Genfit
Parc Eurasanté
885, avenue Eugène Avinée
59120 LOOS
France

An Open Label, Randomized, Multicenter Study to Assess the Pharmacokinetic and Pharmacodynamic Profile and the Safety and Tolerability of Two Dose Levels of Elafibranor (80 mg and 120 mg) in Children and Adolescents, 8 to 17 Years of Age, with Nonalcoholic Steatohepatitis (NASH)

Phase 2a Study

STATISTICAL ANALYSIS PLAN

Product: Elafibranor (GFT505)

Study No: GFT505E-218-1

Date: 20 August 2020

Version: Final 2.0

Reference: INF - SOP STAT 007 - Version 4.0_Statistical Analysis Plan

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STATISTICAL ANALYSIS PLAN APPROVAL FORM

SPONSOR: Genfit

STUDY NUMBER: GFT505-218-1

STUDY TITLE: An Open Label, Randomized, Multicenter Study to Assess the Pharmacokinetic and Pharmacodynamic Profile and the Safety and Tolerability of Two Dose Levels of Elafibranor (80 mg and 120 mg) in Children and Adolescents, 8 to 17 Years of Age, with Nonalcoholic Steatohepatitis (NASH)

STUDY PART: Final

VERSION: Final 2.0 - 20 August 2020

Author

PPD

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Date: 2020.08.21 17:11:30 +02'00'

Name: PPD **Signature** _____ **Date** __/___/____
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Reviewer Inferential

PPD

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Name: PPD **Signature** _____ **Date** __/___/____
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Reviewers Sponsor

PPD

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See all related documents attached

Version History

Version	Date	Author	Description
0.1	08 October 2019	PPD	Initial version
0.2	28 November 2019	PPD	Implementation of comments from Genfit on Draft 0.1
1.0	13 March 2020	PPD	Implementation of comments from Genfit on Draft 0.2
2.0	20 August 2020	PPD	Implementation of comments on version Final 1.0

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List of Abbreviations

AE	Adverse Event
AESI	Adverse Event of Special Interest
ALP	ALkaline Phosphatase
ALT	ALanine amino Transferase
AMA	Antimitochondrial Assay
ApoAI	Apolipoprotein A-I
ApoB	Apolipoprotein B
AST	ASpartate Transaminase
BMI	Body Mass Index
CI	Confidence Interval
CPK	Creatinine Phosphokinase
CV	Coefficient of Variation
DBP	Diastolic Blood Pressure
DRM	Data Review Meeting
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
eGFR	Estimated Glomerular Filtration Rate
EOS	End Of Study
EOT	End Of Treatment
FFA	Fatty Free Acids
GGT	Gamma-Glutamyl Transferase
HAV	Hepatitis A Virus
HbA1c	Hemoglobin A1C
HB	Hepatitis B
HCV	Hepatitis C Virus
HDL	High-Density Lipoprotein
HDL-C	High-Density Lipoprotein Cholesterol
HEV	Hepatitis E virus
HIV	Human Immunodeficiency Virus
HOMA-IR	HOmeostatic Model Assessment for Insulin Resistance
HRQOL	Health-Related Quality of Life

ICH	International Conference on Harmonisation
INR	International Normalized Ratio
ITT	Intent-To-Treat
LDL-C	Low-Density Lipoprotein Cholesterol
LLN	Lower Limit of Normality
LLT	Lower Level Term
MedDRA	Medical Dictionary for Regulatory Activities
N	Number
NASH	NonAlcoholic SteatoHepatitis
NCA	Non-Compartmental Analysis
PD	PharmacoDynamic
PedsQL™	Pediatric Quality of Life
PK	PharmacoKinetic
PT	Prothrombin Time
PT	Preferred Term
Q1	25th percentile
Q3	75th percentile
RBC	Red Blood Cells
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SBP	Systolic Blood Pressure
SD	Standard Deviation
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
TG	Triglycerides
TSH	Thyroid Stimulation Hormone
ULN	Upper Limit of Normality
VLDL-C	Very Low-Density Lipoprotein
WBC	White Blood Cells
WHODD	WHO Drug Dictionary
WHO-DRUG	World Health Organisation-Drug reference list

1. INTRODUCTION

This Statistical Analysis Plan (SAP) outlines and describes the statistical analyses of baseline, efficacy and safety data collected during the course of study GFT505E-218-1.

PharmacoKinetic (PK) analyses will be described in the PK SAP.

1.1 Objectives of the Study

1.1.1 Primary Objective

- To assess the pharmacokinetics of elafibranor and its active metabolite GFT1007, following once daily oral administration of two dose levels of elafibranor (80 mg and 120 mg) to children and adolescents, 8 to 17 years of age.

1.1.2 Secondary Objectives

- To assess changes in serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), and alkaline phosphatase (ALP) and other liver markers,
- To assess changes in markers of glucose homeostasis (homeostatic model assessment for insulin resistance (HOMA-IR) and fasting insulin),
- To assess changes in serum lipid parameters,
- To assess changes in body weight and Body Mass Index (BMI) Z-score,
- To assess changes in waist circumference,
- To assess changes in inflammatory markers,
- To assess the change in pediatric quality of life (PedsQL™) score as completed by the child/adolescent and the parent/legal guardian.

1.1.3 Safety Secondary Objectives

- To assess the safety and tolerability profile of two dose levels of elafibranor (80 mg and 120 mg) in children and adolescents, 8 to 17 years of age.

1.1.4 Exploratory objectives

- CCI [redacted]

1.2 Study Design

1.2.1 Experimental Design

- **Design:** Open-label, randomized, multicenter, sequential cohort study,

- **Centers:** Two planned centers in the United States,
- **Cohorts**: A total of 20 patients will be enrolled across the two cohorts:
  - Cohort 1: ≥12 to ≤17 years of age. A total of approximately 12 patients will be randomized in this cohort,
  - Cohort 2: ≥8 to ≤11 years of age. A total of approximately 8 patients will be randomized in this cohort. Enrollment in this cohort will not start until 80% of the patients in cohort 1 have been evaluated through Visit 4 by the Data Safety Monitoring Board (DSMB).
- **Study groups:** Patients will be randomized 1:1 to receive either dose:
  - 80 mg once daily for 12 weeks (n=10 patients),
  - 120 mg once daily for 12 weeks (n=10 patients).
- **Stratification**: Patients will also be stratified:
  - by age (Group 1: 8 to 11 years of age (approximately 8 patients) and Group 2: 12 to 17 years of age (approximately 12 patients),
  - and according to fibrosis severity (stratum 1: fibrosis stage 0 to 1 and stratum 2: fibrosis stage 2 to 3).
  - At least 4 patients ≥12 to ≤17 years of age and at least 2 patients ≥8 to ≤11 years of age with fibrosis stage 2 or 3 will be enrolled.
- **Treatment:** Daily dose of elafibranor for 12 weeks,
- **Blinding:** not applicable (open-label study),
- **Data collection:** Case Report Form (eCRF).

1.2.2 Study Duration

Each patient will participate in the study for up to approximately 20 weeks (screening through final follow-up visit).

1.2.3 Number of Patients

The primary objective of this study is to characterize individual PK parameters in children and adolescents 8 to 17 years of age (inclusive), by collecting rich PK samples to support non-compartmental analysis (NCA). Inter-patient variability of PK parameters in adults was low to moderate (coefficient of variation [CV]% ranged from 23.3% to 68.3%). Assuming a similar degree of variability in pediatric population, a sample size of 20 patients is set to target a 95% CI [confidence interval] within 60% and 140% of the geometric mean estimates of clearance and volume of distribution for elafibranor with at least 80% power (Wang, 2012). Additionally, 20 patients should be sufficient to evaluate the safety and tolerability and explore the responsiveness (efficacy) of once daily oral dosing of 80 mg and 120 mg of elafibranor for up to 12 weeks.

1.3 Study Parameters

1.3.1 Primary Endpoint

- Plasma concentrations of elafibranor and its active metabolite GFT1007.

1.3.2 Secondary Efficacy Endpoints

- Change from baseline in serum ALT, AST, GGT, ALP and other liver markers,
- Change from baseline in glucose homeostasis makers (fasting plasma glucose, HOMA-IR and fasting insulin),
- Change from baseline in serum lipid parameters,
- Change from baseline in body weight and BMI Z-score,
- Change from baseline in waist circumference,
- Change from baseline in inflammatory markers,
- Change from baseline in PedsQL™ scores.

1.3.3 Safety Parameters

- Incidence and severity of treatment emergent adverse events (TEAEs) and their relationship to study drug,
- Incidence of clinically meaningful changes from baseline in safety laboratory parameters, physical examination, electrocardiogram (ECG) and vital signs.

1.3.4 Exploratory parameters

- CCI [redacted]

1.3.5 Compliance

From Visit 1 and at each subsequent visit while the patient is being treated with study drug up to the End of Treatment (EOT) visit, the patient will be instructed to bring back all used and unused cartons and wallets containing blisters. Compliance will be checked by the Investigator or their designee during those visits and recorded in the eCRF. If treatment is interrupted, whatever the cause, duration and reason for the interruption should be documented in the dosing diary and on the source documentation.

1.4 Flow Chart

Table 1 Study General Assessment Schedule

	Screening Period		Treatment Period						Follow-up Period
Visit	**SV1**	**SV2**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6/End of Treatment[1]**	**V7/End of Study**
Week	***-4 to -1***	***-1 week***	***0***	***2***	***4***	***4***	***8***	***12***	***16***
Visit Day with Permitted Margin	**-28 to -7**	**-5 (±2 days)**	**1**	**15 (±2 days)**	**29 (±2 days)**	**Day 30**	**57 (±2 days)**	**85 (±2 days)**	**113 (±2 days)**
Obtain informed consent / assent	x								
Medical history / demographics	x								
Check inclusion / exclusion criteria	x		x						
Life Style Modifications (diet and exercise recommendations)	●	—	—	—	—	—	—	—	●
Physical examination	x		x	x	x		x	x	x
Vital signs, height and weight measurement (calculation of BMI Z-score)	x		x	x	x		x	x	x
Waist circumference	x		x	x	x		x	x	x
12-Lead Electrocardiogram			x					x	
Pediatric Quality of Life (PedsQL™)			x					x	
Lab evaluation (see table "study biological assessment schedule")	x		x	x	x		x	x	x
PK blood sampling			x[2]		x[2]	x[2]		x[2]	
Phone call to the patient		x							
Randomization			x						
Review prior/concomitant medication	x		x	x	x		x	x	x
Adverse events	●	—	—	—	—	—	—	—	●
Study Drug Dispensing			x		x		x		

	Screening Period		Treatment Period						Follow-up Period
Visit	**SV1**	**SV2**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6/End of Treatment[1]**	**V7/End of Study**
Week	***-4 to -1***	***-1 week***	***0***	***2***	***4***	***4***	***8***	***12***	***16***
Study Drug Dosing			**Daily[3]**						
Compliance Check (pill count and dosing diary)				x	x		x	x	

Table 2 Study Biological Schedule

	Screening period	Treatment Period						Follow-up period
Visit	**SV1**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6/EOT[1]**	**V7/EOS**
Week	***(-4 to -1)***	***0***	***2***	***4***	***4***	***8***	***12***	***16***
Visit Day with Permitted Margin	**-28 to -7**	**1**	**15 ± 2 days**	**29 ± 2 days**	**29**	**57 ± 2 days**	**85 ±2 days**	**113 ± 2 days**
Labs – Hematology and Coagulation Parameters haemoglobin, haematocrit, RBC, WBC, differential count, platelet count, reticulocytes count, prothrombin time (PT) and international normalized ratio (INR)	x	x	x	x		x	x	x
Labs – Urinary Pregnancy tests[4]	x	x	x	x		x	x	x
Labs – Serology HIV, HAV, HBs and HEV serology	x							
Labs – other parameters for eligibility assessment[5] Antimitochondrial Antibody (AMA), Alpha-1-Antitrypsin Phenotype, Ceruloplasmin, Ferritin, Transferrin Saturation (Serum Iron , Total Iron Binding Capacity)	x[5]							
Labs – Biochemistry								
creatinine, creatinine clearance (eGFR), total protein, albumin, electrolytes (sodium, potassium, chloride, calcium), uric acid, urea, CPK, AST, ALT, GGT, alkaline phosphatase, total and conjugated bilirubin, hsCRP, fasting plasma glucose, fasting insulin, HOMA-IR, fructosamine, C-peptide, FFA, HbA1c, TSH, Cystatin C, eGFR from Cystatin C	x	x	x	x		x	x	x
Labs – Lipids								
Total Cholesterol, Non HDL-C, HDL-C, TG, calculated VLDL-C, ApoAI, ApoB, LDL-C	x	x	x	x		x	x	x

