A Randomized, Double-Blind, Placebo-Controlled, Multiple-Dosing, Dose-Escalating Phase 1b Study to Evaluate the Safety, Pharmacokinetics, Pharmacodynamics and Immunogenicity of N-Rephasin® SAL200 after Continuous Intravenous Infusion in Healthy Volunteers

ClinicalTrials.gov ID: NCT03446053

Statistical Analysis Plan

Study Title

A Randomized, Double-Blind, Placebo-Controlled, Multiple-Dosing, Dose-Escalating Phase 1b Study to Evaluate the Safety, Pharmacokinetics, Pharmacodynamics and Immunogenicity of N-Rephasin® SAL200 after Continuous Intravenous Infusion in Healthy Volunteers

Protocol No.	ITB-101_1b
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Revision History

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1.0	2019/12/04	-	

Table of Contents

1. Introduction

This document contains details in the statistical analyses including pharmacokinetic, pharmacodynamic and safety that described in the protocol of clinical study of ITB-101_1b. Analysis which don't described specified is performed in accordance with the SOP of the Department of Clinical Pharmacology, Seoul National University College of Medicine, Seoul, Korea and iNtRON Biotechnology, Inc.

2. Study Objectives

To evaluate the safety of N-Rephasin® SAL200 after one hour of continuous intravenous infusion single and multiple time in healthy male volunteers and to explore its pharmacokinetic and pharmacodynamic characteristics.

Primary endpoint: To evaluate safety/tolerability of N-Rephasin® SAL200 after multiple administrations.

Secondary endpoint: To evaluate pharmacokinetics* and pharmacodynamics of N-Rephasin® SAL200 after multiple administrations.

**Pharmacokinetic evaluation of urine didn't conduct our trials.*

3. Investigational Plan

3.1. Overall Study Design

Subjects who have voluntarily provided written consent to participate in the clinical study will undergo screening procedures. Subjects who are eligible to participate in this study admit to the hospital 1 day prior to the drug administration. Subjects randomize

to receive SAL200 or placebo at a ratio of 8:2 for each dose groups. At 9 am the day after admission, all subjects receive intravenous infusions of SAL200 or placebo for 1 hours, depending on the dose group. And they followed by clinical trials according to the planned study schedule.

Post-study visit tests are performed on all subjects who have received one or more doses, and the test for immunogenicity evaluation is performed until approximately 50 days after dosing.

3.2. Drug Administration

Dose	Active Drug	Placebo
6 mg/kg (single)	6	2
3 mg/kg/d (multiple, BID)	6	2
6 mg/kg/d (multiple, BID)	6	2
9 mg/kg/d (multiple, BID)	6	2
12 mg/kg/d (multiple, BID)*	6	2

12 mg/kg/d cohort did not conduct because Interim results up to cohort 4 evaluated good safety/tolerability result and enough pharmacokinetic/pharmacodynamic characteristics.

3.3. Schedule of Study

3.3.1. Single administration

	Schedule of Clinical Study								
	Screening Period	Admission Period			Outpatient Period				Post-study Visit
Visit Number	SCV	V1			V2	V3	V4	V5	V6
	Screening	Hospitalization			FU1	FU2	FU3	FU4	PSV
	-28D~-2D	-1D	1D	2D	8D±1D	15D±1D	**22D±1D**	29D±1D	50D±2D
Informed consent	✘								
Demographic information/medical history	✘								
In/Exclusion criteria	✘	✘							
Randomization		✘							
Admission/discharge		✘		✘					
Administration			✘						
Vital signs	✘	✘	✘	✘	✘	✘	✘	✘	✘
ECGs	✘		✘	✘		✘			✘
Clinical laboratory test	✘		✘	✘	✘	✘			✘
Alcohol breath test	✘								
Physical examination	✘	✘	✘	✘	✘	✘	✘	✘	✘
PK blood sampling			✘	✘					
PD blood sampling			✘						
Immunogenicity sampling			✘	✘	✘	✘	✘	✘	✘
Allergic antigen test	✘	✘			✘	✘		✘	
AE monitoring		✘	✘	✘	✘	✘	✘	✘	✘
Comedication monitoring	✘	✘	✘	✘	✘	✘	✘	✘	✘

