A Phase 1, Randomized, Double-Blind, Placebo-Controlled, Single-Centre Study of Single, Twice Daily (BID) Doses, and Repeated BID Dosing of Ascending Doses, to Evaluate the Safety, Tolerability, and Systemic Exposure of Intranasal Apo-Si-K170A-C76 in Healthy Adult Subjects

Statistical Analysis Plan for study Apo-Si-K170A-C76.
Based on study protocol version 2.0 dated 29 February 2024.

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SIGNATURE PAGE

Authored By:

Orpaz Eilon Senior Biostatistician and SAS Programmer Medistat Ltd	DocuSigned by: Orpaz Eilon F9D1CCBC9BA94B1...	4/24/2024
Name, Title, Company	Signature	Date

Approver's Signature:

Hagit Grimberg CTO SirVit Ltd	DocuSigned by: Hagit Grimberg 951FA068FD9A46C...	5/1/2024
Name, Title, Company	Signature	Date

LIST OF ABBREVIATIONS

ATC	Anatomical Therapeutic Chemical
BID	Twice a day
BL	Baseline
BLQ	Below the Limit of Quantification
CI	Confidence Interval
eCRF	Electronic Case Report Form
CSRs	Clinical study reports
CTC	Common Terminology Criteria
DSMC	Data Safety Monitoring Committee
EOS	End of Study
ET	Early Termination
FDA	Food and Drug Administration
ICF	Informed Consent Form
ITT	Intent-to-Treat
IP	Investigational product
MedDRA	Medical Dictionary for Regulatory Activities
NA	Not applicable
NOAEL	No-Observed-Adverse-Effect Level
PI	Principal Investigator
PK	Pharmacokinetic
QA	Quality Assurance
RU	Research Unit
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis Software
SD	Standard Deviation
SE	Standard Error
SSC	Safety Steering Committee
TNSS	Total Nasal Symptom Score
WHO	World Health Organization

1. STUDY DETAILS

1.1. Study Design

This is a prospective, randomized, double-blind, placebo-controlled study designed to assess the safety, tolerability, and systemic exposure of single, BID dosed and repeated BID dosing of ascending doses of intranasal Apo-Si-K170A-C76 in healthy adult subjects.

Upon signing the informed consent, the subjects will undergo a screening period for eligibility evaluation. Subjects will be admitted to the Research Unit (RU) on Day 1 and eligibility will be confirmed again. Eligible subjects, as determined by the Principal Investigator (PI), will be randomized as close as possible prior to 1st drug administration on Day 1 to receive either intranasal Apo-Si-K170A-C76 or matching placebo. Dosing will depend on the cohort the subjects are assigned to.

Intranasal (IN) administration is performed to both nostrils of all participants. The nasal spray device contains the Study Drug at 20 mg/mL and delivers 0.1 mL volume per actuation. The subjects will receive 1-3 actuations per nostril according to dosing group. After each actuation, an inspiration will be performed, and around a 5-second delay will be introduced between each new actuation. Thus, during each administration cohort, dosages registered as dose/nostril are received twice per subject, one dose to each nostril.

1.2. Blinding & Randomization

All study staff (with the exception of specified unblinded pharmacy staff), study subjects, and the Sponsor will remain blinded to study drug/placebo allocation.

The study will be composed of 7 dosing cohorts. Each subject will participate in one cohort. Subjects will be screened and randomized to active Apo-Si-K170A-C76 or matching placebo in a 3:1 ratio.