	Screening period	Treatment Period						Follow-up period
Visit	**SV1**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6/EOT[1]**	**V7/EOS**
Week	***(-4 to -1)***	***0***	***2***	***4***	***4***	***8***	***12***	***16***
Visit Day with Permitted Margin	**-28 to -7**	**1**	**15 ± 2 days**	**29 ± 2 days**	**29**	**57 ± 2 days**	**85 ±2 days**	**113 ± 2 days**
Inflammatory markers fibrinogen, haptoglobin, TNF-α, IL-6, PAI-1		x		x		x	x	x
Liver markers: CK18 (M65 & M30), adiponectin, ferritin, FGF19 & FGF21, α2 macroglobulin, hyaluronic acid, PIIINP, TIMP-1		x		x		x	x	x
Urinalysis α1 microglobulin, β-NAG, N-Gal, albumin, creatinine, microscopic analysis[6]		x		x		x	x	x
Labs – Urinalysis (dipstick) Specific gravity, pH, protein, glucose, ketones, bilirubin, urobilinogen, blood, nitrite, leukocytes		x		x		x	x	x
Labs – Additional samples	x	x					x	
Blood Volume Collected Each Visit	**30.3 mL**	**33 mL**	**17.3 mL**	**37.5 mL**	**1 mL**	**29.5 mL**	**32 mL**	**29.5 mL**
Total Volume of Blood Collected Over the Study Period: 210.1 mL								

1: If patient prematurely discontinues, EOT visit procedures must be performed and patient will be encouraged to return for EOS one month later.

2: PK sample collected on Day 1 To (prior to first dose), Day 29, T0 (trough), 0.5 hour (±2 minutes), 1 hour (±2 minutes), 1.5 hour (±2 minutes), 2 hours (±5 minutes), 4 hours (±5 minutes), 6 hours (±10 minutes), and 8 hours (±10 minutes) post dose, Day 30, 24 hours (±10 minutes) after the dose administered the previous day, and Day 85 24 hours (±10 minutes) after the dose administered the previous day.

3: From V1 to V5 the study dosing occurs at site during the visit.

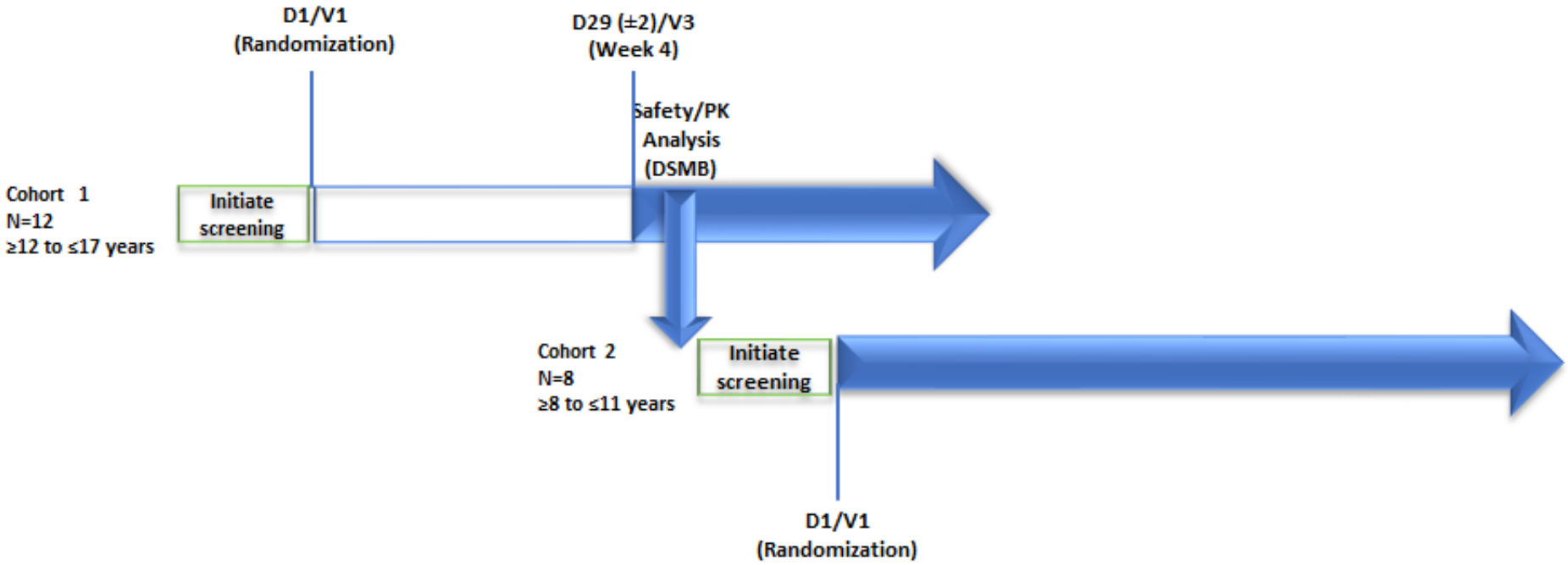
4: Females of childbearing potential (FOCBP) only.

5: Parameters to be analyzed at SV1 only if not screened in the past for these tests (with available results in source documentation).

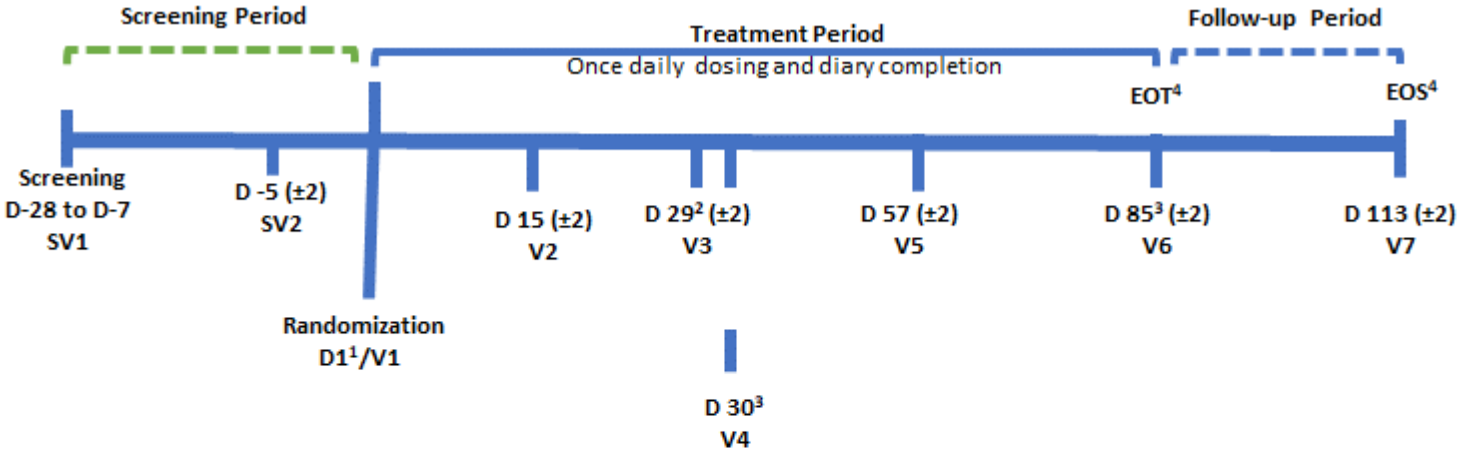
6: Microscopic analysis is performed centrally in case urinalysis dipstick is abnormal.

Figure 1 Study Schematic

A: Enrollment



B: Visit Schedule



Abbreviation: D = day; EOS = end of study; EOT = end of treatment; V = visit
[1] PK sample prior to first dose.
[2] Collection of PK samples: T0 (trough), 0.5 hour (±2 minutes), 1 hour (±2 minutes), 1.5 hour (±2 minutes), 2 hours (±5 minutes), 4 hours (±5 minutes), 6 hours (±10 minutes), and 8 hours (±10 minutes) post dose.
[3] PK sample 24 hour (±10 minutes) after the dose administered the previous day.
[4] Patients that prematurely discontinue study drug, will complete V6 and will be encouraged to complete V7.

1.5 Protocol Amendments

- Protocol v1.0 dated 04 January 2019
- Protocol v2.0 dated 24 September 2019
- Protocol v3.0 dated 21 February 2020

1.6 Treatment

Patients will receive either 80 mg or 120 mg of elafibranor once daily by the oral route for 12 weeks.

2. CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

2.1 Protocol Amendments

Description of amendments to the clinical study protocol which may have impacted the statistical analyses:

Not applicable.

2.2 Changes in the Statistical Analysis Plan

The following change was made in the SAP before database lock with regards to the analyses as compared to the analyses planned in protocol version V3.0:

- Addition of a listing describing Adverse Event of Special Interest (AESI).

3. STATISTICAL CONSIDERATIONS

Statistical analyses will be performed using the SAS® software (SAS Institute, Cary, NC, USA) version 9.4.

Continuous data will be summarized using the number of observations, mean, standard deviation (SD), median, 25% (Q1) and 75% (Q3) percentiles, minimum and maximum.

The same number of decimal places as in the raw data will be presented when reporting median, minimum, maximum, Q1 and Q3, 1 more decimal place than in the raw data will be presented when reporting mean and SD.

Dichotomous and categorical data will be presented in tables along with the number and percentages of patients by category.

No statistical test will be performed. All analyses will be descriptive.

4. STUDY PATIENTS

4.1 Disposition of Patients

The following descriptions will be performed either on all enrolled patients (See Section 4.3.1 for definition) or on all included patients (See Section 4.3.2 for definition) globally, by dose group (80 mg vs 120 mg), by age group (8 to 11 years vs 12 to 17 years) and by fibrosis severity (stage 0-1 vs stage 2-3), unless specified otherwise:

- Disposition of patients (See Table 14.1.1.1.1 by dose group, Table 14.1.1.1.2 by age group and Table 14.1.1.1.3 by fibrosis severity) on all enrolled patients: Screened patients, Included patients, Randomized patients, Randomized and treated patients, Treated patients, Patients who completed the study.
- Patients screen failed and Reason for screen failures (See Table 14.1.1.2) on all enrolled patients.
- Patients not randomized and Reason for non randomized patients (See Table 14.1.1.3) on all included patients.
- Patients not treated and Reason for non treated patients (See Table 14.1.1.4 by dose group) on all included patients.
- Patients prematurely withdrawn from the study and Reason for premature withdrawal (See Table 14.1.1.5.1 by dose group, Table 14.1.1.5.2 by age group and Table 14.1.1.5.3 by fibrosis severity) on all included patients.
- Patient disposition by visit (See Table 14.1.1.6.1 by dose group, Table 14.1.1.6.2 by age group and Table 14.1.1.6.3 by fibrosis severity) on all included patients: number of patients by visit.
- Patients with major protocol deviations throughout the study (See Table 14.1.2.1.1 by dose group, Table 14.1.2.1.2 by age group and Table 14.1.2.1.3 by fibrosis severity) on all included patients: number and percentage of patients with at least one major protocol deviation by category (See Section 4.2 for more details).
- Patients with minor protocol deviations throughout the study (See Table 14.1.2.2 by dose group) on all included patients: number and percentage of patients with at least one minor protocol deviation by category (See Section 4.2 for more details).
- Analysis sets (See Table 14.1.3.1.1 by dose group, Table 14.1.3.1.2 by age group and Table 14.1.3.1.3 by fibrosis severity) on all included patients: number and percentage of patients in the PK population(s), in the Intent-To-Treat (ITT) population and in the Safety population (See Section 4.3.3, Section 4.3.4 and Section 4.3.5, respectively).
- Exclusion from analysis sets (See Table 14.1.3.2.1 by dose group, Table 14.1.3.2.2 by age group and Table 14.1.3.2.3 by fibrosis severity): number and percentage of patients excluded from the PK population(s), from the ITT population and from the Safety population (See Section 4.3.3, Section 4.3.4 and Section **Error! Reference source not found.**, respectively). Reasons why patients have been excluded from analysis sets will also be described.