Medical intervention monitoring		✘	✘	✘	✘	✘	✘	✘	✘

3.3.2. Multiple administrations

	Schedule of Clinical Study											
	Screening Period	Admission Period						Outpatient Period				Post-study Visit
Visit Number	SCV	V1						V2	V3	V4	V5	V6
	Screening	Hospitalization						FU1	FU2	FU3	FU4	PSV
	-28D ~ -2D	-1D	1D	2D	3D	4D	5D	8D±1D	15D±1D	**22D±1D**	29D±1D	50D±2D
Informed consent	✘											
Demographic information/medical history	✘											
In/Exclusion criteria	✘	✘										
Randomization		✘										
Admission/discharge		✘					✘					
Administration			✘	✘	✘	✘						
Vital signs	✘	✘	✘	✘	✘	✘	✘	✘	✘	✘	✘	✘
ECGs	✘		✘	✘	✘	✘	✘		✘			✘
Clinical laboratory test	✘		✘	✘	✘	✘	✘	✘	✘			✘
Alcohol breath test	✘											
Physical examination	✘	✘	✘	✘	✘	✘	✘	✘	✘	✘	✘	✘
PK blood sampling			✘	✘	✘	✘	✘					
PD blood sampling			✘			✘						
Immunogenicity sampling			✘				✘	✘	✘	✘	✘	✘
Allergic antigen test	✘	✘						✘	✘		✘	
AE monitoring			✘			✘						

Comedication monitoring		✘	✘	✘	✘	✘	✘	✘	✘	✘	✘	✘
Medical intervention monitoring	✘	✘	✘	✘	✘	✘	✘	✘	✘	✘	✘	✘
Informed consent		✘	✘	✘	✘	✘	✘	✘	✘	✘	✘	✘

3.4. Determination of the Sample Size

This study is a phase I clinical trial to evaluate PK/PD characteristics and safety/tolerability. Since the purpose of this clinical trial in healthy volunteers is explorative and descriptive in nature, the study is different from the studies for statistical hypothesis testing, so that it is reasonable to undergo with the minimum number of subjects required empirically. It is planned to enroll a total of 8 subjects in each dose group, with the randomization of 6: 2 in active versus placebo.

4. Documentation of Variables

4.1. Demographic Variables

Sex, age, height, weight, BMI, Smoking, Alcohol of Subjects

4.2. Safety Variables

4.2.1. Adverse Events

4.2.1.1. Treatment-Emergent Adverse Events (TEAE)

An adverse event which was new in onset or worsened in severity after the first study drug intake

4.2.1.2. Adverse Drug Reaction (ADR)

An adverse drug reaction (ADR) refers to all noxious and unintended responses to a medicinal (investigational) product related to any dose. The phrase "responses to a medicinal (investigational) product" means that a causal relationship between medicinal

(investigational) product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

4.2.1.3. Unexpected adverse drug reaction (Unexpected ADR)

The investigator and iNtRON Biotechnology, Inc. determine whether the adverse reaction is expected or unexpected, if the adverse reaction is related to the clinical trial drug.

- Expected: For investigational drugs, adverse reactions that match the nature, severity, frequency, and characteristics described in the investigator's brochure or protocol are defined as "Expected".

- Unexpected: Adverse reaction that are not included in the "Expected" range

4.2.2. Vital Signs

Blood pressure (sitting position), Pulse rate, Body temperature (tympanic)

4.2.3. Clinical Laboratory Test

4.2.3.1. Hematology Test

WBC with differential count (segmented neutrophil, lymphocyte, monocyte, eosinophil, basophil), RBC, hemoglobin, hematocrit, platelets

4.2.3.2. Blood Chemistry Test

Calcium, phosphorus, glucose, BUN, uric acid, cholesterol, total protein, albumin, total bilirubin, alkaline phosphatase, AST, ALT, γ-GT, CPK, LDH, creatinine, sodium, potassium, chloride, triglyceride, amylase, lipase, ESR, hs-CRP

4.2.3.3. Urine Test

Color, pH, specific gravity, albumin, bilirubin, glucose, urobilinogen, ketone, nitrite, occult blood, leukocyte, microscopy

4.2.3.4. Blood Coagulation Test

aPTT (Activated partial thromboplastin time), PT (Prothrombin Time)/INR (International Normalized Ratio)

4.2.4. 12-Lead Electrocardiogram Test

Ventricular rate, PR, QRS, QT and QTc intervals

4.2.5. Physical Examination

4.2.6. Anaphylatoxin test

C3a, C4a, mast cell tryptase, IL-1b, IL-2, IL-6, TNF-alpha

4.3. Pharmacokinetic Variables

4.3.1. Pharmacokinetic Measurements

1) Single administration

pre-dose, 0.25 h, 0.5 h, 0.75 h, 1 h, 1.5 h, 2 h, 3 h, 4 h, 5 h, 6 h, 8 h, 10 h, 12 h, 24 h

2) Multiple administrations

1D: pre-dose, 0.25 h, 0.5 h, 0.75 h, 1 h, 1.5 h, 2 h, 3 h, 4 h, 5 h, 6 h, 8 h, 10 h, 12 h.