Part 1	Dose Concentration	Number of Subjects	
		Apo-Si-K170A-C76	Placebo
Cohort 1	2mg/nostril, 4mg/both nostrils	6	2
Cohort 2	4mg/nostril, 8mg/both nostrils	6	2
Cohort 3	6mg/nostril, 12mg/both nostrils	6	2
Cohort 4	4mg/nostril, 8 mg/both nostrils BID (16mg/day/both nostrils)	6	2
Cohort 5	6mg/nostril, 12 mg/both nostrils BID (24mg/day/both nostrils)	6	2
Cohort 6	4mg/nostril, 8 mg/both nostrils BID (16mg/day/both nostrils) for 5 days	6	2
Cohort 7	6mg/nostril, 12 mg/both nostrils BID (24mg/day/both nostrils) for 5 days	6	2
Total Subjects		**42**	**14**

1.3. Sample Size

Fivety six(56) healthy subjects are planned to be enrolled (42 active and 14 placebo subjects).

The sample size is not based on power calculations. It is chosen based on clinical experience and typical SAD and multiple administration designs and considered to be adequate to fulfil the objectives of the study.

1.4. Study Duration

The total duration for each participating subject is up to 35 days: Up to 21 days of screening and 14 days (7±2 days after last dose) including treatment and the follow up visit period (depending on the cohort the subject is assigned to).

1.5. Study Objectives

a) Primary Objectives

To evaluate the safety and tolerability of single, BID doses and repeated BID, ascending doses of Apo-Si-K170A-C76 administered intranasally (IN) in healthy adult subjects.

b) Secondary Objective

To evaluate the systemic exposure of Apo-Si-K170A-C76 following intranasal administration in healthy adult subjects.

1.6. Study Endpoints

1.6.1. Safety and Tolerability Endpoints

a. Frequency and severity of Adverse Events (AEs), including Serious Adverse Events (SAEs) and Treatment-emergent AEs (TEAEs) occurring at any time during the study.

b. Change from Baseline to End of Study (EOS) in: Laboratory tests including urinalysis and blood tests, Vital signs, Physical examination, & Total Nasal Symptom Score (TNSS).

1.7. Schedule of Assessments

a. Cohort 1, 2, 3 (Single Dose):

	Screening[1] -21 to Day 1	Treatment administration Day 1[2]	Day 2	EOS: Day 8 (± 2 day) F/U
Visit No.	**1**	**2**	**3**	**4**
Informed consent[3]	X			
Complete medical history	X			
Height[4], weight, and BMI calculation	X			
Vital signs[5]	X	X	X	X
TNSS[6]	X	X	X	X
Complete physical examination[7]	X			
Focused physical examination[8]		X	X	X
12-lead safety ECGs[9]	X	X	X	X
Blood and urine for safety analyses[10]	X			X
SARS-CoV-2 screening test[11]	X	X		
Blood sampling for systemic exposure[12]		X	X	
Blood for hep B, hep C, HIV serology	X			
Alcohol test and urine test for drugs of abuse, cotinine and pregnancy[13]	X	X		
Eligibility confirmation	X[3]	X[3]		
Randomization[14]		X		
IN administration of treatment		X		
Assess for AEs[15]	X	X	X	X
Prior and concomitant medications[16]	X	X	X	X
Examination of nasal cavity	X		X	X

1 Screening must occur within 21 days prior to the start of dosing. Screening will take place only once for each participant.
2 Overnight confinement to the clinic between Day 1 and Day 2 is mandatory (through 24 hours post dose); i.e., subjects will be discharged on Day 2 after all required assessments and procedures have been completed for that day. The PI or designee will confirm that the subject is fit for discharge on Day 2.
3 Informed Consent must be obtained prior to initiating any study procedure. Subject eligibility should be confirmed also on Day 1 prior to dosing.
4 Height to be measured only at screening.
5 Vital signs will be obtained at Screening, within 2 hours prior to and 1, 2, 4, and 8 hours (all ± 20 minutes) post dose on Day 1, at 24 hours (± 1 hour) post dose on Day 2 and at F/U. Vital signs should be captured after 5 minutes of rest while the subject is in a supine or seated position.