The following data will be listed:

- Patients' final status in the study in Listing 16.2.1.1,
- Study withdrawals in Listing 16.2.1.2, including the specification of other reason for withdrawal,
- Visit dates in Listing 16.2.1.3,
- Inclusion criteria not respected in Listing 16.2.1.4,
- Exclusion criteria not respected in Listing 16.2.1.5,
- Randomization data in Listing 16.2.1.6,
- Analysis data sets in Listing 16.2.1.7,
- Reason for exclusion from analysis data sets in Listing 16.2.1.8.

These listings will be sorted by patient number.

4.2 Protocol Deviations

All protocol deviations will be identified and declared major or minor at a data review meeting (DRM) that will occur before the lock of the database of the study. The list of major and minor protocol deviations will be finalized during the meeting.

Major protocol deviations will be listed by patient in Listing 16.2.2.1 and minor protocol deviations will be listed by patient in Listing 16.2.2.2. The listings will include all deviation descriptions and the coded category of deviation. They will be sorted by patient and deviation category. Patients without any protocol deviation will not be included in the listings.

4.3 Data Sets Analyzed

The following sets of population will be used for the statistical analyses and patient individual data listings: all enrolled patients, all included patients, the PK Population(s), the ITT population and the Safety Population.

4.3.1 All Enrolled Patients

All enrolled patients will include all patients who signed their informed consent form, *i.e.* all screened patients (including screen failures). This set will be used for patient disposition summaries and patient individual data listings.

4.3.2 All Included Patients

All included patients will comprise all enrolled patients who were included in the study. This set will be used for patient disposition summaries.

4.3.3 Pharmacokinetic Population(s)

See PK SAP.

4.3.4 Intent-To-Treat (ITT) Population

The ITT population will comprise all included patients who were randomized and who received at least one dose of study drug. This set will be used for statistical analyses of baseline and efficacy data.

Analyses on the ITT population will be performed according to the randomization dose group regardless of the dose actually received.

4.3.5 Safety Population

The Safety population will comprise all included patients who received at least one dose of study drug and have at least one post-baseline safety assessment. This set will be used for statistical analyses of safety data.

In case the Safety population differs significantly from the ITT population, selected baseline data may be described on this population in addition to being described on the ITT population.

Analyses on the Safety population will be performed according to the dose actually received.

4.4 Dose Switch During the Study

In the unlikely event of a patient receiving an incorrect treatment kit at any time during the study which would result in a switch of dose (i.e., switch to a dose group different from the one of the kit received at Day 1), the patient will be analyzed as planned in the dose group corresponding to the kit received at Day 1. All efficacy data will be analyzed in the ITT population. Safety data, compliance and exposure data will be analyzed up to the timepoint when the switch occurred. Data collected after the switch will be considered as missing. The corresponding values will be flagged in the patient individual data listings with the indication of the dose group to which the patient was switched.

5. DEMOGRAPHICS AND OTHER BASELINE CHARACTERISTICS

Demographics and baseline characteristics will be evaluated using the following assessments (the list of parameters is detailed in the next sections):

- Demographic characteristics at Screening,
- NASH Diagnosis at Screening,
- Alcohol Use Disorders Identification Test (AUDIT) at Screening,
- Laboratory screen tests:
  - Serology at Screening,
  - Other parameters for eligibility assessment at Screening,
  - Urine Pregnancy test at Screening,
- Medical and surgical history,
- Prior medications,
- Prior Procedures.

Depending on the assessment, data will be either listed in patient individual data listings or descriptive statistics of baseline data will be presented (See statistical considerations in Section 3**Error! Reference source not found.**).

Unless specified otherwise, descriptive statistics will be presented on the ITT population globally, by dose group (80 mg vs 120 mg), by age group (8 to 11 years vs 12 to 17 years) and by fibrosis severity (stage 0-1 vs stage 2-3).

Height, Weight, BMI z-score, waist circumference, physical examination, vital signs, 12-lead ECG, Pediatric Quality of Life (PedsQL™) and laboratory data collected at screening and/or Day 1 and at post-baseline visits will be described with the efficacy and safety criteria in Section 7.1.2, Section 9.4 and in Section 9.5.

5.1.1 Demographic Characteristics

Baseline data for demographic characteristics will correspond to those collected at Screening. Descriptive statistics will be presented (See Table 14.1.4.1.1 by dose group, Table 14.1.4.1.2 by age group and Table 14.1.4.1.3 by fibrosis severity) for:

- Sex (Male; Female),
- Age as continuous and categorical variable (8 to 11 years and 12 to 17 years; See Section 11.2 for computation of age),
- Race (American Indian or Alaska Native; Native Hawaiian or other Pacific Islander; Asian; White; Black or African American; Other),
- Ethnicity (Hispanic, Latino or Spanish origin; Not Hispanic, Latino or Spanish origin; Unknown; Not Reported).

Listing 16.2.4.1 will list demographic data for all enrolled patients, including “Assent date”, “Mother / legal guardian informed consent date” (or not applicable), “Father /

legal guardian informed consent date" (or not applicable). The specification of other race will also be displayed. The listing will be sorted by patient number.

5.1.2 NASH Diagnosis

The following data collected at Screening for NASH diagnosis will be described (See Table 14.1.4.2.1 by dose group, Table 14.1.4.2.2 by age group and Table 14.1.4.2.3 by fibrosis severity):

- NASH type (Type 1; Type 2; Undetermined),
- Fibrosis stage (Stage 0; Stage 1; Stage 2; Stage 3).

Listing 16.2.4.2 will list data collected for NASH diagnosis including the date of liver biopsy confirming the diagnosis for all enrolled patients.

5.1.3 Alcohol Use Disorders Identification Test (AUDIT)

Alcohol screening was performed at Screening using the AUDIT questionnaire. The following data will be described (See Table 14.1.4.3.1 by dose group, Table 14.1.4.3.2 by age group and Table 14.1.4.3.3 by fibrosis severity):

- Collection method (Interview in English; Interview with a translator),
- Overall score.

AUDIT data will be listed in Listing 16.2.4.3 for all enrolled patients.

5.1.4 Medical and Surgical History

Medical and surgical history data recorded at screening visit will be coded using the MedDRA dictionary version 23.0. All data will be summarized (See Table 14.1.4.4.1 by dose group, Table 14.1.4.4.2 by age group and Table 14.1.4.4.3 by fibrosis severity) by Primary System Organ Class (SOC) and Preferred Term (PT).

The tables will be sorted by descending frequency of SOC, and, within each SOC, by descending frequency of PT in all patients.

Medical and surgical history data will be listed in Listing 16.2.4.4 for all enrolled patients. Start date, whether the condition is ongoing and/or treated and stop date (if applicable) will also be displayed. The listing will be sorted by patient number, start date, Primary SOC and PT.

5.2 Prior Medications

Prior medications ended before (<) the first study treatment intake will be coded using the World Health Organization (WHO) Drug Dictionary (WHODD) version of March 2020 (B3 format) (See Section 11.3 for more details).

The number and percentage of patients taking prior medications will be summarized (See Table 14.1.4.5.1 by dose group, Table 14.1.4.5.2 by age group and Table 14.1.4.5.3 by fibrosis severity) overall and by Anatomical Therapeutic Chemical

Classification (ATC) Therapeutic Subgroup (ATC level 2), Chemical Subgroup (ATC level 4) and WHO Drug Name.

The tables will be sorted by descending frequency of ATC Therapeutic Subgroup, and, within each ATC Therapeutic Subgroup, by descending frequency of ATC Chemical Subgroup, and, within each ATC Chemical Subgroup, by descending frequency of Who Drug Name in all patients.

Prior medications will be listed in Listing 16.2.4.5 for all enrolled patients. The listing will be sorted by patient number, medication start date and stop date, ATC Therapeutic Subgroup, ATC Chemical Subgroup and WHO Drug Name. Indication (Adverse Event; Medical History; Other specification), dose, frequency (Daily; Twice per day; 3 times per day; 4 times per day; Every other day; Every week; Every month; Once; As needed; Intermittent; Continuous; Per year; Unknown; Other specification), unit (mg; g; ug; ml; tablet; capsule; puff; drop; application; IU; Other specification; Not applicable; Unknown), route (Oral; Topical; Subcutaneous; Intramuscular; Intravenous; Sublingual; Inhalation; Epidural; Rectal; Ophthalmic; Intraocular; Other specification; Unknown) will also be displayed.

In case non-pharmacological treatments are reported, a specific listing will be provided for these treatments.

5.3 Prior Procedures

Prior procedures ended before (<) the first study treatment intake will be coded using the MedDRA dictionary version 23.0. All data will be summarized (See Table 14.1.4.6.1 by dose group, Table 14.1.4.6.2 by age group and Table 14.1.4.6.3 by fibrosis severity) by Primary System Organ Class (SOC) and Preferred Term (PT).

The tables will be sorted by descending frequency of SOC, and, within each SOC, by descending frequency of PT in all patients.

Prior procedures will be listed in Listing 16.2.4.6 for all enrolled patients. Start date, whether the procedure is ongoing and stop date (if applicable) will also be displayed. The listing will be sorted by patient number, start date, Primary SOC and PT.

5.4 Laboratory Screen Tests

Data collected at Screening for laboratory screen tests will only be listed in patient individual data listings for all enrolled patients:

- Listing 16.2.4.7.1 will list serology parameters (Human Immunodeficiency Virus (HIV), Hepatitis A Virus (HAV), Hepatitis B (HBs), Hepatitis C Virus (HCV) and Hepatitis E virus (HEV)),

- Listing 16.2.4.7.2 will list other laboratory parameters for eligibility assessment (Antimitochondrial Antibody (AMA), Alpha-1-Antitrypsin Phenotype, Ceruloplasmin, Ferritin, Transferrin Saturation (Serum Iron, Total Iron Binding Capacity)),

- Listing 16.2.4.7.3 will list for women only, the data on urine pregnancy test (test performed ? Yes No; Date of urine pregnancy test; Result: Positive; Negative) at Screening. This listing will additionally present the results of urine pregnancy tests collected at Day 1, Day 15, Day 29, Day 57, Day 85 (EOT) and Day 113 (EOS).

The listings will be sorted by patient number and visit (when applicable).

6. TREATMENT COMPLIANCE

The compliance of study treatment will be summarized (See Table 14.1.5.1 by dose group, Table 14.1.5.2 by age group and Table 14.1.5.3 by fibrosis severity) for the Safety population both as a continuous and categorical variables (< 80%, 80% to 120%, > 120%) by visit (Day 29 and Day 85) and overall.

The details on treatment compliance definition and computation can be found in Section 11.4.

Data on treatment compliance, including kit and study treatment dispensation data, number of tablets taken, number of tablets returned and kit replacement information (if applicable), will be listed in Listing 16.2.5.1 for all enrolled patients.

7. EFFICACY EVALUATION

7.1.1 Primary Efficacy Analysis

Not applicable.

7.1.2 Secondary Efficacy Analyses

Values at visits and changes from baseline corresponding to secondary efficacy endpoints will be described by visit on the ITT population by dose group, by age group, by fibrosis severity and overall.

Baseline value will be defined as the last measurement before the first intake of treatment including unscheduled/retest that could have been performed. Depending on endpoints, Screening and/or Day 1 data will be taken into account to obtain the baseline value:

- Change from baseline in serum ALT, AST, GGT, ALP and other liver markers (CK18 (M65 & M30), adiponectin, ferritin, FGF19 & FGF21, α2 macroglobulin, hyaluronic acid, PIIINP, TIMP-1):
  - Visits: baseline, Day 15 (except other liver markers), Day 29, Day 57, Day 85 (EOT), Day 113 (EOS),
  - Baseline: Last measurement before first intake of treatment taking including Screening and Day 1.

- Change from baseline in glucose homeostasis makers (Fasting plasma glucose, HOMA-IR and fasting insulin):
  - Visits: baseline, Day 15, Day 29, Day 57, Day 85 (EOT), Day 113 (EOS),
  - Baseline: Last measurement before first intake of treatment including Screening and Day 1.

