MEDPACE

STATISTICAL ANALYSIS PLAN

Protocol Title:	A PHASE 2A, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY EVALUATING THE SAFETY AND EFFICACY OF EFRUXIFERMIN IN SUBJECTS WITH NONALCOHOLIC STEATOHEPATITIS (NASH)
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Investigational Product:	Efruxifermin (EFX)
Sponsor:	Akero Therapeutics, Inc [redacted]
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CONFIDENTIAL

SIGNATURE PAGE

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We, the undersigned, have reviewed and approved this Statistical Analysis Plan:

Signature **Date**

[redacted]

VERSION HISTORY

Version	Version Date	Description
1.0	04 January 2021	Original signed version
1.1	26 January 2021	Adjust language for Liver Biopsy Evaluable Analysis Set
1.2	10 February 2021	Updated per Sponor request: Indicate two sets of biopsy data (local read v.s. central read); Added an analysis for ELF Week 12 data if available, and adjust analysis visit windown for Week 12 ELF; F4 Safety Set added for selected safety analysis
2.0	05 March 2021	Second signed version

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LIST OF ABBREVIATIONS

Abbreviation	Definition
ADA	Anti-drug Antibodies
AE	Adverse Event
AESI	Adverse Event of Special Interest
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
ANCOVA	Analysis of Covariance
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
BLQ	Below Limit of Quantification
BMI	Body Mass Index
BSAP	Bone Specific Alkaline Phosphatase
C3M	Neo-epitope of MMP-9 Mediated Degradation of Type III Collagen
CLDQ-NAFLD	Chronic Liver Disease Questionnaire-Nonalcoholic Fatty Liver Disease
CP	Child Pugh
CRN	Clinical Research Network
CRF	Case Report Form
CSR	Clinical Study Report
cT1	Corrected T1
CTCAE	Common Terminology Criteria for Adverse Events
DILI	Drug-Induced Liver Injury
DMC	Data Monitoring Committee
DXA	Dual Energy X-ray Absorptiometry
eDISH	Evaluation of Drug-Induced Serious Hepatotoxicity
ECG	Electrocardiogram
EFX	Efruxifermin
ELF™	Enhanced Liver Fibrosis Panel
EOT	End of Treatment
FAS	Full Analysis Set
GGT	Gamma Glutamyl Transferase
HRQoL	Health-Related Quality of Life
INR	International Normalized Ratio
LLOQ	Low Limit of Quantification
MedDRA	Medical Dictionary for Regulatory Activities
MELD	Model for End-Stage Liver Disease
MMRM	Mixed-Model Repeated-Measures
NAb	Neutralizing Antibody
NAFLD	Nonalcoholic Fatty Liver Disease
NAS	NAFLD Activity Score
NASH	Nonalcoholic Steatohepatitis
PK	Pharmacokinetics
PPAS	Per Protocol Analysis Set
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SF-36	Short Form 36 Health Survey

Abbreviation	Definition
SOC	System Organ Class
TB	Total Bilirubin
TEAE	Treatment-Emergent Adverse Event
TESAE	Treatment-Emergent Serious Adverse Event
TFLs	Tables, Figures, and Listings
WHO	World Health Organization
WPAI	Work Productivity and Activity Impairment

1 INTRODUCTION

The purpose of this Statistical Analysis Plan (SAP) is to provide a description of the statistical methods to be implemented for the analysis of the Cohort C data from Akero Therapeutics, Inc. Protocol AK-US-001-0101. A separate SAP has been provided for the analysis of Main Study data from Akero Therapeutics, Inc. Protocol AK-US-001-0101. The SAP will be finalized prior to unblinding of the Cohort C database. Any deviations from the SAP after database unblinding will be documented in the final Clinical Study Report (CSR).

2 STUDY OVERVIEW

2.1 Study Objectives

2.1.1 Primary Objective

The primary objective of this study is:

- To assess the safety and tolerability of EFX in NASH subjects with compensated cirrhosis

2.1.2 Secondary Objectives

The secondary objectives of this study are:

- To evaluate the change from baseline in liver stiffness as evaluated by FibroScan® at Week 16
- To evaluate the change from baseline in non-invasive plasma (serum) fibrosis biomarkers including liver fibrosis by ELF™ Test score and pro-C3 levels

2.1.3 Exploratory Objectives

The exploratory objectives of this study are:

- Change from baseline in markers of liver injury and function including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), bilirubin, International Normalized Ratio (INR), albumin, Model for End-Stage Liver Disease (MELD) score, and Child Pugh (CP) score
- Change from baseline in body weight and waist-to-hip ratio
- Change from baseline in bone mineral density of the lumbar spine, femoral neck, and total hip as measured by Dual Energy X-ray Absorptiometry (DXA)
- The proportion of subjects – whose fibrosis regresses by ≥ 1-stage according to the NASH CRN classification
- The proportion of subjects who had no worsening in NAS with improvement in fibrosis stage
- The proportion of subjects who had at least 2 points improvement in NAS with no worsening in fibrosis stage
- The proportion of subjects who had ≥ 1 point improvement in NAS, fibrosis, steatosis, lobular inflammation or hepatocellular ballooning

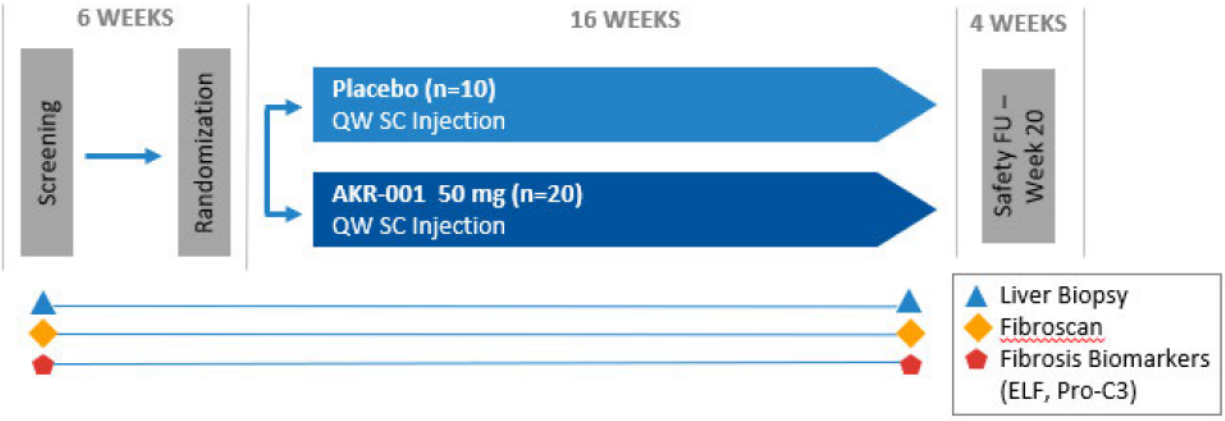
- Changes from baseline in health-related quality of life (HRQoL)
- Changes from baseline in lipoprotein profile and markers of lipid metabolism, insulin sensitivity and glycemic control
- Change from baseline in body fat distribution as measured by DXA total body composition
- Plasma concentrations of EFX
- To evaluate decompensated liver disease events including ascites, hepatic encephalopathy (HE), or variceal bleeding