2D : 0 h, 1 h, 12 h.

3D : 0 h, 1 h, 12 h.

4D : 0 h, 0.25 h, 0.5 h, 0.75 h, 1 h, 1.5 h, 2 h, 3 h, 4 h, 5 h, 6 h, 8 h, 10 h, 12 h.

5D : 0 h.

4.3.2. Pharmacokinetic Parameters

1) Single administration: AUC_{last}, AUC_{inf}, C_{max}, T_{max}, $T_{1/2}$, CL, V_{ss}

2) Multiple administrations:

Day 1: AUC_{last}, AUC_{inf}, AUC_{t}, C_{max}, T_{max}, $T_{1/2}$, CL, V_{ss}

Day 4: AUC_{last}, AUC_{inf}, $AUC_{t,ss}$, $C_{max,ss}$, $C_{min,ss}$, $T_{max,ss}$, $T_{1/2,ss}$, CL_{ss}, V_{ss} R, Rs, PTF

Parameter	Unit	Significant Digits	Definition
AUC_{last}	μg·h/mL	3	Area under the blood concentration-time curve from the single administration to the last blood collection point
AUC_{inf}	μg·h/mL	3	Area under the blood concentration-time curve under the serum concentration-time curve from time to infinity after administration
C_{max}	μg/mL	3	Maximum drug concentration after single administration
T_{max}	h	3	Time to reach the peak blood concentration after single administration
$T_{1/2}$	h	3	Elimination half-life after single administration
CL	L/h	3	Drug clearance after single administration
$AUC_{t,ss}$	μg·h/L	3	Area under the blood concentration-time curve between dosing intervals at steady state after multiple administrations
$C_{max,ss}$	μg/mL	3	Maximum drug concentration at steady state after multiple administrations
$C_{min,ss}$	μg/mL	3	Minimum drug concentration at steady state after multiple administrations
$T_{max,ss}$	h	3	Time to reach peak blood concentration at steady state after multiple administrations
$T_{1/2,ss}$	h	3	Elimination half-life at steady state after multiple administrations
CL_{ss}	L/h	3	Drug clearance at steady state after multiple administrations

V_{ss}	L	3	Volume of distribution calculated as Dose*AUMC/(AUC)^2
R		3	Accumulation Ratio: The ratio of the area under the curve compared the single administration to that of multiple administrations ($AUCt_{ss}$ / AUCt)
Rs		3	Time-Invariance Ratio: The ratio of the area under the curve compared the single administration to that of multiple administrations (AUCtss / AUCinf)
PTF	%	3	Peak to trough fluctuation

4.4. Pharmacodynamic Variables

4.4.1. Pharmacodynamic Measurements

1) Single administration

1D: pre-dose, 1h, 1.5h, 2h

2) Multiple administrations

1D: pre-dose, 1h, 1.5h, 2h

4D: 0h, 1h, 1.5h, 2h

4.4.2. Pharmacodynamic Parameters

ex vivo antibacterial activity as assessed by bactericidal effects of the serum specimens collected from the trials were compared with calibration samples range of 0.05 to 1.0 μg/mL N-Rephasin® SAL200 (see Appendix 4 of the protocol).

4.5. Immunogenicity Variables

4.5.1. Immunogenicity Measurements

1) Single administration

1D: pre-dose

2D: 0h

2) Multiple administrations

1D: pre-dose

5D : 0h

4.5.2. Immunogenicity Parameters

Anti-drug antibody titer

5. Definitions of the Analysis Sets

5.1. Randomized set

Demographic information is analyzed by randomized set which randomized and subject who obtained the random number (Intention-To-Treat).

5.2. Safety set

Safety analysis are conducted in safety sets that receive at least one administration of the investigational drug (safety set).

5.3. PK/PD set

Pharmacokinetic, pharmacodynamic, and immunogenicity assessments (PK / PD sets) are subject to completion of all testing procedures. However, if the subject is dropped

out after receiving the drug, the test results obtained from the subject up to the point of suspension and dropout will be reviewed.