- Change from baseline in serum lipid parameters (Total Cholesterol, Non High-density lipoprotein cholesterol (HDL-C), HDL-C, TG (Triglycerides), calculated VLDL-C (Very low-density lipoprotein), Apolipoprotein A-I (ApoAI), Apolipoprotein B (ApoB), Low-density lipoprotein cholesterol (LDL-C)):
  - Visits: baseline, Day 15, Day 29, Day 57, Day 85 (EOT), Day 113 (EOS),
  - Baseline: Last measurement before first intake of treatment including Screening and Day 1.

- Change from baseline in body weight and BMI Z-score:
  - Visits: baseline, Day 15, Day 29, Day 57, Day 85 (EOT), Day 113 (EOS),
  - Baseline: Last measurement before first intake of treatment including Screening and Day 1.

- Change from baseline in waist circumference:
  - Visits: baseline, Day 15, Day 29, Day 57, Day 85 (EOT), Day 113 (EOS),

  - Baseline: Last measurement before first intake of treatment including Screening and Day 1.

- Change from baseline in inflammatory markers (fibrinogen, haptoglobin, TNF-α, IL-6, PAI-1):
  - Visits: baseline, Day 29, Day 57, Day 85 (EOT), Day 113 (EOS),
  - Baseline: Last measurement before first intake of treatment including Day 1.

- Change from baseline in PedsQL™ scores:
  - Visits: baseline, Day 85 (EOT),
  - Baseline: Last measurement before first intake of treatment including Day 1.

Analyses of Secondary endpoints will be presented in the tables below:

Endpoint	**Tables**		
	By dose group and overall	**By age group and overall**	**By fibrosis severity and overall**
Change from baseline in serum ALT, AST, GGT and ALP (absolute and relative changes)	14.2.2.1.1	14.2.2.1.2	14.2.2.1.3
Change from baseline in other liver markers (absolute changes)	14.2.2.2.1	14.2.2.2.2	14.2.2.2.3
Change from baseline in glucose homeostasis makers (absolute changes)	14.2.2.3.1	14.2.2.3.2	14.2.2.3.3
Change from baseline in serum lipid parameters (absolute changes)	14.2.2.4.1	14.2.2.4.2	14.2.2.4.3
Change from baseline in height (cm), body weight (kg) and BMI Z-score (absolute changes)	14.2.2.5.1	14.2.2.5.2	14.2.2.5.3
Change from baseline in waist circumference (absolute changes)	14.2.2.6.1	14.2.2.6.2	14.2.2.6.3
Change from baseline in inflammatory markers (absolute changes)	14.2.2.7.1	14.2.2.7.2	14.2.2.7.3
Change from baseline in PedsQL™ scores (absolute changes)	14.2.2.8.1	14.2.2.8.2	14.2.2.8.3

Details of the computation of BMI Z-score and PedsQL™ score can be found in Section 11.5.

Where applicable, results will be presented in Standard International (SI) units.

Date for secondary efficacy endpoints will be listed for each included patient in Listings 16.2.6.1 to 16.2.6.7 (see Section 12.7 for details).

Additionally, data collected on changes in patients' lifestyle diet at post baseline visits will be listed in Listing 16.2.6.8.

7.1.3 Statistical / Analytical Issues

7.1.3.1 Adjustments for Covariates

Not applicable. Analyses will only be descriptive.

7.1.3.2 Handling of Dropouts or Missing Data

No replacement of missing values (including those of drop outs) will be performed.

7.1.3.3 Interim Analyses and Data Monitoring

No interim analysis is planned.

7.1.3.4 Multicenter Studies

No analysis by center is planned.

7.1.3.5 Multiple Comparison/Multiplicity

Not applicable.

7.1.3.6 Use of an 'Efficacy' Subset of Patients

Not applicable.

7.1.3.7 Active-Control Studies Intended to Show Equivalence

Not applicable.

7.1.3.8 Examination of Subgroups

No subgroup analysis is planned.

7.1.4 Tabulation of Individual Response Data

Date for secondary efficacy endpoints will be listed for each included patient in Listings 16.2.6.1 to 16.2.6.7 (see Section 12.7 for details).

7.1.5 Drug Dose, Drug Concentration and Relationships to Response

Not applicable.

7.1.6 Drug-Drug and Drug-Disease Interactions

Not applicable.

8. PHARMACOKINETIC EVALUATION

See PK SAP.

9. SAFETY EVALUATION

All safety parameters will be analyzed on the Safety population by dose group, by age group and overall. Individual data will be presented in listings for all included patients.

9.1 Exposure, Study and Treatment Durations

The study duration (days), treatment duration (days) and duration of exposure to study treatment (days) will be summarized (See Table 14.3.1.1 by dose group and Table 14.3.1.2 by age group). The definitions of study duration, treatment duration and duration of exposure can be found in Section 11.6.

Data on study duration, treatment duration and duration of exposure, including study treatment interruption data, will be listed in Listing 16.2.5.2 for all included patients. The listing will be sorted by patient number.

9.2 Adverse Events

AEs will be coded using the MedDRA Dictionary version 23.0.

In this study, seriousness, severity, relationship to study treatment, relationship to study procedures, action taken, action taken with study treatment and outcome were recorded for each episode of an AE. Specific information related to the definitions and conventions used for descriptions of AEs based on these data can be found in Section 11.7.

Unless specified otherwise, descriptions of AEs will be performed by dose group, by age group, by fibrosis group and overall on the Safety Population.

Also, unless specified otherwise, tables by primary SOC and PT will be sorted by descending frequency of SOC, and, within each SOC, by descending frequency of PT in all patients.

9.2.1 Summary of AEs

An overview of AEs (See Table 14.3.2.1.1.1 by dose group and Table 14.3.2.1.1.2 by age group) will be provided displaying the number of events along with the number and percentages of patients with at least one:

- AE,
- TEAE,
- TEAE related to study treatment,
- TEAE related to study procedures,
- SAE,
- Serious TEAE,
- Serious TEAE related to study treatment,

- Serious TEAE related to study procedures,
- AE leading to treatment withdrawal,
- TEAE leading to treatment withdrawal,
- AE leading to study withdrawal,
- TEAE leading to study withdrawal,
- Fatal AE,
- Fatal TEAE,
- AESI.

A summary of AEs (See Table 14.3.2.1.2.1 by dose group and Table 14.3.2.1.2.2 by age group) displaying the number of AEs along with the number and percentage of patients with at least one AE will be provided according to:

- Seriousness (Serious; Not serious),
- Relationship to study treatment (Related; Possibly related; Unlikely related; Not related; Not assessable),
- Relationship to study procedures (Related; Not Related),
- Severity (Mild; Moderate; Severe),
- Action taken (None; Procedure required; Withdrawn from clinical trial due to AE; Treatment required; Hospitalisation or prolonged hospitalisation; Other),
- Action taken with study treatment (Drug withdrawn, Drug interrupted, Dose not changed, Unknown, Not applicable),
- Outcome (Recovering / Resolving; Not recovered / not resolved; Recovered / resolved; Recovered / resolved with sequelae; Fatal; Unknown).

A summary of TEAEs (See Table 14.3.2.1.3.1 by dose group and Table 14.3.2.1.3.2 by age group) displaying the number of TEAEs along with the number and percentage of patients with at least one TEAE will be provided according to: Seriousness, Relationship to study treatment, Relationship to study procedures, Severity, Action taken, Action taken with study treatment and Outcome.

A summary of SAEs (See Table 14.3.2.4.1 by dose group and Table 14.3.2.4.2 by age group) displaying the number of SAEs along with the number and percentage of patients with at least one SAE will be provided according to: Relationship to study treatment, Relationship to study procedures, Severity, Action taken, Action taken with study treatment and Outcome, and additionally according to:

- Seriousness criteria (Death; Initial or prolonged hospitalisation; Life threatening; Congenital anomaly or birth defect; Persistent or significant disability/incapacity; Medically important event not covered by other serious criteria).

The number and percentage of patients will be presented according to the number of AEs (1, 2 or 3 or more AEs: See Table 14.3.2.1.2.3 by dose group and Table 14.3.2.1.2.4 by age group), the number of TEAEs (1, 2 or 3 or more TEAEs: See Table 14.3.2.1.3.3 by dose group and Table 14.3.2.1.3.4 by age group) and the

number of SAEs (1, 2 or 3 or more SAEs: See Table 14.3.2.1.4.3 by dose group and Table 14.3.2.1.4.4 by age group).

9.2.2 Display of Adverse Events

9.2.2.1 Adverse Events

The number of AEs along with the number and percentage of patients with at least one AE will be presented (See Table 14.3.2.2.1.1 by dose group and Table 14.3.2.2.1.2 by age group) according to Primary SOC and PT.

9.2.2.2 Treatment Emergent AEs

The number of TEAEs along with the number and percentage of patients with at least one TEAE will be presented (See Table 14.3.2.2.2.1 by dose group and Table 14.3.2.2.2.2 by age group) according to Primary SOC and PT.

9.2.2.3 Treatment Emergent AEs Related to Study Treatment

The number of TEAEs related to the study treatment along with the number and percentage of patients with at least one TEAE related to study treatment will be presented (See Table 14.3.2.2.3.1 by dose group and Table 14.3.2.2.3.2 by age group) according to Primary SOC and PT.

9.2.2.4 Treatment Emergent AEs Related to Study Procedures

The number of TEAEs related to the study procedures along with the number and percentage of patients with at least one TEAE related to study treatment will be presented (See Table 14.3.2.2.4.1 by dose group and Table 14.3.2.2.4.2 by age group) according to Primary SOC and PT.

9.2.2.5 Treatment Emergent AEs by Maximum Event Severity

The number of TEAEs along with the number and percentage of patients with at least one TEAE will be presented (See Table 14.3.2.2.5.1 by dose group and Table 14.3.2.2.5.2 by age group) according to Primary SOC, PT and maximum event severity (when available).

The tables will be sorted by descending frequency of SOC, and, within each SOC, by descending frequency of PT for all severities combined in all patients.

9.2.2.6 Serious AEs

The number of SAEs along with the number and percentage of patients with at least one SAE will be presented (See Table 14.3.2.2.6.1 by dose group and Table 14.3.2.2.6.2 by age group) according to Primary SOC and PT.

9.2.2.7 Serious Treatment Emergent AEs

The number of serious TEAEs along with the number and percentage of patients with at least one serious TEAE will be presented (See Table 14.3.2.2.7.1 by dose group and Table 14.3.2.2.7.2 by age group) according to Primary SOC and PT.

9.2.2.8 Serious Treatment Emergent AEs Related to Study Treatment

The number of serious TEAEs related to the study treatment along with the number and percentage of patients with at least one serious TEAE related to the study treatment will be presented (See Table 14.3.2.2.8.1 by dose group and Table 14.3.2.2.8.2 by age group) according to Primary SOC and PT.

9.2.2.9 Serious Treatment Emergent AEs Related to Study Procedures

The number of serious TEAEs related to the study procedures along with the number and percentage of patients with at least one serious TEAE related to the study procedures will be presented (See Table 14.3.2.2.9.1 by dose group and Table 14.3.2.2.9.2 by age group) according to Primary SOC and PT.

9.2.2.10 Serious Treatment Emergent AEs by Maximum Event Severity

The number of serious TEAEs along with the number and percentage of patients with at least one serious TEAE will be presented (See Table 14.3.2.2.10.1 by dose group and Table 14.3.2.2.10.2 by age group) according to Primary SOC, PT and maximum event severity (when available).

The tables will be sorted by descending frequency of SOC, and, within each SOC, by descending frequency of PT for all severities combined in all patients.

9.2.2.11 AEs Leading to Treatment Withdrawal

The number of AEs leading to treatment withdrawal along with the number and percentage of patients with at least one AE leading to treatment withdrawal will be presented (See Table 14.3.2.2.11.1 by dose group and Table 14.3.2.2.11.2 by age group) according to Primary SOC and PT.

9.2.2.12 Treatment Emergent AEs Leading to Treatment Withdrawal

The number of TEAEs leading to treatment withdrawal along with the number and percentage of patients with at least one TEAE leading to treatment withdrawal will be presented (See Table 14.3.2.2.12.1 by dose group and Table 14.3.2.2.12.2 by age group) according to Primary SOC and PT.

9.2.2.13 AEs Leading to Study Withdrawal

The number of AEs leading to study withdrawal along with the number and percentage of patients with at least one AE leading to study withdrawal will be presented (See Table 14.3.2.2.13.1 by dose group and Table 14.3.2.2.13.2 by age group) according to Primary SOC and PT.