2.2 Study Design

2.2.1 Overview

This is a Phase 2a, randomized, double-blind, placebo-controlled study evaluating the safety and efficacy of EFX in subjects with NASH.

Cohort C will enroll approximately 30 subjects with biopsy-proven NASH. All subjects in Cohort C will have F4 fibrosis. Subjects meeting the study's entry criteria will be randomly assigned in a 1:2 ratio into 2 treatment groups as shown in the figure below:



There will be no stratification for Cohort C. Study drug will be administered subcutaneously once weekly (QW) for a total of 16 weeks. After 16 weeks of treatment, a safety follow-up visit will occur at Week 20. Following 16 weeks of treatment, subjects will be given the option to collect an end of treatment biopsy.

This study will be conducted at approximately 30 sites in the U.S. Additional sites may be added, depending on subject accrual rates.

2.2.2 Sample Size Determination

Since the primary objective is to assess the safety and tolerability of EFX in NASH subjects with compensated cirrhosis, the sample size is determined based on clinical considerations, and the treatment comparisons of efficacy measurements are not powered.

2.3 Study Endpoints

2.3.1 Secondary Efficacy Endpoints

The secondary endpoints are:

- Change from baseline in liver stiffness as evaluated by FibroScan® at Week 16
- Changes from baseline in non-invasive biomarkers including Pro-C3 at Weeks 12, 16 and 20, and liver fibrosis by ELF™ Test score at Weeks 6, 12 and 16

2.3.2 Exploratory Efficacy Endpoints

The exploratory endpoints are:

- Change from baseline in markers of liver injury and function including ALT, AST, ALP, GGT, bilirubin, INR, albumin, MELD score, and CP score at Weeks 12, 16 and 20
- Change from baseline in body weight and waist-to-hip ratio at Weeks 12, 16 and 20
- Change from baseline in bone mineral density of the lumbar spine, femoral neck, and total hip as measured by DXA at Week 16
- The proportion of subjects at Week 16 whose fibrosis regresses by ≥ 1-stage according to the NASH CRN classification
- The proportion of subjects at Week 16 who had no worsening in NAS with improvement in fibrosis stage
- The proportion of subjects at Week 16 who had at least 2 points improvement in NAS
- The proportion of subjects at Week 16 who had ≥ 1point improvement in NAS, fibrosis, steatosis lobular inflammation or hepatocellular ballooning
- The proportion of subjects at Week 16 who had NASH resolution (0-1 Point Inflammation, 0 Point Ballooning)
- The proportion of subjects at Week 16 who had fibrosis improvement ≥ 2-stage
- Changes from baseline in HRQoL (SF-36, CLDQ-NAFLD, WPAI) at Weeks 12 and 16
- Changes from baseline in lipoprotein profile and markers of lipid metabolism, insulin sensitivity and glycemic control at Weeks 12, 16 and 20
- Change from baseline in body fat distribution as measured by DXA total body composition at Week 16
- Plasma concentrations of EFX
- The incidence and severity of any decompensated liver disease events including ascites, hepatic encephalopathy (HE), or variceal bleeding
- Changes from baseline in Neo-epitope of MMP-9 Mediated Degradation of Type III Collagen (C3M)
- Changes from baseline in platelets at Weeks 12, 16 and 20
- Change from baseline in liver steatosis as evaluated by FibroScan® (CAP) at Week 16

2.3.3 Safety Endpoints

The safety endpoint is the safety and tolerability of EFX in NASH subjects with compensated cirrhosis.

Safety analyses include: summaries of extent of exposure, adverse events (AEs), laboratory evaluations, electrocardiogram (ECG), vital sign assessments, body weight, anti-drug antibody (ADA) and neutralizing antibody (NAb) assessments, and concomitant medication usage.

3 STATISTICAL METHODOLOGY

3.1 General Considerations

3.1.1 Analysis Day

Analysis day will be calculated from the date of first dose of study drug. The day of the first dose of study drug will be Day 1, and the day immediately before Day 1 will be Day -1. There will be no Day 0, in alignment with international data standards for clinical trials. Analysis day will be calculated as (date of clinical event – date of first dose of study drug) + 1 if the date of the event is on or after the date of first dose and as (date of clinical event – date of first dose of study drug) if the date of event is before the date of first dose.

3.1.2 Analysis Visits

Scheduled visits will be assigned to analysis visits as recorded on the Case Report Form (CRF). Unscheduled and early termination visits for ELF™ will be assigned to analysis visits according to the following visit windows:

Analysis Visit	Target Analysis Day	Low Analysis Day	High Analysis Day
Week 6	43	22	64
Week 12	85	65	99
Week 16	113	100	141
Note: if the unscheduled collection or early term collection is >21 days after the last dose of study drug, it will not be used in analyses.			

For ALT, markers of liver injury and function, waist-to-hip ratio, biomarkers, pro-C3 and HRQoL, unscheduled and early termination visits will be assigned to analysis visits according to the following visit windows:

Analysis Visit	Target Analysis Day	Low Analysis Day	High Analysis Day
Week 1	8	2	15
Week 4	29	16	43
Week 8	57	44	71
Week 12	85	72	99
Week 16	113	100	127
Week 20 Safety follow-up	141	128	EOS
Note: if the unscheduled collection or early term collection is >14 days after the last dose of study drug, it will not be used in analyses.			