6 Subjects will complete the TNSS scale to rate their nasal symptoms. TNSS will be tested at screening, within 2 hours prior to dosing, and 1 hour (± 20 minutes) after dosing. Also, TNSS will be recorded on Day 2, 24 hours (± 1 hour) after the dose administered on Day 1, and at the EOS visit.
7 A complete physical examination (i.e., general appearance, head, ears, eyes, nose, throat, dentition, thyroid, chest [heart, lungs], abdomen, skin, neurological, extremities, back, neck, musculoskeletal, lymph nodes) will be performed at Screening.
8 A focused physical examination consisting of the chest (heart, lungs), abdomen, skin, neurological, and musculoskeletal examinations will be performed within 2 hours prior to dosing of Treatment, upon discharge on Day 2, and at the F/U visit.
9 Safety ECGs will be obtained at Screening Visit. A single 12-lead safety ECG will also be obtained on Day 1, pre-dose (within 2 hours prior to dosing) and at 1 hour ± 20 minutes and 24 hours (± 1 hour) post dose. Safety ECGs will be obtained at F/U. The ECGs should be captured after 5 minutes of rest in a semi-supine / supine position.
10 Blood samples will be collected for chemistry, hematology, and coagulation at Screening and at F/U. Urine samples will be collected for urinalysis (and urine microscopy if urinalysis is + or above for red blood cells, white blood cells, protein, or nitrite) at Screening and at F/U.
11 Performed locally using a kit.
12 On Day 1, obtain blood for systemic exposure prior to dosing (within 1 hour before), at 30 and 60 minutes (all ± 5 minutes) and 2, 3, and 4 hours (all ± 10 minutes), 6 and 8 hours (all ± 20 minutes) post dose. A 24-hour (± 1 hour) post dose sample will be collected on Day 2.
13 At screening, alcohol and pregnancy will be tested in blood and drugs and cotinine in urine (all central lab). On Day 1 prior to dosing, alcohol, drugs, cotinine, and β-HCG will be tested locally in urine.
14 Randomization to placebo or active will occur as close as possible prior to the first administration of Treatment.
15 Adverse events will be collected from the time of informed consent through the F/U visit.
16 Prior and concomitant medication history includes all medications (including over-the-counter medications, vitamins, and supplements) taken from 30 days prior to informed consent signing through the F/U visit.

b. Cohort 4&5 (BID dose):

	Screening[1] -21 to Day 1	Day 1 Treatment administration[2]	Day 2	EOS: Day 8 (± 2 day) F/U
Visit No.	**1**	**2**	**3**	**4**
Informed consent[3]	X			
Complete medical history	X			
Height[4], weight, and BMI calculation	X			
Vital signs[5]	X	X	X	X
TNSS[6]	X	XX	X	X
Complete physical examination[7]	X			
Focused physical examination[8]		X	X	X
12-lead safety ECGs[9]	X	X	X	X
Blood and urine for safety analyses[10]	X			X
SARS-CoV-2 screening test[11]	X	X		
Blood sampling for systemic exposure[12]		X	X	
Blood for hep B, hep C, HIV serology	X			
Alcohol test and urine test for drugs of abuse, cotinine and pregnancy [13]	X	X		
Eligibility Confirmation	X[3]	X[3]		
Randomization[14]		X		
IN administration of treatment		XX (BID)		
Assess for AEs[15]	X	X	X	X
Prior and concomitant medications[16]	X	X	X	X
Examination of nasal cavity	X		X	X

c. Cohort 6&7 (repeated dose BID):