9.2.2.14 Treatment Emergent AEs Leading to Study Withdrawal

The number of TEAEs leading to study withdrawal along with the number and percentage of patients with at least one TEAE leading to study withdrawal will be presented (See Table 14.3.2.2.14.1 by dose group and Table 14.3.2.2.14.2 by age group) according to Primary SOC and PT.

9.2.2.15 Fatal AEs

The number of fatal AEs along with the number and percentage of patients with at least one fatal AE will be presented (See Table 14.3.2.2.15.1 by dose group and Table 14.3.2.2.15.2 by age group) according to Primary SOC and PT.

9.2.2.16 Fatal Treatment Emergent AEs

The number of fatal TEAEs along with the number and percentage of patients with at least one fatal TEAE will be presented (See Table 14.3.2.2.16.1 by dose group and Table 14.3.2.2.16.2 by age group) according to Primary SOC and PT.

9.2.3 Analysis of Adverse Events

Not applicable.

9.2.4 AEs Listings

AEs will be listed in Listing 16.2.7.1 for all included patients. This listing will present a complete description of all episodes of AEs including SOC, PT and other MedDRA terms as well as investigator description, episode number, start date and time, end date as applicable, time to onset since treatment intake as applicable (days), duration (days), severity, seriousness, relationship to study treatment, relationship to study procedures, action taken, action taken with study treatment and outcome. Flags will indicate which AEs are treatment emergent.

The listing will be sorted by patient number, start date, end date, SOC, PT and investigator description.

9.2.5 Adverse Events of Special Interest

AESI are TEAEs corresponding to the conceptual definition of:

- CPK elevations of severe intensity or leading to permanent study drug discontinuation
- Muscle injury symptoms of severe intensity corresponding to:
  - Muscle pain or Myalgia
  - Muscle spasms or Tremor
  - Muscle weakness
- Transaminases elevations from baseline of severe intensity or leading to permanent study drug discontinuation

- Liver injury events of severe intensity corresponding to:
  - Hepatic impairment
  - Hepatic failure
- Gastrointestinal symptoms of severe intensity corresponding to:
  - Abdominal pain
  - Constipation
  - Diarrhea
  - Nausea
  - Vomiting
  - Acute cholecystis
  - Acute pancreatitis
- Fatigue and Asthenia of severe intensity
- Serum creatinine elevations of severe intensity or leading to permanent study drug discontinuation
- Renal injury events of moderate or severe intensity corresponding to:
  - Renal failure
  - Renal impairment
  - Renal colic

All of the above categories will be identified via a list of MedDRA queries of PT codes.

All AESIs will be listed with the SOC and the PT in Listing 16.2.7.2. The listing will be sorted as described above for Listing 16.2.7.1.

9.3 Deaths, Other Serious AEs and Other Significant AEs

9.3.1 Listings of Deaths, Other Serious AEs and Other Significant AEs

Deaths, if any, SAEs and other significant AEs, *i.e.* AEs leading to treatment withdrawal and AEs leading to study withdrawal, will be listed (See Table 14.3.3.1, Table 14.3.3.2, Table 14.3.3.3 and Table 14.3.3.4, respectively).

The listings will be sorted as described above for Listing 16.2.7.1.

9.3.2 Narratives of Deaths, Other Serious AEs and Other Significant AEs

Not applicable.

9.4 Clinical Laboratory Evaluation

General remarks concerning laboratory data can be found in Section 11.8.

9.4.1 Listings of Individual Laboratory Measurements

All laboratory data will be listed for all included patients by patient number, parameter and visit in Listing 16.2.8.1 for hematology and coagulation parameters, Listing 16.2.8.2 for biochemistry parameters and Listing 16.2.8.3 for urinalysis parameters.

In case of retest, a flag will indicate which assessment was retained for the analysis. Where applicable, values outside the laboratory reference ranges will also be flagged and presented along with assessments of clinically significant values by the investigator. Date of sampling or reason why samples were not collected will be displayed. Where applicable, specifications reported in open text fields for “Other” categories will also be displayed.

The listings will be sorted by patient number and visit.

9.4.2 Evaluation of Each Laboratory Parameter

Unless specified otherwise, descriptive statistics of laboratory parameters will be presented by dose group, by age group, by fibrosis severity and overall on the Safety Population.

Continuous descriptive statistics of laboratory data will be presented by parameter and visit (baseline, Day 15, Day 29, Day 57, Day 85 (EOT), Day 113 (EOS)) (See Table 14.3.4.1.1 by dose group and Table 14.3.4.1.2 by age group for hematology and coagulation parameters; See Table 14.3.4.2.1 by dose group and Table 14.3.4.2.2 by age group for biochemistry parameters; See Section 11.8.1 for the list of parameters).

Descriptive statistics at post-baseline visits of absolute changes from baseline in laboratory parameters as well as number and percentage of patients by category according to reference range (< lower limit of normality (LLN); Normal, i.e. ≥ LLN and ≤ upper limit of normality (ULN); > ULN and < 3 ULN; ≥ 3 ULN and < 5 ULN; ≥ 5 ULN) will also be presented in the tables. Relative changes from baseline will additionally be presented in the tables for ALP, GGT, AST and ALT.

Shift tables showing each individual patient's Baseline values by category according to reference range (see above categories) versus values by category according to reference range at Day 85 (EOT) will be provided (See Table 14.3.4.3.1 by dose group and Table 14.3.4.3.2 by age group for hematology and coagulation parameters; See Table 14.3.4.4.1 by dose group and Table 14.3.4.4.2 by age group for biochemistry parameters; See Section 11.8.1 for the list of parameters).

Descriptive statistics at baseline and post-baseline visits (baseline, Day 15, Day 29, Day 57, Day 85 (EOT), Day 113 (EOS)) of urinalysis parameters (See Section 11.8.1 for the list of parameters) will be presented (See Table 14.3.4.5.1 by dose group and Table 14.3.4.5.2 by age group for urinalysis parameters.

Continuous descriptive statistics of urinalysis (dipstick) parameters (Specific Gravity, pH and Urobilinogen) will be presented by parameter and visit (baseline, Day 29,

Day 57, Day 85 (EOT), Day 113 (EOS)) (See Table 14.3.4.6.1 by dose group and Table 14.3.4.6.2 by age group for urinalysis (dipstick) parameters). Descriptive statistics at post-baseline visits of absolute changes from baseline in urinalysis (dipstick) parameters (Specific Gravity, pH and Urobilinogen) as well as number and percentage of patients by category according to reference range (< lower limit of normality (LLN); Normal, i.e. ≥ LLN and ≤ upper limit of normality (ULN); > ULN) will also be presented in the tables.

Furthermore, number and percentage of patients by category (Positive; Negative) at baseline and post-baseline visits of urinalysis (dipstick) parameters (Protein, Glucose, Ketones, Bilirubin, Blood, Nitrites, Leukocytes) will also be presented in the tables.

Baseline value will be defined as the last measurement, including Screening and Day 1 taking into account unscheduled assessments/retests that could have been performed, before the first intake of treatment.

9.5 Vital Signs, Physical Findings and Other Observations Related to Safety

9.5.1 Vital Signs

Unless specified otherwise, descriptive statistics of vital sign parameters will be presented by dose group, by age group, by fibrosis severity and overall on the Safety Population.

Continuous descriptive statistics for vital signs (Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg), Heart rate (beats/min)) after 5 minutes rest in the seating position will be presented by parameter and visit (baseline, Day 15, Day 29, Day 57, Day 85 (EOT), Day 113 (EOS)) (See Table 14.3.5.1.1 by dose group and Table 14.3.5.1.2 by age group).

Descriptive statistics at baseline and post-baseline visits of changes from baseline in vital sign parameters as well as the number and percentage of patients by out of range significance category (Not Clinically Significant; Clinically Significant) will also be presented in the tables.

Baseline value will be defined as the last measurement, including Screening and Day 1 taking into account unscheduled assessments that could have been performed, before the first intake of treatment.

Vital sign data will be listed in Listing 16.2.9.1 for all included patients, including vital sign measurement date and time or the reason why measurement was not performed. The listing will be sorted by patient number, parameter and visit.

9.5.2 Other Observations Related to Safety

9.5.2.1 Physical Examination

Unless specified otherwise, descriptive statistics of physical examination parameters will be presented by dose group, by age group, by fibrosis severity and overall on the Safety Population.

Physical examination findings (Not Clinically Significant; Clinically Significant) were collected according to pre-defined body systems: General Appearance; Skin; Eyes; Ears; Nose; Throat; Neck and Thyroid; Lungs; Heart; Upper/lower Extremities; Lymph Nodes; Abdomen; Musculoskeletal System; Basic Neurological Assessment; Other.

The number and percentage of patients with a physical examination abnormality will be summarized by visit (baseline, Day 15, Day 29, Day 57, Day 85 (EOT), Day 113 (EOS)) overall and by pre-defined body system (See Table 14.3.5.2.1.1 by dose group and Table 14.3.5.2.1.2 by age group). Within each visit, the table will be sorted by descending frequency of body system in all patients.

The number and percentage of patients with clinically significant abnormal physical examination will be presented in the same way (See Table 14.3.5.2.2.1 by dose group and Table 14.3.5.2.2.2 by age group).

Baseline value will be defined as the last measurement, including Screening and Day 1 taking into account unscheduled assessments/retests that could have been performed, before the first intake of treatment.

Physical examination data will be listed in Listing 16.2.9.2 by patient, visit and pre-defined body system for all included patients, including physical examination date or the reason why physical examination was not performed. Specification of body system “Other” will also be displayed. The listing will be sorted by patient number.

9.5.2.2 Electrocardiogram

Unless specified otherwise, descriptive statistics of 12-lead ECG parameters will be presented by dose group, by age group, by fibrosis severity and overall on the Safety Population.

Descriptive statistics at baseline and Day 85 (EOT) of whether the ECG was performed (Yes; No) and of the interpretation of the ECG (Normal; Abnormal, Not Clinically Significant; Abnormal, Clinically Significant) will be presented in the tables (See Table 14.3.5.3.1 by dose group and Table 14.3.5.3.2 by age group).

Baseline value will be defined as the last measurement, including Day 1 taking into account unscheduled assessments that could have been performed, before the first intake of treatment.

12-lead ECG data will be listed in Listing 16.2.9.3 for all included patients, including ECG date or the reason why ECG was not performed. The listing will be sorted by patient number and visit.

9.6 Concomitant Medications

Concomitant medications ended after or on the date (≥) of the first study treatment intake will be coded using the World Health Organization (WHO) Drug Dictionary (WHODD) version of March 2020 (B3 format) (See Section 11.3 for more details).

Unless specified otherwise, concomitant medications will be described by dose group, by age group, by fibrosis severity and overall on the Safety Population.

The number and percentage of patients taking concomitant medications will be summarized overall and by Anatomical Therapeutic Chemical Classification (ATC) Therapeutic Subgroup (ATC level 2), Chemical Subgroup (ATC level 4) and WHO Drug Name (See Table 14.3.6.1 by dose group and Table 14.3.6.2 by age group).

The tables will be sorted by descending frequency of ATC Therapeutic Subgroup, and, within each ATC Therapeutic Subgroup, by descending frequency of ATC Chemical Subgroup, and, within each ATC Chemical Subgroup, by descending frequency of Who Drug Name in all patients.

Concomitant medications will be listed in Listing 16.2.10.1 for all included patients. The listing will be sorted by patient number, medication start date and stop date, ATC Therapeutic Subgroup, ATC Chemical Subgroup and WHO Drug Name. Indication (Adverse Event; Medical History; Other specification), dose, frequency (Daily; Twice per day; 3 times per day; 4 times per day; Every other day; Every week; Every month; Once; As needed; Intermittent; Continuous; Per year; Unknown; Other specification), unit (mg; g; ug; ml; tablet; capsule; puff; drop; application; IU; Other specification; Not applicable; Unknown), route (Oral; Topical; Subcutaneous; Intramuscular; Intravenous; Sublingual; Inhalation; Epidural; Rectal; Ophthalmic; Intraocular; Other specification; Unknown) will also be displayed.

In case non-pharmacological treatments are reported, a specific listing will be provided for these treatments.

9.7 Concomitant Procedures

Concomitant procedures ended after or on the date (≥) of the first study treatment intake will be coded using the MedDRA dictionary version 23.0. All data will be summarized (See Table 14.3.7.1 by dose group and Table 14.3.7.2 by age group) by Primary System Organ Class (SOC) and Preferred Term (PT).