For body weight, unscheduled and early termination visits will be assigned to analysis visits according to the following visit windows:

Analysis Visit	Target Analysis Day	Low Analysis Day	High Analysis Day
Week 1	8	2	11
Week 2	15	12	18
Week 3	22	19	25
Week 4	29	26	32
Week 5	36	33	39
Week 6	43	40	46
Week 7	50	47	53
Week 8	57	54	60
Week 9	64	61	67
Week 10	71	68	74
Week 11	78	75	81
Week 12	85	82	88
Week 13	92	89	95
Week 14	99	96	102
Week 15	106	103	109
Week 16	113	110	127
Week 20 Safety follow-up	141	128	EOS
Note: if the unscheduled collection or early term collection is >14 days after the last dose of study drug, it will not be used in analyses.			

The efficacy assessments from two FibroScan® (Screening and Week 16) and the safety assessments from two DXA Scans (Screening and Week 16) will be considered for the analysis regardless of when the second assessment or biopsy takes place. Unscheduled visits after the first dose of study drug and early termination visits will be assigned as post-baseline.

For PK concentration summaries, a concentration that is intended as predose will be excluded from analysis if it is >24 hours before a dose or after the current dose. Beyond this rule, PK concentrations must be within the visit window to be included in summary statistics of PK.

Within an analysis visit window, the measurement from the scheduled visits will be used if available. If no scheduled visit occurs, the measurement from the visit closest to the defined target analysis day within the window will be used. If there is more than one measurement with equal distance to the defined target analysis day, the latter will be used. If no visits occur within a visit window, the measurement for this visit will be treated as missing.

3.1.3 Definition of Baseline

For all variables except lipids and liver enzymes variables, pre-dose measurements on Baseline visit (Day 1) will be considered the baseline values. If the measurement at this visit is not available, the last measurement prior to the first dose of study drug may be used as the baseline value unless it is stated otherwise. The scheduled baseline visit for FibroScan, liver biopsy, DXA scan, and ELF™ is Screening. Baseline lipid variables including Total Cholesterol, HDL-C, LDL-C, Triglycerides, non-HDL cholesterol will be the average of Screening and Baseline visit (Day 1) values. Baseline liver enzymes variables including ALT and AST will be the average of Pre-Baseline and Baseline visit (Day 1) values. If one is missing for lipids and liver enzymes variables, the available one will be used.

3.1.4 Summary Statistics

Categorical data will generally be summarized with counts and percentages of subjects. The denominator used for the percentage calculation will be clearly defined. Continuous data will generally be summarized with descriptive statistics including n (number of non-missing values), mean, median, standard deviation, minimum, and maximum. For certain continuous data, it will be summarized with descriptive statistics including n (number of non-missing values), arithmetic mean, arithmetic standard deviation, geometric mean, geometric coefficient of variation, median, minimum, and maximum. PK concentrations will be summarized with the set of continuous parameters including geometric mean and will add the statistic of number of samples below the limit of quantification (nblq).

All individual subject data will be listed as measured.

3.1.5 Hypothesis Testing

The statistical hypotheses will be tested at the 2-sided, 0.05 significance for the parameters with neutral direction unless specified otherwise.

3.1.6 Handling of Dropouts and Missing Data

Missing data can have an impact on the interpretation of the trial data. In general, values for missing data will not be imputed.

Where appropriate, safety data for subjects that did not complete the study will be included in summary statistics. For example, if a subject received study drug, the subject will be included in a summary of AEs according to the treatment received; otherwise, if the subject is not dosed then they will be excluded from the summary. If safety laboratory results for a subject are missing for any reason at a time point, the subject will be excluded from the calculation of summary statistics for that time point. If the subject is missing a pre-dose value, then the subject will be excluded from the calculation of summary statistics for the pre-dose value and the change from pre-dose values.

Values for missing safety laboratory data will not be imputed; however, a missing baseline result will be replaced with a screening result, if available. If no pre-treatment laboratory value is available, the baseline value will be assumed to be normal (i.e., no grade [Grade 0]) for the summary of graded laboratory abnormalities.

Values for missing vital signs data will not be imputed; however, a missing baseline result will be replaced with a screening result, if available.

Below limit of quantification (BLQ) PK concentration at pre-dose at Baseline will be imputed as zero and the other pre-dose BLQ PK concentrations will be imputed as half of the low limit of quantification (0.5*LLOQ).

3.2 Analysis Populations

3.2.1 Full Analysis Set (FAS)

The FAS will include all subjects who were randomized into the study. The FAS will be the primary analysis set for efficacy analyses.

Subjects who receive a dose of study drug other than that to which they were randomized for the entire duration of treatment will be analyzed according to treatment group to which they were randomized.

3.2.2 Safety Set

The Safety Set will include all subjects who received at least one dose of study drug. The Safety Set will be the primary analysis set for safety analyses.

Subjects who received a dose of study drug other than that to which they were randomized for the entire duration of treatment will be analyzed according to the dose of study drug received. All data collected during treatment plus 30 days after last dose of study drug will be included in the safety summaries.

3.2.3 F4 Safety Set

The F4 Safety Set will be a subset of the Safety Set. It will exclude Safety Set subjects who are not confirmed F4 fibrosis by histology central reads.

3.2.4 PK Analysis Set

The PK Analysis Set will include all randomized subjects who took at least one dose of study drug and for whom concentration data of EFX is available.

3.2.5 Biomarker Analysis Set

The Biomarker Analysis Set will include data from subjects in the Safety Set who have the baseline and at least one on-study measurement to provide interpretable results for ELF™ Test score or pro-C3 levels.

3.2.6 Per Protocol Analysis Set (PPAS)

The PPAS is defined as any subject who is randomized, receives at least one dose of study drug without any major protocol deviations. A full detail of inclusions and exclusions from PPAS will be in the classifications specifications and finalized before unblinding.

3.2.7 Liver Stiffness Evaluable Analysis Set

The Liver Stiffness Evaluable Analysis Set will be a subset of the FAS. It will include all FAS subjects who have Baseline and Week 16 liver stiffness as evaluated by FibroScan.

3.2.8 Liver Biopsy Evaluable Analysis Set

Liver Biopsy Evaluable Analysis Set will be a subset of the FAS. It will include all FAS subjects with confirmed F4 fibrosis at baseline by central reads who have Baseline and Week 16 liver biopsy results. It will be the analysis population for the responders based on histologic evaluation of NAS system and fibrosis stage.

