (Mean), standard deviation (SD), median, minimum (Min) and maximum (Max) by treatment groups for baseline and scheduled all visits (i.e. baseline to Week 24 visits).

To check the mean significance difference between baseline and scheduled visit for Week 24, a paired t-test at 5% level of significance will be used.

Following sample SAS code will be used for paired t-test:

```
proc ttest data=data sides=2 alpha=0.5;
paired BASE*AVAL;
run;
```

Where AVAL: variable with post baseline value; BASE: variable with baseline value.

The primary efficacy endpoint, the change from baseline in hepatic fat content at Week 24 will be analyzed using an analysis of covariance (ANCOVA) model. The model will include change in the hepatic fat content values from baseline as dependent variable, treatment group as a fixed effect and baseline values as a covariate.

The estimate the LS means for treatment groups and its 95% confidence interval, the difference of LS Mean for treatment group (Saroglitazar magnesium 4 mg – Placebo) and its 95% confidence interval of the difference of LS Mean for treatment group, and p-value to check the significance difference at 5% level of significance will be generated using ANCOVA model.

The following sample SAS code pertains to the ANCOVA analysis:

```
proc mixed data=DATA;
class TRT;
model CHG = BASE TRT/solution;
lsmeans TRT/ stderr pdiff cl alpha=0.05;
ods output diffs = DIFFS lsmeans = LSMEANS;
run;
```

Where, CHG: variable with change from baseline values; BASE: variable with baseline values; TRT: variable with treatment values.

The effectiveness of the investigational product (Saroglitazar Magnesium 4 mg) compared to placebo will be obtained and thus the null and alternative hypothesis will be state as follows:

Null hypothesis, H0: $S \leq P$

i.e., Mean change in hepatic fat content for treatment group (Saroglitazar magnesium 4 mg) – Mean change in hepatic fat content for control group (Placebo) ≤ 0

Alternative hypothesis, H1: $S > P$

i.e., Mean change in hepatic fat content for treatment group (Saroglitazar magnesium 4 mg) – Mean change in hepatic fat content for control group (Placebo)> 0

Where, S = Treatment effect of Saroglitazar Magnesium 4 mg, P = Treatment effect of Placebo.

The effectiveness of the investigational product (Saroglitazar magnesium 4 mg) will be achieved using the lower bound of the 95% confidence interval of the LS Mean difference between the treatment groups. If the lower bound of the 95% confidence interval of the LS Mean difference between the treatment groups is greater than 0, Investigational product (Saroglitazar magnesium 4 mg) will lead to the conclusion that the treatment effect of Saroglitazar Magnesium 4 mg is statistically significantly greater than the treatment effect of placebo group and hence the test drug is more effective than placebo, and the study will be considered a success.

9.7.1.4 Handling of Missing values

For the primary analysis, resulting missing values will be replaced using MI procedure (like a hypothetical strategy in the estimand framework). The data will be separated into two subsets based on the treatment groups which will ensure that the imputation process accounts for potential difference between these

groups. Complete dataset will be generated using PROC MI and recombine the data set for subsequent analysis. The number of imputed data set should be sufficient to ensure reliable result. The number of imputations (m) may be determined using fraction of missing information and the percentage of missing data. Generally, 5 to 20 imputations are required to perform to ensure robust result. A productive mean approach or regression method can be used for the imputation. PROC MIANALYZE will be used to combine the results of complete dataset results.

9.7.1.5 Sensitivity Analysis

In order to test robustness of results following analyses will be performed:

- Change in hepatic fat content from baseline to Week 24 will be analyzed using analysis of covariance (ANCOVA) model for PP population. No missing values will be imputed for the analysis.
- Change in hepatic fat content from baseline to Week 24 will be analyzed using analysis of covariance (ANCOVA) model for mITT population, where missing values will be imputed as per above strategy.

9.7.1.6 Subgroup Analysis

The primary endpoint will be analyzed separately based on the prespecified ALT scores and geographical region as subgroups, and the treatment effect estimates will be presented for each subgroups. The model used for the primary analysis will be applied within each subgroup to estimate the treatment effect. The PP and mITT populations – Imputed will be used for primary endpoint subgroup analysis.