The tables will be sorted by descending frequency of SOC, and, within each SOC, by descending frequency of PT in all patients.

Concomitant procedures will be listed in Listing 16.2.10.2 for all included patients. Start date, whether the procedure is ongoing and stop date (if applicable) will also be

displayed. The listing will be sorted by patient number, start date, Primary SOC and PT.

9.8 Collection of PK Blood Samples

Information on collection of PK blood samples reported in the eCRF will not be described. These data will only be listed.

Data on collection of PK blood samples at visits and timepoints will be listed in Listing 16.2.11.1 for all included patients, including whether the sample was taken, the sample date and time and treatment administration first and last dates and times. The listing will be sorted by patient number, visit and timepoint.

10. TABLES, FIGURES AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT

10.1 General Remarks about Tables

Results presented in section 14 of ICH report will be created using SAS version 9.4. All table templates can be found in Attachment. This section lists all tables in the order in which they are expected to appear in the study report.

10.2 Demographic Data Summary and Figures

10.2.1 Study Patients

Table 14.1.1.1.1 Disposition of Patients by Dose Group - All Enrolled Patients

Table 14.1.1.1.2 Disposition of Patients by Age Group - All Enrolled Patients

Table 14.1.1.1.3 Disposition of Patients by Fibrosis Severity - All Enrolled Patients

Table 14.1.1.2 Reason for Screen Failures - All Enrolled Patients

Table 14.1.1.3 Reason for Non Randomized Patients - All Included Patients

Table 14.1.1.4 Reason for Non Treated Patients by Dose Group - All Included Patients

Table 14.1.1.5.1 Reason for Premature Withdrawals by Dose Group - All Included Patients

Table 14.1.1.5.2 Reason for Premature Withdrawals by Age Group - All Included Patients

Table 14.1.1.5.3 Reason for Premature Withdrawals by Fibrosis Severity - All Included Patients

Table 14.1.1.6.1 Disposition of Patients by Visit and Dose Group - All Included Patients

Table 14.1.1.6.2 Disposition of Patients by Visit and Age Group - All Included Patients

Table 14.1.1.6.3 Disposition of Patients by Visit and Fibrosis Severity - All Included Patients

Table 14.1.2.1.1 Major Protocol Deviations by Dose Group - All Included Patients

Table 14.1.2.1.2 Major Protocol Deviations by Age Group - All Included Patients

Table 14.1.2.1.3 Major Protocol Deviations by Fibrosis Severity - All Included Patients

Table 14.1.2.2 Minor Protocol Deviations by Dose Group - All Included Patients

Table 14.1.3.1.1 Analysis Sets by Dose Group - All Included Patients

Table 14.1.3.1.2 Analysis Sets by Age Group - All Included Patients

Table 14.1.3.1.3 Analysis Sets by Fibrosis Severity - All Included Patients

Table 14.1.3.2.1 Reasons for Exclusion From Analysis Sets by Dose Group - All Included Patients

Table 14.1.3.2.2 Reasons for Exclusion From Analysis Sets by Age Group - All Included Patients

Table 14.1.3.2.3 Reasons for Exclusion From Analysis Sets by Fibrosis Severity - All Included Patients

10.2.2 Demographics and Patient Characteristics

Table 14.1.4.1.1 Demographic Characteristics at Baseline by Dose Group - Intent-To-Treat Population

Table 14.1.4.1.2 Demographic Characteristics at Baseline by Age Group - Intent-To-Treat Population

Table 14.1.4.1.3 Demographic Characteristics at Baseline by Fibrosis Severity - Intent-To-Treat Population

Table 14.1.4.2.1 Nash Diagnosis at Baseline by Dose Group - Intent-To-Treat Population

Table 14.1.4.2.2 Nash Diagnosis at Baseline by Age Group - Intent-To-Treat Population

Table 14.1.4.2.3 Nash Diagnosis at Baseline by Fibrosis Severity - Intent-To-Treat Population

Table 14.1.4.3.1 Alcohol Use Disorders Identification Test (AUDIT) at Baseline by Dose Group - Intent-To-Treat Population

Table 14.1.4.3.2 Alcohol Use Disorders Identification Test (AUDIT) at Baseline by Age Group - Intent-To-Treat Population

Table 14.1.4.3.3 Alcohol Use Disorders Identification Test (AUDIT) at Baseline by Fibrosis Severity - Intent-To-Treat Population

Table 14.1.4.4.1 Surgical and Medical History by Dose Group - Intent-To-Treat Population

Table 14.1.4.4.2 Surgical and Medical History by Age Group - Intent-To-Treat Population

Table 14.1.4.4.3 Surgical and Medical History by Fibrosis Severity - Intent-To-Treat Population

Table 14.1.4.5.1 Prior Medications by ATC Therapeutic Subgroup, Chemical Subgroup, WHO Drug Name and Dose Group - Intent-To-Treat Population

Table 14.1.4.5.2 Prior Medications by ATC Therapeutic Subgroup, Chemical Subgroup, WHO Drug Name and Age Group - Intent-To-Treat Population

10.2.3 Treatment Compliance

10.3 Efficacy Data Summary Figures and Tables

10.3.1 Secondary Efficacy Variables

10.4 Safety Data Summary Figures and Tables

10.4.1 Exposure, Study and Treatment Durations

10.4.2 Displays of Adverse Events

10.4.2.1 Summary of Adverse Events

10.4.3 Listings of Deaths, Other Serious and Significant Adverse Events

Table 14.3.3.2 Listing of Serious Adverse Events - Safety Population

Table 14.3.3.3 Listing of Adverse Events Leading to Treatment Withdrawal - Safety Population

Table 14.3.3.4 Listing of Adverse Events Leading to Study Withdrawal - Safety Population

10.4.4 Narratives of Deaths, Other Serious and Significant Adverse Events

Not applicable.

10.4.5 Abnormal Laboratory Value Listing

See patient individual data Listings 16.2.8.1 and 16.2.8.2.

10.4.6 Display of Laboratory Data

Table 14.3.4.1.1 Hematology and Coagulation Parameters by Dose Group - Safety Population

Table 14.3.4.1.2 Hematology and Coagulation Parameters by Age Group - Safety Population

Table 14.3.4.2.1 Biochemistry Parameters by Dose Group - Safety Population

Table 14.3.4.2.2 Biochemistry Parameters by Age Group - Safety Population

Table 14.3.4.3.1 Shift Table of Hematology and Coagulation Parameters by Dose Group - Safety Population

Table 14.3.4.3.2 Shift Table of Hematology and Coagulation Parameters by Age Group - Safety Population

Table 14.3.4.4.1 Shift Table of Biochemistry Parameters by Dose Group - Safety Population

Table 14.3.4.4.2 Shift Table of Biochemistry Parameters by Age Group - Safety Population

Table 14.3.4.5.1 Urinalysis Parameters by Dose Group - Safety Population

Table 14.3.4.5.2 Urinalysis Parameters by Age Group - Safety Population

Table 14.3.4.6.1 Urinalysis (Dipstick) Parameters by Dose Group - Safety Population

Table 14.3.4.6.2 Urinalysis (Dipstick) Parameters by Age Group - Safety Population

10.4.7 Vital Signs, Physical Findings and Other Observations Related to Safety

Table 14.3.5.1.1 Vital Signs Parameters by Dose Group - Safety Population

Table 14.3.5.1.2 Vital Signs Parameters by Age Group - Safety Population

Table 14.3.5.2.1.1 Physical Examination Abnormalities by Dose Group - Safety Population

Table 14.3.5.2.1.2 Physical Examination Abnormalities by Age Group - Safety Population

Table 14.3.5.2.2.1 Physical Examination Clinically Significant Abnormalities by Dose Group - Safety Population

Table 14.3.5.2.2.2 Physical Examination Clinically Significant Abnormalities by Age Group - Safety Population

Table 14.3.5.3.1 12-Lead ECG Parameters by Dose Group - Safety Population

Table 14.3.5.3.2 12-Lead ECG Parameters by Age Group - Safety Population

10.4.8 Concomitant Medications

Table 14.3.6.1 Concomitant Medications by ATC Therapeutic Subgroup, Chemical Subgroup, WHO Drug Name and Dose Group - Safety Population

Table 14.3.6.2 Concomitant Medications by ATC Therapeutic Subgroup, Chemical Subgroup, WHO Drug Name and Age Group - Safety Population

10.4.9 Concomitant Procedures

Table 14.3.7.1 Concomitant Procedures by Primary System Organ Class, Preferred Term and Dose Group - Safety Population

Table 14.3.7.2 Concomitant Procedures by Primary System Organ Class, Preferred Term and Age Group - Safety Population

11. DOCUMENTATION OF STATISTICAL METHODS

11.1 Missing and Partially Known Dates

Missing dates will not be replaced. Unless specified otherwise, partially known dates will be defined as follows for duration computation:

- Partially known begin date:
  - If only the day is missing, it is estimated as the first day of the month or first visit date if the month/year are the same as the month/year of the first visit.
  - If month and day are missing, they are estimated as January 1 or first visit date if the year is the same as the year of the first visit.
  - The first visit date will be the date of screening (or the date of study treatment intake in case of treatment emergent AE duration computation).
- Partially known end date:
  - If only the day is missing, it is estimated as the last day of the month or last visit date if the month/year are the same as the month/year of the last visit.
  - If month and day are missing, they are estimated as December 31 or last visit date if the year is the same as the year of the last visit.
  - The last visit date will be the date of Early Termination visit or End of Study visit.

The original dates without estimation will be presented in the listings.

11.2 Demographics and Other Baseline Characteristics

The following rules will be applied for the computation of age:

- **Age** will be calculated in years using the following formula: **age** = (initial visit date – birth date) / 365.25. Date of initial visit will be taken at baseline visit. Results will be expressed with one decimal.

11.3 Medications

Medications will be coded using the WHO Drug dictionary version of March 2020 (B3 format). Tables and listings will be presented by Anatomical Therapeutic Chemical Classification (ATC) Therapeutic Subgroup (ATC level 2), Chemical Subgroup (ATC level 4) and WHO Drug Name.

A **prior medication** is a medication which was ended before the first study treatment intake (medication end date < first study treatment intake date). A **concomitant medication** is a medication which ended after or on the date of the first study treatment intake (medication end date ≥ first study treatment intake date).

When the end date of a medication intake is missing, the medication will be considered as concomitant with the study treatment.

When start and/or end dates of a medication intake are only partially known, medications will be categorized as prior treatment or concomitant using the following rules:

- If the partial end date is before (<) the first study treatment intake (*i.e.* year or year & month is/are before (<) the first study treatment intake date) then the medication is categorized as prior.
- If the partial end date is after or on the date (≥) of the first study treatment intake (*i.e.* year or year & month is/are after or on the date (≥) of the first study treatment intake date) then the medication is categorized as concomitant.

11.4 Treatment Compliance

- **Treatment compliance (%) at a post-baseline visit** will be calculated as follows: number of tablets taken between the previous visit and the current visit divided by number of tablets that should be taken between the previous visit and the current visit.

  With:

  - Number of tablets taken = number of tablets dispensed at the previous visit - number of tablets returned at the visit. For Visit 3 (Day 29), the previous visit when tablets were dispensed is Visit 1 (Day 1).
  - Number of tablets that should be taken = one tablet per day x theoretical treatment duration between the previous visit and the current visit, i.e. (date of current visit - date of previous visit + 1) - number of days when the tablets have not been taken.
  - Number of days when the tablets have not been taken, i.e., number of days of treatment interruption = Min(date restarted, date of current visit) - Max(interruption start date, date of previous visit) + 1.

- **The overall treatment compliance (%)** will be calculated as follows: total number of tablets taken divided by total number of tablets that should be taken.

  With:

  - Total number of tablets taken = sum over the visits of (number of tablets dispensed at the previous visit - number of tablets returned at the visit).
  - Total number of tablets that should be taken = one tablet per day x theoretical treatment duration, i.e. (last post baseline visit date - date of Visit 1 (Day 1) + 1) - total number of days when the tablets have not been taken.
  - Total number of days when the tablets have not been taken, i.e., total number of days of treatment interruption = sum over the visits of (date restarted - interruption start date + 1).