3.2.9 Stratification

Not Applicable.

3.3 Subject Data and Study Conduct

3.3.1 Subject Disposition

Counts and percentages of subjects who were screened (signed informed consent), discontinued early during screening (screen failures), and randomized will be summarized in total based on all screened subjects. Reasons for early discontinuation will also be summarized. In addition, discontinuation contributed by COVID-19 will be summarized.

Counts and percentages of subjects in each of the following disposition categories will be presented by treatment and in total based on all randomized subjects:

- Subjects who were randomized
- Subjects who started study drug
- Subjects who completed the treatment
- Subjects who withdrew from the treatment
- Subjects who completed the study
- Subjects who withdrew from the study

For randomized subjects who withdraw from the treatment and withdraw from the study, the primary reason for the withdrawal will be summarized. In addition, early discontinuation from the treatment contributed by COVID-19 and early discontinuation from the study contributed by COVID-19 will be summarized.

3.3.2 Protocol Deviations

Protocol deviations will be defined in the Protocol Deviation Plan. Counts and percentages of subjects with CSR reportable protocol deviations by deviation category will be summarized by treatment and in total based on all randomized subjects. All protocol deviations and COVID-19 related protocol deviations will be listed.

3.3.3 Analysis Populations

Counts and percentages of subjects in each analysis population will be summarized by treatment and in total based on all randomized subjects.

3.3.4 Demographic and Baseline Characteristics

The following demographic and baseline characteristics will be summarized:

- Age (years) and age categories (<45 years, ≥45 to <65 years, ≥65 years)
- Sex
- Race
- Ethnicity
- Height (cm) at Screening
- Weight (kg) at Baseline
- Body mass index (BMI) (kg/m^2) at Baseline and BMI categories at Baseline (<30 kg/m^2, ≥30 kg/m^2)
- Waist circumference (cm) at Baseline
- Hip circumference (cm) at Baseline

- Waist-to-hip ratio at Baseline
- Type 2 diabetes status at Screening
- Statin Use at Baseline
- Vitamin E/Thiazolidinedione Use at Baseline
- Fibrosis stage (local read) at Screening
- Biopsy diagnosis (local read) at Screening
- NAS and NAS components (local read) at Screening
- Fibrosis stage (central read) at Screening
- Biopsy diagnosis (central read) at Screening
- NAS and NAS components (central read) at Screening
- Liver Stiffness as Evaluated by FibroScan at Screening (kiloPascals [kPa])
- Liver Steatosis as Evaluated by FibroScan at Screening (Controlled Attenuation Parameter [CAP])
- Alanine aminotransferase (U/L) and Aspartate Aminotransferase (U/L) at Baseline
- Triglyceride (mg/dL), Total Cholesterol (mg/dL), LDL-C (mg/dL), HDL-C (mg/dL), and non-HDL-C (mg/dL) at Baseline
- Hemoglobin A1c (%) at Baseline
- Endogenous FGF21 at Baseline
- MELD Score at Baseline
- CP Score at Baseline
- ELF Score at Baseline
- Pro-C3 (ug/L) at Baseline
- ALT >= 3xULN at Baseline
- AST >= 3xULN at Baseline

Demographic and baseline characteristics will be summarized with descriptive statistics or counts and percentages of subjects as appropriate by treatment and in total for all randomized subjects and each defined analysis population if the analysis population composition is different than all randomized subjects.

3.3.5 Medical History

Medical history will be coded to system organ class (SOC) and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA) version 22.0. Counts and percentages of subjects with medical history by SOC and preferred term will be summarized by treatment and in total based on all randomized subjects.

3.3.6 Concomitant Medications

Concomitant medications will be coded to anatomical therapeutic chemical (ATC) class and preferred term using the World Health Organization (WHO) Drug Dictionary version 2019G B3. For summary purposes, medications will be considered prior medications if they stopped prior to the first dose of study drug and concomitant medications if they were taken at any time on or after the first dose of study drug (i.e. started prior to the first dose of study drug and were ongoing or started after the first dose of study drug).

Counts and percentages of subjects taking concomitant medications by ATC class and preferred term will be summarized by treatment and in total based on the Safety Set. The use of any prior medication or concomitant medication will be listed for all randomized subjects.

3.3.7 Study Drug Exposure and Compliance

Weeks of exposure to study drug will be calculated as:

(date of last dose of study drug - date of first dose of study drug + 1) / 7

Weeks of exposure to study drug will be summarized by treatment based on the Safety Set with descriptive statistics and with counts and percentages of subjects with exposure in the following categories:

- >0 to ≤4 weeks
- >4 to ≤8 weeks
- >8 to ≤12 weeks
- >12 to ≤16 weeks
- >16 weeks

The total number of injections administered will be calculated for each subject. A contingency table will be provided to display the number and percentage of subjects in each treatment group with the following number of injections: 1-3, 4-6, 7-9, 10-12, 13-15, >=16.

Subjects that miss 2 or more doses of study drug over the course of study participation are considered noncompliant. The frequency and percentage of subjects who are compliant and noncompliant will be summarized by treatment group.

3.4 Efficacy Assessment

Efficacy data will be summarized and analyzed by randomized treatment based on the FAS unless otherwise specified. For the secondary endpoints, the boxplots over time will be provided.

3.4.1 Secondary Efficacy Endpoints

3.4.1.1 Change from baseline in liver stiffness as evaluated by FibroScan® at Week 16

Liver stiffness will be assessed using FibroScan® at Screening and Week 16. Summary statistics at all visits for the values, change from baseline and percent change from baseline will be provided.

The change and percent change from baseline at Week 16 in liver stiffness expressed in kPa will be analyzed with an analysis of covariance (ANCOVA) model with treatment group as a factor and baseline liver stiffness as evaluated by FibroScan® as a covariate using the FAS. The treatment effect estimate, 95% CI and pvalues will be provided. Missing values at Week 16 will be imputed using the last-observed-carried-forward (LOCF) method. The same analysis will be repeated on the Liver Stiffness Evaluable Analysis Set and the PPAS, and no imputation will be performed.