The subgroups are defined as follows:

a) ALT Scores

- ALT values at baseline >= 38
- ALT values at baseline < 38

b) Geographical region (Country):

- Mexico
- USA

9.7.2 Secondary Efficacy Analysis

9.7.2.1 Endpoints

The secondary efficacy endpoints are:

1. Change from baseline in Liver Enzymes/LFTs (ALT, AST, ALP, GGT, serum protein, albumin and total bilirubin) at Week 12 and Week 24.
2. Change from baseline in Insulin resistance (IR) measured by Homeostasis Model Assessment (HOMA) at Week 12 and Week 24.
3. Change from baseline in CK-18, hs-CRP, TNFα and liver stiffness measured by transient elastography/FibroScan at Week 24.

4. Change from baseline in controlled attenuation parameter measured by transient elastography/ FibroScan at Week 24.
5. Change from baseline in body weight, body mass index (BMI) and waist circumference at Week 12 and Week 24.
6. Change from baseline in MRI-derived total liver fat index and total liver volume at Week 24.
7. Change from baseline in serum lipid profile and lipoproteins (TG, TC, HDL, LDL, sdLDL, VLDL, ApoA and ApoB) at Week 12 and Week 24.
8. Change from baseline in Sex hormone binding globulin (SHBG) level at Week 12 and Week 24.
9. Change from baseline in ovarian function (Total testosterone, 17-hydroxyprogesterone, free testosterone, luteinizing hormone, follicle-stimulating hormone, LH-to-FSH ratio and estradiol) at Week 12 and Week 24.
10. Change from baseline in free androgen index at Week 12 and Week 24.

9.7.2.2 Analysis Strategy

The analysis for the secondary efficacy endpoints performed as below:

For the analysis of the secondary endpoints, i.e., Change from baseline in Liver Enzymes/LFTs, Insulin resistance (IR) measured by HOMA, CK-18, hs-CRP, TNFα, liver stiffness, controlled attenuation parameter, body weight, body mass index (BMI), waist circumference, total liver fat index, total liver volume, serum lipid profile and lipoproteins, sex hormone binding globulin level, ovarian function parameters and free androgen index. The analysis of covariance ANCOVA model will be applied separately at each visit as appropriate. The model will include treatment as a fixed effect and the corresponding baseline values of the endpoint as a covariate.

For each visits the estimate of the LS Means for treatment groups and its 95% confidence interval, LS Mean for treatment group difference (Saroglitazar magnesium 4 mg – Placebo) and its 95% confidence interval of the LS Mean for treatment group difference, and p-value to check the significance difference at 5% level of significance will be generated from ANCOVA model. These analyses will provide the treatment effect at each visit while controlling for baseline differences

Descriptive summaries will be provided for all the secondary efficacy endpoints at each scheduled visit by treatment group. All secondary efficacy analysis will be conducted primarily based on the PP population and analysis, based on mITT population will be considered as supportive analyses .

9.7.3 Exploratory Efficacy Analysis

Not applicable

9.7.4 Pharmacokinetics Analysis

Pharmacokinetic analyses plan (PAP) will be prepared separately.

9.8 Safety Analysis

9.8.1 Adverse Events

The applicable definition of an Adverse Event (AE) is any unfavorable or unintended sign, symptom or disease temporally associated with the use of study drug whether or not considered related to study drug. as per the study protocol. Treatment-emergent AEs are defined as any AE that started after the first dose of study drug or started before the first dose but increased in severity or frequency after administration of the initial dose of study drug. The period for treatment-emergent AE analysis starts from the first exposure to the study drug until the participant exits the study.

All the AEs, serious adverse events (SAEs), treatment emergent adverse event (TEAEs) and expected adverse event reported throughout the study, shall be coded and classified according to the standards of latest version of MedDRA (Medical Dictionary for Regulatory Activities) and grouped by preferred term (PT) and system organ class (SOC).

All adverse events for each participant, including the same event on several occasions should be listed for safety population giving both preferred term and original term used by the investigator.