  In case one of the dates is missing or incomplete in the above computations then the duration (number of days) is missing. See Section 11.1 for handling partially known dates in case dates are only partially known. If one of the variables necessary to compute the patient compliance is missing, the compliance will be set to missing. Results will be expressed with one decimal.

11.5 Efficacy Variables

- The **height** and the **waist circumference** can be collected in two different units: cm and inch. All results will be presented in cms. Therefore, the conversion from inch to cm is the following:

$$1\ inch = 2.54\ cms$$

- The **weight** can be collected in two different units: kg and lb. All results will be presented in kgs. Therefore, the conversion from lb to kg is the following:

$$1\ lb = 0.453592\ kgs$$

- The **Body Mass Index** - BMI (Kg/m²) of patients will be calculated using the following formula:

$$\text{BMI} = \frac{\text{weight}}{(0.01 \times \text{height})^2}$$

  where height is in centimeters (cm) and weight in kilograms (kg). Results will be expressed with one decimal.

- The **BMI Z-score** of patients will be calculated using the following formula:

$$BMI\ Z - score = \left[\left(\frac{BMI}{M} \right)^{L} - 1 \right] / (L * S)$$

  where BMI is the Body Mass Index and M, L and S are values depending on sex and age (month) displayed in the table in Appendix.

- The child, adolescent and parent/legal guardian **PedsQL™ (Version 4.0) Generic Core Scales** is composed of 23 items comprising 4 dimensions (Physical Functioning, Emotional Functioning, Social Functioning, and School Functioning).

  The scoring of PedsQL™ will be performed as follows:

  - Items will be reversed scored and linearly transformed to a 0-100 scale, so that higher scores indicate better HRQOL (Health-Related Quality of Life). To reverse score, transform the 0-4 scale items to 0-100 as follows: 0=100, 1=75, 2=50, 3=25, 4=0.
  - To create Scale Scores, the mean will be computed as the sum of the items over the number of items answered for the corresponding dimension. If more than 50% of the items in the dimension are missing, the Scale Score should not be computed.
  - To create the Psychosocial Health Summary Score, the mean will be computed as the sum of the items over the number of items answered in the Emotional, Social, and School Functioning Scales. The Physical Health Summary Score is the same as the Physical Functioning Scale Score.

- To create the Total Score, the mean will be computed as the sum of all the items over the number of items answered on all the dimensions.

11.6 Exposure and Durations

Study duration will be defined in days as: Early Termination visit date (in case of withdrawal from the study) or End of Study visit date minus Screening visit date plus 1.

Treatment duration will be defined in days as last treatment intake date minus first treatment intake date plus 1. First treatment intake date corresponds to study treatment administration date collected at Visit 1 (Day 1). Last treatment intake date corresponds to last study treatment administration date collected at EOT (in case of withdrawal from the study) or at Visit 6 (Day 85).

Duration of exposure will be defined in days as duration of study treatment minus the number of days when the tablets have not been taken, i.e. study drug interruption: sum over the visits of (date restarted - interruption start date + 1).

In case one of the dates is missing or incomplete in the above computations then the duration is missing. See Section 11.1 for handling partially known dates in case dates are only partially known.

11.7 Adverse Events

All AEs will be categorized as treatment emergent or not treatment emergent as follows:

- **Not treatment emergent**: all events which started before (<) the date of first study treatment intake (at least one episode with start date/time before (<) the first study treatment intake date/time).
- **Treatment emergent**: 1) all events which started after or on the date (≥) of first study treatment (all episodes with start date/time after or on the date (≥) of the first study treatment intake date/time) or 2) all events which started before the date of first study treatment intake and worsened or became serious after or on the date of the first study treatment intake (in case of multiple episodes of the same event before the date of first treatment intake, the severity of the episode closest to the date of first treatment intake will be taken into account).

  In case of missing severity, the emergence of adverse events will be determined as showed in the table below:

Table 3 Assessment of Treatment Emergent Adverse Events

Severity			AE considered as
Closest episode before the date of first dose intake	**Episode(s) after the date of first treatment intake (included)**		
Missing	Missing	⇨	Emergent
Missing	Mild	⇨	Non emergent
Missing	Moderate	⇨	Emergent
Missing	Severe	⇨	Emergent
Mild	Missing	⇨	Emergent
Moderate	Missing	⇨	Emergent
Severe	Missing	⇨	Non emergent

If a start date is missing or unknown for an episode of an adverse event and the end date/time is either missing or after or on the date (≥) of the first study treatment intake date/time, the episode will be considered as starting after or on the date of the first study treatment intake.

When start and/or end dates of an episode of an adverse events are only partially known, episodes will be categorized as starting before or after/on the date of the first treatment intake using the following rules:

- If the partial end date is before (<) the first study treatment intake (*i.e.* year or year & month is/are before (<) the first study treatment intake date) then the episode will be considered as starting before the first study treatment intake,
- If the partial start date is after or on the date (≥) of the first study treatment intake (*i.e.* year or year & month is/are after or on the date (≥) of the first study treatment intake date) then the episode will be considered as starting after or on the date of the first study treatment intake.

Seriousness, severity, relationship to the study treatment, action taken and outcome are recorded for each episode of an adverse event. The following rules will be applied for the descriptions of AEs:

- For descriptions based on **seriousness**: if one episode of the AE is serious (whatever the time it occurs), the whole event will be considered as serious.
- For descriptions based on **severity**: the worst intensity among all episodes of the AE during the studied period will be taken into account.
- For descriptions based on **relationship to study treatment (Yes/No)**: if one episode of the AE is Related or Possibly Related or relationship to the study treatment is Not assessable (after or on the date of first treatment intake), the whole event will be considered as related to the study treatment.
- For descriptions based on **relationship to study treatment by category**: the whole event will be categorized according to the episode (after or on the date of

first treatment intake) associated with the “highest” category according to the following order: Not related < Unlikely related < Possibly related < Related. Not assessable relationship is considered as related to the study treatment.

- For descriptions based on **relationship to study procedures (Yes/No)**: if one episode of the AE is Related to the study procedures or if relationship to the study procedures is Not assessable (after or on the date of first treatment intake), the whole event will be considered as related to the study treatment.
- For descriptions based on **action taken**: if one episode of the AE leads to **study withdrawal**, the whole event will be considered as leading to study withdrawal. Otherwise, the action taken of the AE will be the action taken of the episode occurring on or after the day of emergence of the AE.
- For descriptions based on **action taken with study treatment**: if one episode of the AE leads to **study treatment withdrawal**, the whole event will be considered as leading to study treatment withdrawal. Otherwise, the action taken with study treatment of the AE will be the action taken of the episode occurring on or after the day of emergence of the AE.
- For descriptions based on **outcome:** the information of the last episode of the AE will be taken into account.

The **maximum event severity** is the greatest severity associated with a PT for a patient according to the following order: Mild < Moderate < Severe. Missing severity is considered as severe (except for the definition of emergence: See Table 3).

The **duration of an adverse event** will be computed in days as the difference between the end date of the last episode and the start date of the first episode using the following formula: end date of the last episode - start date of the first episode +1 (See Section 11.1 for handling missing and partially known dates).

Time to onset since first treatment intake of a treatment emergent adverse event will be computed in days as the difference between the start date of the first episode after the first treatment intake and the date of first treatment intake using the following formula: start date of the first episode after the first treatment intake - date of first treatment intake +1 (See Section 11.1 for handling missing and partially known dates).

11.8 Laboratory Data

11.8.1 Laboratory Evaluation

Laboratory measurements that will be summarized in the report are those defined in the study protocol:

- **Hematology and coagulation parameters**: haemoglobin, haematocrit, red blood cells (RBC), white blood cells (WBC), differential count, platelet count, reticulocytes count, prothrombin time (PT) and international normalized ratio (INR).

- **Biochemistry**: creatinine, creatinine clearance (eGFR), total protein, albumin, electrolytes (sodium, potassium, chloride, calcium), uric acid, urea, Creatinine Phosphokinase (CPK), AST, ALT, GGT, ALP, total and conjugated bilirubin, hsCRP, fasting plasma glucose, fasting insulin, HOMA-IR, fructosamine, C-peptide, Fatty Free Acids (FFA), Hemoglobin A1C (HbA1c), Thyroid Stimulation Hormone (TSH), Cystatin C, eGFR from Cystatin C.

  Note: some biochemistry parameters will be quantitively described both as efficacy and safety data. Safety analyses will additionally include descriptions according to reference range and shift tables.

- **Urinalysis**: α1 microglobulin, β-NAG, N-Gal, albumin, creatinine, microscopic analysis6.

- **Urinalysis (dipstick)**: Specific gravity, pH, protein, glucose, ketones, bilirubin, urobilinogen, blood, nitrite, leukocytes.

Results will be presented Standard International (SI) units.

In case of multiple results at the baseline visit for a same laboratory parameter and a same patient, only the result of the reliable (*i.e.* analyzable) test which date is closer and before (<) the intake of study treatment date will be retained for analysis.

In case of multiple results at follow-up visit for a same laboratory parameter and a same patient:

- Only the result of the first (earlier date) analyzable test will be retained for descriptive analysis by visit.
- The result of the first (earlier date) analyzable test will be retained for shift table by visit, unless the first test value is within range and the retest value (from analyzable test) is out of range, in which case the retest (later date) will be retained in the shift table at the corresponding visit.

All laboratory tests will be presented in the data listings for each patient.

11.8.2 Reference Ranges

For each laboratory parameter, reference ranges used to categorize the results as “below lower limit of normality”, “normal” or “above upper limit of normality” will be those provided by the laboratories which performed the tests and that were entered in the database.

Results expressed with symbols, like “< LLN”, *i.e.* below lower limit of normality, and “> ULN”, *i.e.* above upper limit of normality, will be considered for the quantitative analyses of laboratory parameters as LLN/2 and ULN, respectively.

Original results (with symbols) as reported in the database will be displayed in the individual data listings.

12. PATIENT DATA LISTINGS

12.1 General Remarks about Listings

Listings presented in section 16.2 of ICH report will be created with SAS version 9.4. In each listing, the patients will be presented by patient number and, when relevant, parameter, visit and timepoint.

The following sections present the listings in the order in which they are planned to appear in the study report.

12.2 Disposition of Patients

Listing 16.2.1.1 Patients' Final Status in the Study
Listing 16.2.1.2 Study Withdrawals
Listing 16.2.1.3 Visit Dates
Listing 16.2.1.4 Inclusion Criteria Not Respected
Listing 16.2.1.5 Exclusion Criteria Not Respected
Listing 16.2.1.6 Randomization Data
Listing 16.2.1.7 Analysis Data Sets
Listing 16.2.1.8 Patients Excluded From Analysis Data Sets

12.3 Protocol Deviations

Listing 16.2.2.1 Major Protocol Deviations
Listing 16.2.2.2 Minor Protocol Deviations

12.4 Patients Excluded from Efficacy Analysis

Not applicable.