The SAS sample code is listed:

```
**********************************************************************
  TREATMENT: 0 (Placebo), 1 (EFX 50 mg)
  BASE: Baseline liver stiffness as evaluated by FibroScan
  CHG: Change from baseline to Week 16 in liver stiffness
**********************************************************************;
```

```
proc glm;
  class TREATMENT;
  model CHG = TREATMENT BASE / p;
  lsmeans TREATMENT / stderr pdiff cl;
  estimate "EFX 50 mg : Placebo" TREATMENT -1 1;
run;
```

The Shapiro-Wilk normality test will be performed for the residuals from the model above. If the p-value is < 0.01, then non-parametric analyses will be explored.

3.4.1.2 Changes from baseline in non-invasive biomarkers including Pro-C3 at Weeks 12, 16 and 20 , and liver fibrosis by ELF™ Test score at Weeks 6, 12 and 16

ELF™ Test score and its components including hyaluronic acid (HA), procollagen III amino terminal peptide (PIIINP), tissue inhibitor of metalloproteinase 1 (TIMP-1) will be measured at Screening, Week 6 and Week 16. Values and changes from baseline in ELF™ Test score and its components will be summarized descriptively. ANCOVA model with treatment group as a factor and baseline value as a covariate based on the FAS will be used for analyzing the change from baseline to Week 16. LS means, 95% confidence intervals and p-values will be presented. Missing values will be imputed using the LOCF method. The same analysis will be repeated on the Biomarker Analysis Set and the PPAS, and no imputation will be performed. The Shapiro-Wilk normality test will be performed for the residuals from the model above. If the p-value is < 0.01, then non-parametric analyses will be explored. Week 12 of ELF Test score and its components will be included in the summary and the change from baseline to Week 12 will be analyzed using the same ANCOVA model if the data is available.

Pro-C3 will be measured at Screening, Baseline (Day 1), Week 1, Week 4, Week 8, Week 12, Week 16 and Week 20 Safety follow-up. Values and changes from baseline in Pro-C3 will be summarized descriptively. The change and percent change from baseline to Weeks, 4, 8, 12, 16 and 20 will be analyzed using ANCOVA model in a manner similar to the ELF™ Test score and its components.

3.4.2 Exploratory Efficacy Endpoints

The exploratory efficacy endpoints are defined in Section 2.3.3. Descriptive statistics at each scheduled visit for the values and changes from baseline of the exploratory efficacy endpoints will be summarized. For certain efficacy endpoints, logarithmic transformation may be performed prior to fitting the ANCOVA model. Since these endpoints are for exploratory purposes, all the analysis will be based on the observed values and no adjustments for multiplicity will be made expcept for liver steatosis as evaluated by FibroScan® expressed in CAP.

3.4.2.1 Markers of liver injury and function

Markers of liver injury and function including ALT, AST, ALP, GGT, bilirubin, INR, albumin, MELD score, and CP score will be measured at Screening, Pre-Baseline, Baseline (Day 1), Week 1, Week 4, Week 8, Week 12, Week 16 and Week 20 Safety follow-up.

CP score will be calculated as below, ranging from 5-15:

	1 point	**2 point**	**3 point**
Bilirubin (Total)	<2 mg/dL (<34.2 µmol/L)	2-3 mg/dL (34.2-51.3 µmol/L)	>3 mg/dL (>51.3 µmol/L)
Albumin	>3.5 g/dL (>35 g/L)	2.8-3.5 g/dL (28-35 g/L)	<2.8 g/dL (<28 g/L)
INR	<1.7	1.7-2.2	>2.2

Ascites	Absent	Slight	Moderate
Encephalopathy	No Encephalopathy	Grade 1-2	Grade 3-4
Class A = 5-6 points Class B = 7-9 points Class C = 10-15 points			

ANCOVA model with treatment group as a factor and baseline value as a covariate will be used for analyzing the change from baseline to Weeks 4, 8, 12, 16, and 20, as well as the percent change from baseline to Weeks 4, 8, 12, 16 and 20. LS means, 95% confidence intervals and p-values will be presented.

3.4.2.2 Body weight and waist-to-hip ratio

Body weight, waist circumference and hip circumference will be measured at all visits.

ANCOVA model with treatment group as a factor and baseline value as a covariate will be used for analyzing the change from baseline and percent change from baseline to Weeks 4, 8, 12, 16, and 20. LS means, 95% confidence intervals and p-values will be presented.

3.4.2.3 Biomarkers

Lipid metabolism biomarkers and insulin sensitivity & glycemic control biomarkers will be measured at Baseline (Day 1), Week 1, Week 4, Week 8, Week 12, Week 16 and Week 20 Safety follow-up.

ANCOVA model with treatment group as a factor and baseline value as a covariate will be used for analyzing the change from baseline to Week 12, the change from baseline to Week 16, and the change from baseline to Week 20, as well as the percent change from baseline to Week 12, 16 and 20. LS means, 95% confidence intervals and p-values will be presented.

3.4.2.4 DXA scan measurements

DXA scans measurements including bone mineral density of the lumbar spine, femoral neck, total hip and body fat distribution will be performed at Baseline (Day 1) and Week 16.

An analysis will be performed on the change from baseline to Week 16 in DXA Scan measurements using ANCOVA model with treatment group as a factor and baseline value as a covariate. LS means, 95% confidence intervals and p-values will be presented.

3.4.2.5 Liver biopsy

- The proportion of subjects at Week 16 whose fibrosis regresses by ≥ 1-stage according to the NASH CRN classification
- The proportion of subjects at Week 16 who had no worsening in NAS with improvement in fibrosis stage
- The proportion of subjects at Week 16 who had at least 2 points improvement in NAS
- The proportion of subjects at Week 16 who had ≥ 1 point improvement in NAS, fibrosis, steatosis lobular inflammation or hepatocellular ballooning
- The proportion of subjects at Week 16 who had NASH resolution (0-1 Point Inflammation, 0 Point Ballooning)
- The proportion of subjects at Week 16 who had fibrosis improvement ≥ 2-stage

Following 16 weeks of treatment, subjects will be given the option to collect an end of treatment biopsy. Counts and percentages of subjects will be presented by treatment group based on the Liver Biosy Evaluable Analysis Set using central reads.

3.4.2.6 HRQoL

HRQoL including Short Form 36 Health Survey (SF-36), Chronic Liver Disease Questionnaire-Nonalcoholic Fatty Liver Disease (CLDQ-NAFLD) and Work Productivity and Activity Impairment (WPAI) will be collected at Baseline (Day 1), Week 1, Week 4, Week 8, Week 12, and Week 16.