6. General Presentation of Summaries and Analyses

6.1. Summary Statistics

Continuous data, including the changes from the baseline, will be analyzed descriptively as follows (number of subjects, average, standard deviation or CV(%), minimum, median, maximum). Categorical data, including the shift table from the baseline, will be summarized by dose group using frequency tables (frequency and percent)

6.2. Baseline

Baseline data will be set before the first dose for single administration study and before the last dose for multiple administration study.

6.3. Handling of Missing Data

Unless otherwise stated, missing data will be not replaced by other values. Outliers identified in the data presentation will be examined for causality; appropriate action will be taken and commented on in the text of the CSR.

6.4. Software for Statistical Analysis

Statistical analysis will be conducted using SAS® (version 9.4 or later).

6.5. Significance Level

Unless otherwise stated, two one-sided significance level of 5% will be applied for comparison between dose groups and for comparison of the IP to placebo.

7. Methods for Analyses

7.1. Disposition and Protocol Deviations

7.1.1. Subject Disposition

Evaluation of participation in clinical trials will be performed on the screened set. Screened subjects, subjects who dropped out after screening, subjects who completed randomization, subjects who did not receive the investigational drug after randomization, subjects who received the investigational drug and don't, the dropout subjects and subjects who completed the study will be summarized and tabulated by dose group.

For randomized set, individual data in the following section will be presented as a listing.

- Subject Informed Consent
- Inclusion/Exclusion criteria and Enrollment
- Drug Administration

7.1.2. Summary for Analysis Sets

For subjects in each analysis group (Randomized Set, Safety Set, Pharmacokinetic and Pharmacodynamic Analysis Set) will be summarized by dose group, placebo group in each cohort, and pooled placebo group.

7.1.3. Protocol Deviations

Protocol deviation assessment will be performed on all subjects who have passed screening. Each deviation will be summarized by number of subjects, percentage (%),

and number of occurrences for dose group and total subjects, and individual data will be presented as a listing.

7.2. Demographics and Baseline Characteristics

7.2.1. Demographics

The demographic characteristics of the subjects will be assessed against a randomized set. Demographic characteristics are summarized by dose group for the following:

- Sex, age, height, weight, BMI
- Smoking, alcohol

If necessary, statistical analysis may be conducted to evaluate the differences between dose groups in each cohort, and each active dose versus pooled placebo group. Differences between dose groups or IP to placebo for continuous data will be analyzed using the t-test / ANOVA or Mann–Whitney U-test / Kruskal Wallis test and categorical data can be analyzed using the chi-square test or Fisher's exact test.

For demographic analysis, individual data in the following section will be presented as a listing.

- Demographics
- Interview
- Urine Drug Screening
- Serology

7.2.2. Medical History

The evaluation for medical history will be performed on a randomized set. Medical history will be standardized into System Organ Class (SOC) and Preferred Term (PT) using MedDRA® (version 20.0 or later).

Medical history will be summarized the number of subjects, percentage (%), and number of occurrences for each dose group and all subjects. Individual data will be presented as a listing.

7.2.3. Concomitant Medication

Concomitant drug evaluation will be performed on a randomized set. Concomitant medications will be coded using WHO-Drug insight (version 2018 or later) and summarized by number of subjects, percentage (%), and number of occurrences for each dose group and all subjects. Individual data will be presented as a listing.

7.3. Safety Evaluation

Safety evaluation will be performed on a safety set.

7.3.1. Adverse Events/ Serious Adverse Events

All reported TEAE / ADRs will be standardized to SOC and PT using MedDRA® (version 20.0 or later). For dose group and all subjects, the evaluation values of TEAE/ADRs (severity, seriousness, causality, method to treat, outcomes) will be summarized by subject number, percentage (%) the number of occurrences. If necessary, statistical tests such as a chi-square test or Fisher's exact test can be performed to assess the difference in adverse events between the dose groups. Individual data will be presented as a listing.

7.3.2. Vital Signs

Vital signs should be reviewed comprehensively. If clinically significant, it should be described in the CSR and the relationship with the investigational drug should be determined.

The results of each time point for the blood pressure, pulse rate, and body temperature will be summarized by dose group. Changes will be measured relative to baseline if necessary. The results of each time point for blood pressure, pulse rate and body temperature will be summarized by dose group. If necessary, the change from baseline can be presented. Individual data will be presented as a listing.