12.5 Demographic Data

Listing 16.2.4.1 Demographic Characteristics
Listing 16.2.4.2 NASH Diagnosis
Listing 16.2.4.3 Alcohol Use Disorders Identification Test (AUDIT)
Listing 16.2.4.4 Medical and Surgical History
Listing 16.2.4.5 Prior Medications
Listing 16.2.4.6 Prior Procedures
Listing 16.2.4.7.1 Serology Parameters
Listing 16.2.4.7.2 Other Laboratory Parameters for Eligibility Assessment

Listing 16.2.4.7.3 Urine Pregnancy Tests

12.6 Compliance and/or Drug Concentration Data

Listing 16.2.5.1 Treatment Compliance

Listing 16.2.5.2 Exposure, Study and Treatment Durations

12.7 Individual Efficacy Response Data

Listing 16.2.6.1 Liver Markers

Listing 16.2.6.2 Markers of Glucose Homeostasis

Listing 16.2.6.3 Serum Lipid Parameters

Listing 16.2.6.4 Height, Body Weight and Body Mass Index Z-Score

Listing 16.2.6.5 Waist Circumference

Listing 16.2.6.6 Inflammatory markers

Listing 16.2.6.7 Pediatric Quality of Life (PedsQL™)

Listing 16.2.6.8 Lifestyle Diet

12.8 Adverse Event Listings

Listing 16.2.7.1 Adverse Events

Listing 16.2.7.2 Adverse Events of Special Interest

12.9 Listing of Individual Laboratory Measurements

Listing 16.2.8.1 Hematology and Coagulation Parameters

Listing 16.2.8.2 Biochemistry Parameters

Listing 16.2.8.3 Urinalysis Parameters

12.10 Vital signs, Physical Findings and Other Observations Related to Safety

Listing 16.2.9.1 Vital Signs Parameters

Listing 16.2.9.2 Physical Examination

Listing 16.2.9.3 12-Lead ECG Parameters

12.11 Concomitant Medications and Procedures

Listing 16.2.10.1 Concomitant Medications

Listing 16.2.10.2 Concomitant Procedures

12.12 Collection of PK Blood Samples

Listing 16.2.11.1 Collection of PK Blood Samples

13. APPENDIX

Table 4 Data for Computation of BMI Z-score

Sex	Age (month)	L	M	S
Male	96	-1.4629	15.7368	0.09526
Male	97	-1.479	15.7606	0.09567
Male	98	-1.4947	15.7848	0.09609
Male	99	-1.5101	15.8094	0.09651
Male	100	-1.5252	15.8344	0.09693
Male	101	-1.5399	15.8597	0.09735
Male	102	-1.5542	15.8855	0.09778
Male	103	-1.5681	15.9116	0.09821
Male	104	-1.5817	15.9381	0.09864
Male	105	-1.5948	15.9651	0.09907
Male	106	-1.6076	15.9925	0.09951
Male	107	-1.6199	16.0205	0.09994
Male	108	-1.6318	16.049	0.10038
Male	109	-1.6433	16.0781	0.10082
Male	110	-1.6544	16.1078	0.10126
Male	111	-1.6651	16.1381	0.1017
Male	112	-1.6753	16.1692	0.10214
Male	113	-1.6851	16.2009	0.10259
Male	114	-1.6944	16.2333	0.10303
Male	115	-1.7032	16.2665	0.10347
Male	116	-1.7116	16.3004	0.10391
Male	117	-1.7196	16.3351	0.10435
Male	118	-1.7271	16.3704	0.10478
Male	119	-1.7341	16.4065	0.10522
Male	120	-1.7407	16.4433	0.10566
Male	121	-1.7468	16.4807	0.10609
Male	122	-1.7525	16.5189	0.10652
Male	123	-1.7578	16.5578	0.10695
Male	124	-1.7626	16.5974	0.10738
Male	125	-1.767	16.6376	0.1078
Male	126	-1.771	16.6786	0.10823
Male	127	-1.7745	16.7203	0.10865
Male	128	-1.7777	16.7628	0.10906
Male	129	-1.7804	16.8059	0.10948

Sex	Age (month)	L	M	S
Male	130	-1.7828	16.8497	0.10989
Male	131	-1.7847	16.8941	0.1103
Male	132	-1.7862	16.9392	0.1107
Male	133	-1.7873	16.985	0.1111
Male	134	-1.7881	17.0314	0.1115
Male	135	-1.7884	17.0784	0.11189
Male	136	-1.7884	17.1262	0.11228
Male	137	-1.788	17.1746	0.11266
Male	138	-1.7873	17.2236	0.11304
Male	139	-1.7861	17.2734	0.11342
Male	140	-1.7846	17.324	0.11379
Male	141	-1.7828	17.3752	0.11415
Male	142	-1.7806	17.4272	0.11451
Male	143	-1.778	17.4799	0.11487
Male	144	-1.7751	17.5334	0.11522
Male	145	-1.7719	17.5877	0.11556
Male	146	-1.7684	17.6427	0.1159
Male	147	-1.7645	17.6985	0.11623
Male	148	-1.7604	17.7551	0.11656
Male	149	-1.7559	17.8124	0.11688
Male	150	-1.7511	17.8704	0.1172
Male	151	-1.7461	17.9292	0.11751
Male	152	-1.7408	17.9887	0.11781
Male	153	-1.7352	18.0488	0.11811
Male	154	-1.7293	18.1096	0.11841
Male	155	-1.7232	18.171	0.11869
Male	156	-1.7168	18.233	0.11898
Male	157	-1.7102	18.2955	0.11925
Male	158	-1.7033	18.3586	0.11952
Male	159	-1.6962	18.4221	0.11979
Male	160	-1.6888	18.486	0.12005
Male	161	-1.6811	18.5502	0.1203
Male	162	-1.6732	18.6148	0.12055
Male	163	-1.6651	18.6795	0.12079
Male	164	-1.6568	18.7445	0.12102
Male	165	-1.6482	18.8095	0.12125
Male	166	-1.6394	18.8746	0.12148

Sex	Age (month)	L	M	S
Male	167	-1.6304	18.9398	0.1217
Male	168	-1.6211	19.005	0.12191
Male	169	-1.6116	19.0701	0.12212
Male	170	-1.602	19.1351	0.12233
Male	171	-1.5921	19.2	0.12253
Male	172	-1.5821	19.2648	0.12272
Male	173	-1.5719	19.3294	0.12291
Male	174	-1.5615	19.3937	0.1231
Male	175	-1.551	19.4578	0.12328
Male	176	-1.5403	19.5217	0.12346
Male	177	-1.5294	19.5853	0.12363
Male	178	-1.5185	19.6486	0.1238
Male	179	-1.5074	19.7117	0.12396
Male	180	-1.4961	19.7744	0.12412
Male	181	-1.4848	19.8367	0.12428
Male	182	-1.4733	19.8987	0.12443
Male	183	-1.4617	19.9603	0.12458
Male	184	-1.45	20.0215	0.12473
Male	185	-1.4382	20.0823	0.12487
Male	186	-1.4263	20.1427	0.12501
Male	187	-1.4143	20.2026	0.12514
Male	188	-1.4022	20.2621	0.12528
Male	189	-1.39	20.3211	0.12541
Male	190	-1.3777	20.3796	0.12554
Male	191	-1.3653	20.4376	0.12567
Male	192	-1.3529	20.4951	0.12579
Male	193	-1.3403	20.5521	0.12591
Male	194	-1.3277	20.6085	0.12603
Male	195	-1.3149	20.6644	0.12615
Male	196	-1.3021	20.7197	0.12627
Male	197	-1.2892	20.7745	0.12638
Male	198	-1.2762	20.8287	0.1265
Male	199	-1.2631	20.8824	0.12661
Male	200	-1.2499	20.9355	0.12672
Male	201	-1.2366	20.9881	0.12683
Male	202	-1.2233	21.04	0.12694
Male	203	-1.2098	21.0914	0.12704

Sex	Age (month)	L	M	S
Male	204	-1.1962	21.1423	0.12715
Female	96	-1.388	15.681	0.11291
Female	97	-1.3966	15.7107	0.11335
Female	98	-1.4047	15.7415	0.1138
Female	99	-1.4125	15.7732	0.11424
Female	100	-1.4199	15.8058	0.11469
Female	101	-1.427	15.8394	0.11513
Female	102	-1.4336	15.8738	0.11557
Female	103	-1.4398	15.909	0.11601
Female	104	-1.4456	15.9451	0.11644
Female	105	-1.4511	15.9818	0.11688
Female	106	-1.4561	16.0194	0.11731
Female	107	-1.4607	16.0575	0.11774
Female	108	-1.465	16.0964	0.11816
Female	109	-1.4688	16.1358	0.11859
Female	110	-1.4723	16.1759	0.11901
Female	111	-1.4753	16.2166	0.11943
Female	112	-1.478	16.258	0.11985
Female	113	-1.4803	16.2999	0.12026
Female	114	-1.4823	16.3425	0.12067
Female	115	-1.4838	16.3858	0.12108
Female	116	-1.485	16.4298	0.12148
Female	117	-1.4859	16.4746	0.12188
Female	118	-1.4864	16.52	0.12228
Female	119	-1.4866	16.5663	0.12268
Female	120	-1.4864	16.6133	0.12307
Female	121	-1.4859	16.6612	0.12346
Female	122	-1.4851	16.71	0.12384
Female	123	-1.4839	16.7595	0.12422
Female	124	-1.4825	16.81	0.1246
Female	125	-1.4807	16.8614	0.12497
Female	126	-1.4787	16.9136	0.12534
Female	127	-1.4763	16.9667	0.12571
Female	128	-1.4737	17.0208	0.12607
Female	129	-1.4708	17.0757	0.12643
Female	130	-1.4677	17.1316	0.12678
Female	131	-1.4642	17.1883	0.12713

Sex	Age (month)	L	M	S
Female	132	-1.4606	17.2459	0.12748
Female	133	-1.4567	17.3044	0.12782
Female	134	-1.4526	17.3637	0.12816
Female	135	-1.4482	17.4238	0.12849
Female	136	-1.4436	17.4847	0.12882
Female	137	-1.4389	17.5464	0.12914
Female	138	-1.4339	17.6088	0.12946
Female	139	-1.4288	17.6719	0.12978
Female	140	-1.4235	17.7357	0.13009
Female	141	-1.418	17.8001	0.1304
Female	142	-1.4123	17.8651	0.1307
Female	143	-1.4065	17.9306	0.13099
Female	144	-1.4006	17.9966	0.13129
Female	145	-1.3945	18.063	0.13158
Female	146	-1.3883	18.1297	0.13186
Female	147	-1.3819	18.1967	0.13214
Female	148	-1.3755	18.2639	0.13241
Female	149	-1.3689	18.3312	0.13268
Female	150	-1.3621	18.3986	0.13295
Female	151	-1.3553	18.466	0.13321
Female	152	-1.3483	18.5333	0.13347
Female	153	-1.3413	18.6006	0.13372
Female	154	-1.3341	18.6677	0.13397
Female	155	-1.3269	18.7346	0.13421
Female	156	-1.3195	18.8012	0.13445
Female	157	-1.3121	18.8675	0.13469
Female	158	-1.3046	18.9335	0.13492
Female	159	-1.297	18.9991	0.13514
Female	160	-1.2894	19.0642	0.13537
Female	161	-1.2816	19.1289	0.13559
Female	162	-1.2739	19.1931	0.1358
Female	163	-1.2661	19.2567	0.13601
Female	164	-1.2583	19.3197	0.13622
Female	165	-1.2504	19.382	0.13642
Female	166	-1.2425	19.4437	0.13662
Female	167	-1.2345	19.5045	0.13681
Female	168	-1.2266	19.5647	0.137

Sex	Age (month)	L	M	S
Female	169	-1.2186	19.624	0.13719
Female	170	-1.2107	19.6824	0.13738
Female	171	-1.2027	19.74	0.13756
Female	172	-1.1947	19.7966	0.13774
Female	173	-1.1867	19.8523	0.13791
Female	174	-1.1788	19.907	0.13808
Female	175	-1.1708	19.9607	0.13825
Female	176	-1.1629	20.0133	0.13841
Female	177	-1.1549	20.0648	0.13858
Female	178	-1.147	20.1152	0.13873
Female	179	-1.139	20.1644	0.13889
Female	180	-1.1311	20.2125	0.13904
Female	181	-1.1232	20.2595	0.1392
Female	182	-1.1153	20.3053	0.13934
Female	183	-1.1074	20.3499	0.13949
Female	184	-1.0996	20.3934	0.13963
Female	185	-1.0917	20.4357	0.13977
Female	186	-1.0838	20.4769	0.13991
Female	187	-1.076	20.517	0.14005
Female	188	-1.0681	20.556	0.14018
Female	189	-1.0603	20.5938	0.14031
Female	190	-1.0525	20.6306	0.14044
Female	191	-1.0447	20.6663	0.14057
Female	192	-1.0368	20.7008	0.1407
Female	193	-1.029	20.7344	0.14082
Female	194	-1.0212	20.7668	0.14094
Female	195	-1.0134	20.7982	0.14106
Female	196	-1.0055	20.8286	0.14118
Female	197	-0.9977	20.858	0.1413
Female	198	-0.9898	20.8863	0.14142
Female	199	-0.9819	20.9137	0.14153
Female	200	-0.974	20.9401	0.14164
Female	201	-0.9661	20.9656	0.14176
Female	202	-0.9582	20.9901	0.14187
Female	203	-0.9503	21.0138	0.14198
Female	204	-0.9423	21.0367	0.14208

Source: https://www.who.int/growthref/who2007_bmi_for_age/en/

14. ATTACHEMENTS

Table templates: See attached document “Genfit - GFT505-218-1 - SAP - Final 2.0 - Attachment - Tables”.