Day / Visit	Screening[1] -21 to Day 1	Day 1 Treatment administration[2]	Day 2 to Day 4 Continued Dosing of Treatment	Day 5 Final Treatment administration	Day 6	EOS: Day 12 (±2 day) F/U
Visit No.	**1**	**2**	**3, 4, 5**	**6**	**7**	**8**
Informed consent[3]	X					
Complete medical history	X					
Height[4], weight, and BMI calculation	X					
Vital signs[5]	X	X	X	X	X	X
TNSS[6]	X	XX	XX	XX	X	X
Complete physical examination[7]	X					
Focused physical examination[8]		X		X	X	X
12-lead safety ECG[9]	X	X	X	X	X	X
Blood and urine for safety analyses[10]	X		X			X
SARS-CoV-2 screening test[11]	X	X				
Blood sampling for systemic exposure[12]		X	X	X	X	
Blood for hep B, hep C, HIV serology	X					
Alcohol test and urine test for drugs of abuse, cotinine and pregnancy[13]	X	X				
Eligibility Confirmation	X[3]	X[3]				
Randomization[14]		X				
IN administration of treatment[15]		XX (BID)	XX (BID)	XX (BID)		
Assess for AEs[16]	X	X	X	X	X	X
Prior and concomitant medications[17]	X	X	X	X	X	X
Examination of nasal cavity	X		X	X	X	X

2. ANALYSIS SETS

2.1. Intent to Treat Set – ITT

The Intent to Treat (ITT) Set, will include all Enrolled subjects who were randomized.

2.2. Safety Set

The Safety Set will include all enrolled subjects who receive at least one dose of any study intervention, including subjects withdrawn or discontinued from treatment for any reason from the study.

3. DERIVED DATA AND OTHER DEFINITIONS

3.1. General Definitions:

Baseline is considered as the last valid assessment performed before the first administration of study treatment . This value will be measured within 28 days or could be the same day as first treatment administration

Change from baseline (for numerical variables) at time point XX = Value at time point XX – Value at baseline. (No change is 0).

$$Change = current - baseline$$

Relative change from baseline (for numerical variables) at time point XX = (Value at time point XX – Value at baseline)/ Value at baseline × 100%. (No change is 0)

$$Relative\ Change = \frac{current - baseline}{baseline} \times 100$$

Shift from baseline (for categorical variables) at time point XX = Value at baseline to Value at time point XX. (No change is "No Change").

$$Shift = baseline\ to\ current$$

3.2. Study Arms

In each cohort there are 6 subjects with active dose and 2 subjects with placebo. Subjects with placebo will be included in the "Placebo" study arm. All other subjects will be in included in the study arm of their cohort. "Overall" study arm will include all subjects but "Placebo".

3.3. Safety Variables

3.3.1. Medical Coding

Adverse events, Medical history, and Procedures/Therapies will be coded to System Organ Class and Preferred Term using the most updated version of Medical Dictionary for Regulatory Activities (MedDRA) terminology.

Prior and concomitant medications will be coded to Anatomical Therapeutic Chemical (ATC) second, fourth and fifth levels using the WHO (World Health Organization) Drug Public Website Dictionary named WHOCC-ATC/DDD..

4. ANALYSIS METHODS AND DATA PRESENTATION

4.1. General principles

4.1.1. General Considerations

Analyses presented in the clinical report but not mentioned in the SAP are unplanned or ad-hoc analyses. Statistical methods presented in the SAP may be slightly different from those that are presented in the protocol. Differences are clearly stated and the SAP supersedes the protocol only with regard to the way data will be handled and analysed.

4.1.2. Statistical Analysis Software

Data manipulation, tabulation of descriptive statistics, calculation of inferential statistics (if relevant), and graphical representations (if relevant) will be performed using SAS® version 9.4 or higher for Windows. If the use of other software is warranted, the final statistical methodology report will detail which software was used for what purposes.

4.1.3. Handling Missing Data

No data imputation will be performed.

4.1.4. Incomplete dates

All incomplete dates will be entered in the database as they were recorded in the EDC. Thereafter, for calculation purposes, the incomplete dates will be completed using pre-defined rules. If a day or month is recorded as UNK it will be replaced by the first day of the month or January, respectively, provided this does not contradict any other dates recorded. If both day and month are recorded as UNK it will be replaced by the first day of month and January.

4.2. Significance Level and Multiplicity Adjustments

By default, all tests were two-tailed, and a p value of 5% or less will be considered statistically significant.