7.3.3. Clinical Laboratory Test

Clinical laboratory test should be reviewed comprehensively. If clinically significant, it should be described in the CSR and the relationship with the investigational drug should be determined.

The results of each time point for the hematology, blood chemistry, coagulation and urinalysis will be summarized by dose group. Changes can be made relative to baseline if necessary. The results of each time point for blood pressure, pulse rate and body temperature will be summarized by dose group. If necessary, the change from baseline can be presented. Individual data will be presented as a listing.

7.3.4. 12-Lead Electrocardiogram Test

12-lead electrocardiogram test will be reviewed comprehensively. If clinically significant, it should be described in the CSR and the relationship with the investigational drug should be determined. The results of each time point for the ECG test will be summarized. Changes will be evaluated relative to baseline if necessary. Individual data

will be presented as a listing.

7.3.5. Physical Examination

Physical examination will be reviewed comprehensively. If clinically significant, it should be described in the CSR and the relationship with the investigational drug should be determined. Individual data will be presented as a listing.

7.3.6. Anaphylatoxin test

Anaphylatoxin test (C3a, C4a, mast cell tryptase, IL-1b, IL-2, IL-6, TNF-alpha) should be reviewed comprehensively. If clinically significant, it should be described in the CSR and the relationship with the investigational drug should be determined.

If necessary, t-test/ANOVA or Mann–Whitney U-test/Kruskal Wallis test can be performed to assess the difference between the dose groups. Additionally, ANCOVA test will be conducted with other clinical laboratory test or pharmacokinetic parameters. Individual data will be presented as a listing.

7.4. Pharmacokinetics

Pharmacokinetic evaluation will be performed on PK/PD set.

7.4.1. Pharmacokinetic Measurements

Blood concentrations of SAL200 are summarized by nominal time point for each dose group. Individual SAL200 concentration and actual time point will be presented as a listing.

7.4.2. Pharmacokinetic Profiles

The mean serum concentration-time profile of SAL200 will be presented in linear and

log-linear graphs for each dose group.

7.4.3. Pharmacokinetic Parameters

The pharmacokinetic parameters of SAL200 are summarized by dose group and the pharmacokinetic parameters of individual subject will be presented as a listing.

The pharmacokinetic endpoints are calculated by noncompartmental method using pharmacokinetic analysis software (WinNonlin® ver. 7.0 or later, CA, USA) for each subject, and the descriptive statistics for each PK parameter will be presented.

For dose-linearity evaluation, relationship between the dose-related pharmacokinetic parameters (Day 1 C_{max}, AUC_{inf}, AUC_{last}; Day 4: $C_{max,ss}$, AUC (AUC, AUC_{last}, $AUC_{t,ss}$) and dose will be assessed using log-log power model analysis and the dose-adjusted C_{max} and AUC will be compared between the dose groups using a parametric or non-parametric statistical test.

If the pre-dose sample on Day 1 of dosing contains quantifiable SAL200 (potentially a result of assay interference), baseline corrected individual and summary PK concentration and PK parameters will be derived.

7.5. Pharmacodynamics

7.5.1. Pharmacodynamic Measurements

Ex vivo antibacterial activity will be summarized by nominal time point for each dose group. Individual ex vivo antibacterial activity concentration will be presented as a listing.

7.5.2. Pharmacodynamic Profiles

The individual ex-vivo antibacterial activity over time will be presented as a graph

for each dose group. Ex vivo antibacterial activity can be summarized by dose group.

If necessary, statistical tests such as a chi-square test or Fisher's exact test can be performed to assess the differences between dose groups. The ex vivo antibacterial activity of individual subject will be presented as a listing.

7.6. Pharmacokinetic-pharmacodynamic evaluation

To assess the correlation between pharmacokinetic parameter and pharmacodynamic parameters, statistical analysis can be performed between the time matched plasma concentration, C_{max}, AUC (AUC_{last}, AUC_{tau}) and ex vivo bactericidal activity using Pearson correlation coefficient.

7.7. Immunogenicity Evaluation

7.7.1. Immunogenicity measurements

Immunogenicity analysis will be performed using anti-drug antibody(ADA) concentration summarized by nominal time point. Individual ADA concentration will be presented as a listing.