The summary of frequency counts of the number of adverse events (E), and the number of participants with adverse events (n), and the percentages (%) for the number of participants with adverse events will be presented for treatment groups and for overall. For the summaries which count the number of participants, if a participant has more than one TEAE the participant will be counted only once in accordance with SOC and PT. When AEs occur more than once for a participant, the maximal severity (Maximum severity between severity and CTCAE Grade will be considered) and the strongest relationship to the treatment group will be counted. Safety analysis population will be used for adverse events summary tables.

In addition to an overall presentation of all TEAEs, reports will be generated for special classes of TEAEs as follows:

- Overall Summary of AEs
- TEAEs by SOC and PT
- Serious TEAEs by SOC and PT
- TEAEs leading to death by SOC and PT
- TEAEs leading to permanent discontinuation by SOC and PT
- TEAEs by SOC, PT and by Strongest Relationship to Study Drug
- TEAEs by SOC, PT and by Maximum Severity

9.8.2 Laboratory Parameters

Clinical laboratory assessments for renal function test, creatine kinase, urinalysis, BNP, NT-pro BNP, cardiac troponin, CK-MB, Lipase and Amylase will be performed at the Screening, Baseline, Week 2, Week 8, Week 12, Week 16 and Week 24 visits. Laboratory assessments for hs-CRP, TSH, T3, T4 and TNFα will be performed at the Screening and Week 24 visits. All other laboratory assessments will be performed at

Screening, Week 12 and Week 24 visits. Laboratory values will be presented using the International System of Units (SI units).

Observed and changes from baseline values will be summarized descriptively (n, mean, median, standard deviation, minimum, and maximum values) at each assessment. A summary table of the categorical grade shift changes using the normal ranges from baseline to last study visit will be provided based on safety population.

Additionally, A summary of frequency count and percentages for abnormal liver enzyme parameters at each visit as well as worst value across all visits up to EOT will be provided by treatment group for the following categories.

- ALT ≥ 3 x ULN, ≥ 5 x ULN and ≥ 10 x ULN
- AST ≥ 3 x ULN, ≥ 5 x ULN and ≥ 10 x ULN
- Total Bilirubin > 2 x ULN
- ALT ≥3 x ULN and Total Bilirubin ≥2 x ULN
- ALT ≥3 x ULN and Total Bilirubin ≥1.5 x ULN
- AST ≥3 x ULN and Total Bilirubin ≥2 x ULN
- AST ≥3 x ULN and Total Bilirubin ≥1.5 x ULN
- ALP >1.5 x ULN

A summary of abnormal liver enzyme parameters for patients with elevated ALT or AST at baseline (elevated at baseline is defined as, baseline ALT or AST ≥1.5 x ULN) at each visit as well as worst value across all visits up to EOT will be provided by treatment group using frequency count and percentage for the following categories.

- ALT >5 x baseline value at post-baseline visits
- ALT >3 x baseline value at post-baseline visits
- ALT >2 x baseline value at post-baseline visits with either a concomitant Total Bilirubin increase >2 x ULN or INR increase by > 0.2
- AST >5 x baseline value at post-baseline visits
- AST >3 x baseline value at post-baseline visits
- AST >2 x baseline value at post-baseline visits with either a concomitant Total Bilirubin increase >2 x ULN or INR increase by > 0.2

For summary purposes, laboratory values that are listed as above or below particular thresholds will be numerically listed as above or below that threshold, respectively, by the minimum measured amount for that parameter. For example, if a parameter is measured to two decimal places, and has a result of "> 6" then, for summary purposes, the value of 6.01 will be used. Values with "<" or ">" will be classified as Low or High, respectively, unless such classifications aren't applicable for that parameter, in which case they will be classified as Normal.

A by-participants data listing will be provided for safety population, which contains data information for each available laboratory parameter based on safety population.

The plot of correlation between peak Total Bilirubin vs. ALT values will be generated. The horizontal and vertical lines will be as such, divide the graph into quadrants indicate Hy's law thresholds.

9.8.3 Vital Signs

Vital signs parameters include blood pressure, pulse rate, oral temperature and respiratory rates. Vital signs assessments will be performed at screening, baseline, Week 2, Week 8, Week 12, Week 16 and Week 24 visits.