The precision of estimates will be presented using two-sided 95% CIs.

No multiplicity adjustments will be made.

4.3. Displaying of Variables

Measured variables will be listed individually. Measured variables and derived variables will summarised by study arm, for the following descriptive statistics:

Continuous variables will be summarised by the number of observations (n), mean, standard deviation, median, minimum, and maximum and 95% CI for means of variables if appropriate.

Categorical variables will be summarised by frequency (n) counts and percentages (%) for each category. Unless otherwise stated, percentages will be calculated out of the number of patients in the relevant Analysis Set.

4.4. Analysis Method by Section

4.4.1. Patient Disposition

The following Patient disposition outcomes will be summarized. The number of patients in ITT Analysis set who:

- Signed ICF (Note: percentages will not be presented for this number)
- Eligible (not including Screen failure subjects)
- Treated (subjects who went through any intraoperative procedure)
- Completed the study
- Discontinued early from treatment

Where reasons for discontinuation of treatment or withdrawal from study exist, these will be included.
Reasons for Screening Failure will be summarized in a separate table.
All variables above will be listed, including date the Informed Consent Form was signed.

4.4.2. Demographic Data and Baseline Data

Demographic and baseline characteristics data will be listed and summarized by study arm using the ITT Analysis set.

4.4.3. Medical History

All medical history will be listed. The number and percentage of participants with medical history, along with the number of events, will be summarized in appropriate tables by System Organ Class and Preferred Term, by study arm using the ITT Analysis set. Subjects will be counted once for each separate Preferred Term and/or System Organ Class.

For example:

MedDRA System class		VasQ			Control			All		
		N = (events)	N = (subjects)	% (subjects)	N = (events)	N = (subjects)	% (subjects)	N = (events)	N = (subjects)	% (subjects)
System organ class	**Preferred term**									
All	All									
respiratory system	All									
	irritation									
	cough									

4.4.4. Exposure

All exposure data will be listed and summarized.

4.4.5. Adverse Events - Safety Endpoint

All Adverse events will be listed. Details of any deaths will be listed for all patients.

- **Brief Summary of Adverse Events**

An overall summary of the number and percentage of participants, along with the number of events in each category below, will be presented:

a) All AEs
b) Serious AEs
c) Study intervention related AEs
d) AEs with NCI CTCAE ≥ Grade 3
e) Study intervention related AEs with NCI CTCAE ≥ Grade 3
f) AEs leading to treatment discontinuation
g) AEs leading to death

For example:

Brief Summary	Dose X			Dose Y			All		
	N = (events)	N = (subjects)	% (subjects)	N = (events)	N = (subjects)	% (subjects)	N = (events)	N = (subjects)	% (subjects)
All AEs									
Serious AEs									
AEs related to Study Drug									

- **Summary of AEs / Study drug related AEs by System Organ Class and/or Preferred Term for all dose levels and sub-parts**

The number and percentage of participants with AEs / study drug related AEs, along with the number of events, will be summarized in appropriate tables by System Organ Class and Preferred Term, by cohort. Subjects will be counted once for each separate Preferred Term and/or System Organ Class.

For example:

MedDRA System class		Dose X			Dose Y			All		
		N = (events)	N = (subjects)	% (subjects)	N = (events)	N = (subjects)	% (subjects)	N = (events)	N = (subjects)	% (subjects)
System organ class	Preferred term									
All	All									
respiratory	All									
	irritation									
	cough									

- **Summary of AEs by System Organ Class and/or Preferred Term, by CTCAE grade, for all dose levels and sub-parts**

The number and percentage of participants with AEs, will be summarized by System Organ Class and/or Preferred Term, by CTCAE grade, by cohort. Subjects will be counted once for each Preferred Term and/or System Organ Class, according to the worst case of CTCAE grade.