ANCOVA model with treatment group as a factor and baseline value as a covariate will be used for analyzing the change from baseline to Week 12 and the change from baseline to Week 16. LS means, 95% confidence intervals and p-values will be presented.

SF-36: The SF-36 asks 36 questions to measure functional health and well-being from the subject's point of view. It consists of eight health domains in the table below. These health domain scales contribute to the physical health and mental health summary measures.

The scores are weighted sums of the questions in each domain. All the raw scores will be transformed to scores ranging from 0 - 100. Higher scores represent better health. Physical Component Summary (PCS) is calculated by positively weighting the four subscales in the physical domain (PF, RP, BP and GH) and the remaining psychological domain subscales negatively. In contrast, the Mental Component Summary (MCS) is calculated by positively weighting the four mental domain subscales (VT, SF, RE and MH), and negatively weighting the four physical domain subscales.

Domains	Number of Items	Items
Physical functioning (PF)	10	3, 4, 5, 6, 7, 8, 9, 10, 11, 12
Role-physical (RP)	4	13, 14, 15, 16
Bodily pain (BP)	2	21, 22
General health (GH)	5	1, 33, 34, 35, 36
Vitality (VT)	4	23, 27, 29, 31
Social functioning (SF)	2	20, 32
Role-emotional (RE)	3	17, 18, 19
Mental health (MH)	5	24, 25, 26, 28, 30

CLDQ-NAFLD: The CLDQ-NAFLD asks questions related to liver disease and specifically NAFLD, to measure health related quality of life in subjects with chronic liver disease.

The questionnaire has 36 items grouped into six domains: Abdominal Symptoms, Activity, Emotional, Fatigue, Systemic Symptoms, and Worry. Items are scored by a 7-point rating scale from 1 (all of the time) to 7 (none of the time). The higher item values indicate better health. The domain score will be calculated as dividing the sum of the domain's items by the number of items within that domain. The total score will be calculated as an average of the six domain scores.

Domains	Number of Items	Items
Abdominal Symptoms (AS)	3	1, 5, 17
Fatigue (FA)	6	2, 4, 8, 11, 13, 35
Systemic Symptoms (SS)	6	3, 6, 21, 23, 27, 36
Activity (AC)	5	7, 9, 14, 30, 31
Emotional Function (EF)	9	10, 12, 15, 16, 19, 20, 24, 26, 34
Worry (WO)	7	18, 22, 25, 28, 29, 32, 33

WPAI: The questionnaire asks questions regarding the effect of NASH on a person's ability to work and perform regular activities.

The WPAI consists of six questions: 1 = currently employed; 2 = hours missed due to specified problem; 3 = hours missed other reasons; 4 = hours actually worked; 5 = degree problem affected productivity while working; 6 = degree problem affected regular activities. WPAI

outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity. Four main outcomes can be generated and expressed in percentages by multiplying the following scores by 100:

- Percent work time missed due to problem: Q2 / (Q2 + Q4)
- Percent impairment while working due to problem: Q5 / 10
- Percent overall work impairment due to problem:
  Q2 / (Q2 + Q4) + [(1 - (Q2 / (Q2 + Q4))) x (Q5 / 10)]
  For those who missed work and did not actually work in the past seven days, the percent overall work impairment due to problem will be equal to the percent work time missed due to problem.
- Percent activity impairment due to problem: Q6 / 10

3.4.2.7 Lipoprotein profile and free fatty acids

Lipoprotein profile including Total Cholesterol, HDL-C, LDL-C, Triglycerides, and free fatty acids will be measured at Screening, Baseline (Day 1), Week 1, Week 4, Week 8, Week 12, Week 16 and Week 20 Safety follow-up.

Non-HDL cholesterol will be calculated as Total Cholesterol - HDL-C.

ANCOVA model with treatment group as a factor and baseline value as a covariate will be used for analyzing the change from baseline and percent change from baseline to Weeks 4, 8, 12, 16, and 20. LS means, 95% confidence intervals and p-values will be presented.

3.4.2.8 C3M and PRO-C3/C3M Ratio

C3M will be measured at Baseline (Day 1), Week 4, Week 8, Week 12, Week 16, and Week 20. PRO-C3/C3M Ratio will be derived at all available timepoints. ANCOVA model w ith treatment group as a factor and baseline value as a covariate will be used for analyzing the change from baseline to Week 12, and the change from baseline to Week 16. LS means, 95% confidence intervals and p-values will be presented.

3.4.2.9 Platelets

Platelets will be measured at Screening, Baseline (Day 1), Week 1, Week 4, Week 8, Week 12, Week 16 and Week 20 Safety follow-up.

ANCOVA model with treatment group as a factor and baseline value as a covariate will be used for analyzing the change from baseline and percent change from baseline to Weeks 4, 8, 12, 16, and 20. LS means, 95% confidence intervals and p-values will be presented.

3.4.2.10 Liver steatosis as evaluated by FibroScan® at Week 16 expressed in CAP

Liver steatosis will be assessed using FibroScan® at Screening and Week 16. Summary statistics at all visits for the values, change from baseline and percent change from baseline will be provided.

The change and percent change from baseline at Week 16 in liver steatosis expressed in CAP will be analyzed with an analysis of covariance (ANCOVA) model with treatment group as a factor and baseline liver steatosis as evaluated by FibroScan® as a covariate using the FAS. The treatment effect estimate, 95% CI and pvalues will be provided. Missing values at Week 16 will be imputed using the LOCF method. The same analysis will be repeated on the Liver Stiffness Evaluable Analysis Set and the PPAS, and no imputation will be performed.

3.4.3 Subgroups

Subgroup analyses will be performed for the secondary efficacy endpoint. The group variables include statin use, Type 2 diabetes status and baseline Endogenous FGF21.

The glycemic control biomarkers will be summarized and analyzed by the following subgroup: type 2 diabetes status.

The lipoprotein profile will be summarized and analyzed by the following subgroup: statin use.

3.5 Safety Assessment

The safety of EFX will be assessed during the study through the reporting of AEs, clinical laboratory tests, ECG, vital sign assessments, body weight, ADA and NAb assessments, and concomitant medication usage.

All safety data collected on or after the date that study drugs were first dispensed up to the date of last dose of study drugs plus 30 days will be summarized by treatment group. Data for the follow-up period will be included in data listings.