Descriptive summaries (n, mean, median, standard deviation, minimum and maximum values) of observed values (i.e., baseline and post baseline) and change from baseline in each vital sign parameter at each schedule assessment visit will be presented based on the safety population.

A by-participant listing will be provided for the vital sign parameter assessments based on the safety population.

9.8.4 12-Lead ECG

A 12-lead electrocardiogram (ECG) will be performed at Screening (considered as baseline), Week 12 and Week 24 visits. ECG results (normal, abnormal clinically insignificant, abnormal clinically significant) will be summarized by treatment groups for each scheduled visit using change from baseline in each ECG parameters and shifts from baseline in overall ECG assessment tables. Listing of the participants who had gone through the ECG examination will be presented. Safety population will be used for listing and summary table of 12-lead ECG.

9.8.5 General Physical Examination

Physical examination assessments will be performed at screening, baseline, Week 2, Week 8, Week 12, Week 16 and Week 24 visits. Physical examination results (normal/abnormal/ not done) from scheduled visits will be summarized using frequency count and percentage by treatment groups for each body system based on safety population.

A Physical examination results will be listed for the safety population.

9.8.6 Pregnancy Test

Listing will be provided for the pregnancy test for the safety population.

9.8.7 Other Safety Parameters

Not applicable.

9.9 Subgroup Analyses

Primary endpoints i.e., Chang in hepatic fat content, and following secondary endpoints will be analyzed across subgroups using the same analysis as specified for the primary and secondary endpoints., PP and mITT analysis population will be used for subgroup analysis.

1. Liver Enzymes/LFTs (ALT, AST, ALP, GGT, serum protein, albumin, and total bilirubin)

2. Liver stiffness measurement obtained via transient elastography/ FibroScan®
3. MRI-derived total liver fat index and total liver volume
4. Serum lipid profile and lipoproteins (TG, TC, HDL, LDL, sdLDL, VLDL, ApoA and ApoB)

The subgroups are defined as follows:

a) ALT Scores

- ALT values at baseline >= 38
- ALT values at baseline < 38

b) Geographical region (Country):

- Mexico
- USA

10 Deviation from the Study Protocol

The planned analysis will be performed according to the study protocol, its amendments and this statistical analysis plan. Contradictions between the study protocol or its amendments and this statistical analysis plan, the analysis will be performed according to this analysis plan. Any deviation from the planned analysis according to the study protocol has to be reported.

The differences between study protocol and statistical analysis plan are summarized in the following table:

Change	Study protocol	Statistical analysis plan
The terminology Patient(s) and Subject(s) has been replaced with Participant(s) throughout the document.	Patient(s) and Subject(s) has been used.	Used Participant(s) instead.
Missing values imputation	LOCF has been defined for primary and secondary variables imputation.	Only primary variable will be imputed with missing values by using multiple imputation method and secondary variables will be analysed as observed.
Subgroup analysis	No subgroup analysis strategy has been defined.	Primary and defined secondary efficacy analysis endpoints will be analyzed across subgroups as defined in section 9.9 using the same analysis as specified for the primary and secondary endpoints.
Estimand	No estimand framework has been defined	Estimand framework for primary efficacy endpoint has been defined in the SAP.
Statistical significance	Statistical significance of the null hypothesis will be tested at a one-sided p-value <0.025.	The effectiveness of the investigational product (Saroglitazar magnesium 4 mg) will be achieved using the lower bound of the 95% confidence interval of the LS Mean difference between the treatment groups.

11 Database Lock and Unblinding

The SAP will be finalized prior to database lock.

12 References

1. Clinical Study Protocol, Version No. 5.0, Dated 06th February 2020
2. Case Report Form (CRF) final Version No. 2.3, Dated 13th May 2020
3. ICH Harmonized Tripartite Guideline E 3. Structure and Content of Clinical Study Reports, November 1995. (www.ich.org; Guidelines; "Efficacy" Topics)
4. ICH Harmonized Tripartite Guideline E 9. Statistical Principles for Clinical Trials, February 1998. (www.ich.org; Guidelines; "Efficacy" Topics)
5. Guidance for Industry Drug-Induced Liver Injury: Premarketing Clinical Evaluation

13 Appendices

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