For example:

MedDRA System class			Dose X		Dose Y		All	
			N = (subjects)	% (subjects)	N = (subjects)	% (subjects)	N = (subjects)	% (subjects)
System organ class	**Preferred term**	**Severity**						
All	All	All						
		Severe						
		Moderate						
		Mild						
respiratory	All	All						
		Severe						
		Moderate						
		Mild						
	irritation	All						
		Severe						
		Moderate						
	cough	All						
		Mild						

- **Statistical Analysis**

95% Confidence Interval (CI) will be calculated for the proportion of subjects with AE, by cohort.

- **Notes for all AE tables:**

The percentage of participants with a finding in a study group will be calculated by dividing the number of participants with the finding by the total number of participants in the cohort included in the Safety Set.

A TEAE will be considered "Study Drug related" if the investigator indicated the AE as 'possibly related' / 'probably related' / 'related', or, if for some reason, the information is missing.

If there is insufficient data to create a meaningful summary (e.g. for SAEs, AEs leading to death), data will be listed only.

4.4.6. Laboratory Data

All laboratory results will be listed. Out-of-reference range values will be flagged as high (H) or low (L). Laboratory results will be categorized as normal/abnormal and whether clinically significant or not. Laboratory assessments will be summarized. Change and relative change from

baseline will be calculated and summarized as appropriate. Shift from baseline will be calculated and summarized, as appropriate.

4.4.7. Vital Signs

All vital signs data will be listed. Vital signs results will be categorized as normal/abnormal and whether clinically significant or not. Vital signs data, changes and relative changes from baseline will be summarized. Shift from baseline will be calculated and summarized, as appropriate.

4.4.8. Physical Examination

All physical examination data will be listed. Physical Examination will be categorized as normal/abnormal and whether clinically significant or not and summarized by body system. Shift from baseline will be summarized by body system.

4.4.9. Electrocardiogram (12-Lead ECG)

ECG results will be listed. ECG results will be categorized as normal/abnormal and whether clinically significant or not and summarized. Shift from baseline will be summarized.

4.4.10. Prior and Concomitant Medications

The number and percentage of participants with medications, along with the number of medications, will be summarized in appropriate tables by WHO generic name (ATC fifth level), fourth and second level, by study arm using the ITT Analysis set. Subjects will be counted once for each separate ATC fifth level and/or fourth level and/or second level.

For example:

WHOCC-ATC/DDD			VasQ			Control			All		
ATC Level 2	**ATC Level 4**	**WHO Generic Name**	**N = (events)**	**N = (subjects)**	**% (subjects)**	**N = (events)**	**N = (subjects)**	**% (subjects)**	**N = (events)**	**N = (subjects)**	**% (subjects)**
Blood Substitutes And Perfusion Solutions	All	All									
	Blood Substitutes And Plasma Protein Fractions	All									
		Albumin									

	Solutions Affecting The Electrolyte Balance	All									
		Electrolytes									
		Electrolytes With Carbohydrates									

4.4.11. TNSS

The scores for nasal congestion, rhinorrhea, nasal itching, and sneezing are summed to obtain the Total Nasal Symptom Score for a subject at a specific time point. Total Nasal Symptom Score (TNSS) questionnaire results will be listed and summarized. Change and relative change from baseline will be calculated and summarized as appropriate.

4.4.12. Pharmacokinetic (PK)

Pharmacokinetic analysis will be performed upon sponsor request and depending on the available data.
Pharmacokinetic analysis will be performed to evaluate the systemic exposure of study drug Apo-Si-K170A-C76. The analysis will determine the serum concentration of Apo-Si-K170A-C76 over time.

Pharmacokinetics blood samples will be collected at the following time-points:

- Cohorts 1, 2 and 3:
  On Day 1, obtain blood for systemic exposure prior to dosing (within 1 hour before), at 30 and 60 minutes (all ± 5 minutes) and 2, 3 and 4 hours (all ± 10 minutes), 6 and 8 hours (all ± 20 minutes) post dose. A 24-hour (± 1 hour) post dose sample will be collected on Day 2.