Safety data will be summarized by actual treatment received (and in total for selected analyses) based on the Safety Set unless otherwise specified. Selected safety data will be repeated on F4 Safety Set.

3.5.1 Adverse Events

All AEs will be coded to system organ class and preferred term using MedDRA version 22.0 or the latest version.

Treatment-emergent adverse events (TEAEs) are defined as one or both of the following:

- Any AEs with an onset date/time on or after the study drugs start date/time and no later than 30 days after permanent discontinuation of study drugs
- Any AEs leading to premature discontinuation of study drugs.

Injection site reactions, diarrhea, hypoglycemia and drug-induced liver injuries (DILI) will be monitored as AEs of special interests (AESIs) during this study. During the course of the study, additional AESIs may be identified by the Sponsor.

An overview of AEs will be provided including counts and percentages of subjects with the following:

- Any TEAEs (overall and by maximum severity)
- Any study drug related TEAEs (overall and by maximum severity)
- Any study procedure related TEAEs (overall and by maximum severity)
- Any TEAEs of special interest (overall, injection site reactions, diarrhea, hypoglycemia, DILI)
- Any TEAE of decompensated liver disease events including ascites, hepatic encephalopathy (HE), or variceal bleeding
- Any serious AEs (SAEs)
- Any treatment-emergent serious AEs (TESAEs)

- Any TEAEs leading to premature discontinuation of study drug
- Any TEAEs leading to premature discontinuation of study
- Any AEs leading to death

Counts and percentages of subjects will also be presented by system organ class and preferred term for each of the categories in the overview, as well as the common (>=5% in any treatment group) TEAEs. Listings will be provided of all AEs, including AESIs, decompensated liver disease events, SAEs, TEAEs leading to discontinuation of study drug, and AEs leading to death. Counts and percentages of subjects will be presented by preferred term and period (weekly and every 4 weeks) for selected most frequent TEAE.

Counts and percentages of subjects will be repeated on F4 Safety Set for the following:

- An overview of AEs
- Any TEAEs (overall and by maximum severity)
- Any study drug related TEAEs (overall and by maximum severity)
- Any TEAEs leading to premature discontinuation of study drug
- Any TEAEs of special interest (overall, injection site reactions, diarrhea, hypoglycemia, DILI)

3.5.2 Clinical Laboratory Tests

Chemistry, hematology, and coagulation samples will be collected at Screening, Pre-Baseline, Baseline (Day 1), Week 1, Week 4, Week 8, Week 12, Week 16 and Week 20 Safety follow-up.

All continuous laboratory parameters except of liver injury and function markers (see section 2.3.3) will be summarized descriptively by value at baseline and each planned post-baseline visit, together with the corresponding changes from baseline. All categorical laboratory parameters will be tabulated at baseline and each planned post-baseline visit.

For the selected parameters, the incidence of graded treatment-emergent laboratory abnormalities will be presented for laboratory data using the grading scheme in the Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0.

Laboratory	CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4
Chemistry	Alanine aminotransferase increased	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
	Aspartate aminotransferase increased	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
	Blood bilirubin increased	Total Bilirubin >ULN - 1.5 x ULN if baseline was normal;	Total Bilirubin >1.5 - 3.0 x ULN if baseline was normal;	Total Bilirubin >3.0 - 10.0 x ULN if baseline was normal;	Total Bilirubin >10.0 x ULN if baseline was normal;

Laboratory	CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4
		> 1.0 - 1.5 x baseline if baseline was abnormal	>1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 10.0 x baseline if baseline was abnormal	>10.0 x baseline if baseline was abnormal
	Alkaline phosphatase increased	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
	Creatinine increased	>ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 x baseline; >3.0 - 6.0 x ULN	>6.0 x ULN
	CPK increased	>ULN - 2.5 x ULN	>2.5 x ULN - 5 x ULN	>5 x ULN - 10 x ULN	>10 x ULN
	Hyperkalemia	Potassium >ULN - 5.5 mmol/L	Potassium >5.5 - 6.0 mmol/L	Potassium >6.0 - 7.0 mmol/L	Potassium >7.0 mmol/L
	Serum amylase increased	>ULN - 1.5 x ULN	>1.5 - 2.0 x ULN	>2.0 - 5.0 x ULN	>5.0 x ULN
	Hypoglycemia	Glucose <LLN - 55 mg/dL; <LLN - 3.0 mmol/L	Glucose <55 - 40 mg/dL; <3.0 - 2.2 mmol/L	Glucose <40 - 30 mg/dL; <2.2 - 1.7 mmol/L	Glucose <30 mg/dL; <1.7 mmol/L;
	GGT increased	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
Hematology	Anemia	Hemoglobin (Hgb) <LLN - 10.0 g/dL; <LLN - 6.2 mmol/L; <LLN - 100 g/L	Hemoglobin (Hgb) <10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 – 80 g/L	Hemoglobin (Hgb) <8.0 g/dL; <4.9 mmol/L; <80 g/L	
	Hemoglobin increased	Hemoglobin > ULN & Increase in >0 - 2 g/dL	Hemoglobin > ULN & Increase in >2 - 4 g/dL	Hemoglobin > ULN & Increase in >4 g/dL	
	CD4 lymphocytes decreased	<LLN - 500/mm3; <LLN - 0.5 x 10e9 /L	<500 - 200/mm3; <0.5 - 0.2 x 10e9 /L	<200 - 50/mm3; <0.2 x 0.05 - 10e9 /L	<50/mm3; <0.05 x 10e9 /L
	Neutrophil count decreased	<LLN - 1500/mm3; <LLN - 1.5 x 10e9 /L	<1500 - 1000/mm3; <1.5 - 1.0 x 10e9 /L	<1000 - 500/mm3; <1.0 - 0.5 x 10e9 /L	<500/mm3; <0.5 x 10e9 /L
	White blood cell decreased	<LLN - 3000/mm3; <LLN - 3.0 x 10e9 /L	<3000 - 2000/mm3; <3.0 - 2.0 x 10e9 /L	<2000 - 1000/mm3; <2.0 - 1.0 x 10e9 /L	<1000/mm3; <1.0 x 10e9 /L
	Platelet count decreased	<LLN - 75,000/mm3; <LLN - 75.0 x 10e9 /L	<75,000 - 50,000/mm3; <75.0 - 50.0 x 10e9 /L	<50,000 - 25,000/mm3; <50.0 - 25.0 x 10e9 /L	<25,000/mm3; <25.0 x 10e9 /L
Coagulation	INR increased	>1.2 - 1.5; >1 - 1.5 x baseline if on anticoagulation	>1.5 - 2.5; >1.5 - 2.5 x baseline if on anticoagulation	>2.5; >2.5 x baseline if on anticoagulation	

For the other parameters, the incidence of abnormalities (as defined by normal ranges) prior to the first dose of study drug and after the first dose of study drug will be summarized with counts and percentages of subjects.