Immunogenicity rate: Summarize [n (%)] the following by dose group, overall placebo, overall active:

- ADA present at baseline [1]
- ADA negative post baseline [2]
- ADA positive post baseline (regardless of baseline) [3]
- ADA positive post baseline (based only on those negative at baseline) [4]

[1]: Baseline prevalence.

[2]: Only includes subjects who were ADA negative post baseline.

[3]: Includes subjects with ADA-positive results post baseline.

Immunogenicity rate = % of subjects with positive ADA results post-baseline irrespective of baseline.

Percentages(%)are based on the total number of subjects.

[4]: % of subjects with positive ADA results post-baseline based on ADA- at baseline.

7.7.2. Immunogenicity profiles

The mean ADA over time will be presented as a graph by dose group. If necessary, statistical tests can be performed to assess the differences between dose groups. The ADA of individual subject will be presented as a listing.

8. Sensitivity Analysis

In this study, no sensitivity analysis conducted.

9. Interim Analysis

In this study, no interim analysis conducted.

10. Appendix: List of Tables, Figures, and Listings

10.1. Tables

Table No.	Title of table	Notes
1	Subject disposition	Randomized set
2	Demographic characteristics of subjects (Safety set)	Safety set
3	Demographic characteristics of subjects (Pharmacokinetic set)	Pharmacokinetic set
4	Summary of serum pharmacokinetic parameters	Pharmacokinetic set
5	Summary of ex vivo antibacterial activity	Pharmacodynamic set
6	Summary of anaphylatoxin test result by time point	Safety set
7	Summary of ADA test by time point	Pharmacokinetic set, Pharmacodynamic set
8	Summary of ADA rate	Pharmacokinetic set, Pharmacodynamic set
9	Dose proportionality assessment of pharmacokinetic parameters of SAL200	Pharmacokinetic set
10	Summary table for C_{trough} on each dosing day	Pharmacokinetic set
11	PK-PD relationship	Pharmacokinetic set, Pharmacodynamic set
12	Adverse events by SOC PT	Safety set
13	Summary of laboratory test parameters	Safety set
14	Summary of vital signs parameters	Safety set
15	Summary of ECG parameters	Safety set

10.2. Figures

Figure No.	Title of figure	Notes
1	Mean (± SD) profiles of SAL200 serum concentration-time profiles (linear-scale and semi-log scale)	Pharmacokinetic set
2	Individual C_{max} values of SAL200 by each dose group (Upper quartile: 75th percentile, Lower quartile: 25th percentile)	Pharmacokinetic set
3	Individual AUC_{last} values of SAL200 by each dose group (Upper quartile: 75th percentile, Lower quartile: 25th percentile)	Pharmacokinetic set
4	Individual $C_{max,ss}$ values of SAL200 by each dose group (Upper quartile: 75th percentile, Lower quartile: 25th percentile)	Pharmacokinetic set
5	Individual $AUC_{t,ss}$ values of SAL200 by each dose group (Upper quartile: 75th percentile, Lower quartile: 25th percentile)	Pharmacokinetic set
6	Linear regression of logarithmic C_{max} for SAL200 versus logarithmic dose	Pharmacokinetic set
7	Linear regression of logarithmic AUC_{last} for SAL200 versus logarithmic dose	Pharmacokinetic set
8	Linear regression of logarithmic $C_{max,ss}$ for SAL200 versus logarithmic dose	Pharmacokinetic set
9	Linear regression of logarithmic $AUC_{t,ss}$ for SAL200 versus logarithmic dose	Pharmacokinetic set
10	Mean plots of ex vivo antibacterial activity	Pharmacodynamic set
11	Mean plots of ADA result	Pharmacokinetic set, Pharmacodynamic set
12	Mean plots of anaphylatoxin test result	Safety set
13	Relationship between pharmacokinetic parameters and pharmacodynamic parameters	Pharmacokinetic set, Pharmacodynamic set

10.3. Listings

Listing No.	Title of listing	Notes
1	Discontinued subjects	
2	Protocol deviations	
3	Subjects excluded from the pharmacokinetic/ pharmacodynamic analysis	
4	Demographic data	
5	Individual serum SAL200 concentration by time point	
6	Individual serum SAL200 PK parameters	
7	Individual ex vivo antibacterial activity by time point	
8	Individual ADA result by time point	
9	Individual anaphylatoxin test result by time point	
10	Adverse event listings (each subject)	
11	Listing of individual laboratory measurements by subject	
12	Listing of individual vital sign result by subject	
13	Listing of individual 12-lead ECG test result	