- Cohorts 4 and 5:
  On Day 1, obtain blood for systemic exposure prior to dosing (within 1 hour before and then at 30 and 60 minutes (all ± 5 minutes), and 2, 3, and 4 hours (all ± 10 minutes), 6 (pre-2nd dose), 6.5, 7, 8, 9, and 10 hours (all ± 20 minutes), after 1st dosing. A 24-hour (± 1 hour) post 1st dosing sample will be collected on Day 2.

- Cohorts 6 and 7:
  On Day 1, obtain blood for systemic exposure prior to dosing (within 1 hour before and then at 30 and 60 minutes (all ± 5 minutes), and 2, 3 and 4 hours (all ± 10 minutes), 6 (but pre-2nd dose), 6.5, 7, 8, 9, and 10 hours (all ± 20 minutes), after 1st dosing. A 24-hour (± 1 hour) post 1st dosing sample will be collected on Day 2 (this will be the pre-dose sample of Day 2). On Days 2-5, the same time points as Day 1 will be collected. A 24-hour (± 1 hour) post Day 5-1st dosing sample will be collected on Day 6.

In addition to the descriptive statistics described in section 4.3, the descriptive statistics for PK analysis will include also standard error and coefficient of variation (CV%).

BLQ values will be handled prior to calculation according to the following rules:
- BLQ measures will set to zero (0).
- The BLQ will be provided by the sponsor.

Serum PK concentration

Serum PK concentration will be listed and summarized.

One listing will include the PK concentration by subject, by dose and time points.

Another listing will include demographic data of subjects included in the PK analysis.

Another listing will include demographic data of withdrawn subjects.

One table will present descriptive statistics of concentrations by study arm, by dose and time points.

One figure will present graphical presentation of mean ± standard error of concentration by dose, by time-point and treatment.

Another figure will present graphical presentation of concentration by individual patients by dose, by time-point and treatment.

Serum PK parameters (in case a PK analysis will be performed)

The following parameters will be evaluated for all PK variables:

C_{max}	Maximum measured plasma concentration.
T_{max}	Time to maximum measured plasma concentration. If the maximum value is observed at more than one time point, T_{max} will be defined as the first time point observed with this value.
AUC_{last}	The area under the plasma concentration versus time curve from time 0 to the last measurable concentration, as calculated by the linear-log trapezoidal method (linear trapezoidal rule up to Tmax, and log trapezoidal rule for the remainder of the curve)
$AUC_{partial}$	The area under the plasma concentration versus time curve from time 0 to T_{max}, as calculated by the linear trapezoidal method.
λ_z (lambdaz)	Individual estimate of the terminal elimination rate constant, was calculated using log-linear regression of the terminal portions of the plasma concentration-versus-time curves.
AUC_{inf}	The area under the plasma concentration versus time curve from time 0 to infinity. AUC_{inf} is calculated as the sum of AUC_{last} and the ratio of the last measurable plasma concentration to the elimination rate constant. $$AUC_{inf} = AUC_{last} + \frac{C_{last}}{\lambda_z}$$

T½	Apparent first-order terminal elimination half-life defined as $0.693/\lambda_z$.

In cases that concentration time profile do not exhibit a terminal loglinear phase, i.e. there are not three non-null measurements after Tmax:AUC_{inf}, λ_z and T½ cannot be calculated. The statistical summaries (mean, median,…) will use AUCT instead of AUCinf (see table below).

Plasma PK parameters will be listed and summarized by dose and by study arm.

One listing will include the calculated PK parameters by subject and by dose.

One table will present descriptive statistics of parameters by dose and by study arm.

5. RELATED DOCUMENTS

Protocol: 'Protocol Apo-Si-K170A-C76 Amendment 1 29 Feb 2024 clean final.pdf'

6. REFERENCES

Not Applicable

7. APPENDICES

Not Applicable