The incidence of treatment-emergent laboratory abnormalities, defined as values that increase at least one toxicity grade from baseline at any time post baseline up to and including the date of last dose of study drugs plus 30 days, will be summarized with counts and percentages of subjects by treatment group. If baseline data are missing, then any graded abnormality (i.e., at least a Grade 1) will be considered treatment-emergent. If no pre-treatment laboratory value is available, the baseline value will be assumed to be normal (i.e., no grade [Grade 0]) for the summary of graded laboratory abnormalities.

Evaluation of drug-induced serious hepatotoxicity (eDISH) plot will be provided to display peak serum ALT and Total Bilirubin (TB) levels for each subject. The peak serum AST versus TB levels for each subject will also be provided.

3.5.3 Vital Signs

Height will be measured without shoes at Screening. Other vital signs (body weight, BMI, systolic and diastolic blood pressure, pulse, respiration rate and oral temperature) will be measured at each visit. Triplicate blood pressure and heart rate will be measured at Baseline (Day 1) and at 48 - 96 hours post-dose on Weeks 4 and Week 8.

Values and changes from baseline to each visit and timepoint for vital signs will be summarized descriptively. Triplicate measurements will be averaged prior to summary.

3.5.4 12-Lead Electrocardiograms

12-lead ECG will be measured at Screening, Baseline (Day 1) and Week 16.

Values and changes from baseline of ECG parameters (heart rate, PR interval, QRS Interval, QT interval, QTcB interval, QTcF interval and RR interval) and overall interpretation will be summarized by visit. The number and percentage of subjects with absolute QTc interval values in the pre-specified categories (>450, >480, and >500 msec), and QTc interval change (>30 and >60 msec) will be summarized.

3.5.5 Other Safety Assessments

ADA, NAb and other safety data will be listed. Additionally, the subject visits impacted by COVID-19 will be listed.

3.6 Pharmacokinetic (PK) Assessment

PK sampling will be obtained pre-dose at Baseline (Day 1), Week 1, Week 4, Week 8, Week 12, Week 16, Week 20 Safety follow-up, and at 48-96 hours post-dose on Week 4 and Week 8.

Plasma EFX concentrations will be listed and summarized by treatment group, visit, and time point for the PK Analysis Set.

3.7 Pharmacodynamic (PD) Assessment

Saliva cortisol testing will be obtained pre-dose at Baseline (Day 1), Week 1, Week 4, Week 8, Week 12, Week 16, Week 20 Safety follow-up, and at 48-96 hours post-dose on Week 4 and Week 8.

Values of Saliva cortisol and changes from baseline to each visit will be summarized descriptively on Safety Set.

ANCOVA model with treatment group as a factor and baseline value as a covariate will be used for analyzing the absolute change from baseline to Week 16. LS means, 95% confidence intervals and p-values will be presented. The analysis will be based on the ovbserved values and no adjustments for multiplicity will be made.

3.8 Bone Biomarker Assessment

Bone biomarkers samples (Osteocalcin, P1NP, CTX-1, BSAP, PTH, and Vitamin D) will be collected at Baseline (Day 1), Week 1, Week 4, Week 8, Week 12, Week 16 and Week 20 Safety follow-up.

Values of bone biomarkers and changes from baseline to each visit will be summarized descriptively on Safety Set.

ANCOVA model with treatment group as a factor and baseline value as a covariate will be used for analyzing the absolute change from baseline to Week 16. LS means, 95% confidence intervals and p-values will be presented. The analysis will be based on the ovbserved values and no adjustments for multiplicity will be made.

4 DATA MONITORING COMMITTEE (DMC)

An external DMC that consists of two hepatologists, one cardiologist and a statistician will review the progress of the study.

The DMC's specific activities will be defined by a mutually agreed charter, which will define the DMC's membership, conduct, and meeting schedule.

While the DMC will be asked to advise Akero regarding future conduct of the study, including possible early study termination based on the stopping rules from the protocol, Akero retains final decision-making authority on all aspects of the study.

5 INTERIM ANALYSIS

No formal interim analysis is planned.

6 CHANGES FROM PROTOCOL-SPECIFIED STATISTICAL ANALYSES

The following exploratory endpoints related to liver biosy are added for Cohort C:

- The proportion of subjects at Week 16 who had NASH resolution (0-1 Point Inflammation, 0 Point Ballooning)
- The proportion of subjects at Week 16 who had fibrosis improvement ≥ 2-stage

The exploratory endpoint related to liver biosy is updated for Cohort C "The proportion of subjects at Week 16 who had at least 2 points improvement in NAS" from "The proportion of subjects who had 2 points improvement in NAS with no worsening in fibrosis stage"

The subgroup analysis is added for lipoprotein profile by statin use, and for glycemic control biomarkers by type 2 diabetes status.

Week 12 will be analyzed for ELF and its components if the data is available.

The following exploratory endpoints are added for Cohort C:

- ALT is added as one of the markers of liver injury and function.
- C3M
- PRO-C3/C3M ratio
- Change from baseline in platelets at Weeks 12, 16 and 20
- Change from baseline in liver steatosis as evaluated by FibroScan® (CAP) at Week 16

7 PROGRAMMING SPECIFICATIONS

Analyses will be performed using SAS® version 9.4 or higher. All available data will be presented in subject data listings which will be sorted by subject and visit date as applicable. Detailed Programming Specifications will be provided in a separate document.

APPENDIX A: REFERENCES

Sanyal A, Charles ED, Neuschwander-Tetri BA, Loomba R, Harrison SA, Abdelmalek MF, et al. Pegbelfermin (BMS-986036), a PEGylated fibroblast growth factor 21 analogue, in patients with non-alcoholic steatohepatitis: a randomised, double-blind, placebo-controlled, phase 2a trial. Lancet. 2019; 392(10165) :2705-2717.