Protocol Title:	Pharmacokinetic Study Comparing MB05 (Proposed Palivizumab Biosimilar), EU-sourced Synagis® and US-sourced Synagis® in Healthy Volunteers.
NCT Number:	NCT05121246
Protocol version date:	Version 2.0, 07 June 2022

TITLE PAGE

PROTOCOL NUMBER:	**MB05-A-01-21**
STUDY TITLE:	FANTASY–A Randomised, Double-Blind, 3-arm Parallel Study to Compare the Pharmacokinetics, Safety, Immunogenicity and Tolerability of MB05 (Proposed Palivizumab Biosimilar), EU-sourced Synagis® and US-sourced Synagis®, Administered as a Single Dose Intramuscular Injection in Healthy Volunteers.
PHASE:	I
INVESTIGATIONAL AGENT:	MB05 (proposed palivizumab biosimilar)
ROUTE OF ADMINISTRATION:	Intramuscular Injection
SPONSOR:	[redacted] Spain mAbxience From lab to life
SPONSOR REPRESENTATIVE:	[redacted] (Medical Advisor)
PROTOCOL VERSION:	2.0
PROTOCOL DATE:	07 Jun 2022

CONFIDENTIALITY STATEMENT
Information contained in this protocol should not be disclosed, other than to those directly involved in the execution or ethical review of the study, without written authorisation from mAbxience. It is, however, permissible to provide information to a volunteer in order to obtain consent.

SPONSOR SIGNATURE PAGE

Study Title: FANTASY–A Randomised, Double-Blind, 3-arm Parallel Study to Compare the Pharmacokinetics, Safety, Immunogenicity and Tolerability of MB05 (Proposed Palivizumab Biosimilar), EU-sourced Synagis® and US-sourced Synagis®, Administered as a Single Dose Intramuscular Injection in Healthy Volunteers.

Signature of Sponsor Representative [redacted]
Printed Name of Sponsor Representati [redacted]
Sponsor Representative Role/Designation Medical Advisor
By my signature, I confirm that I have reviewed this protocol and find its content to be acceptable.

SITE PRINCIPAL INVESTIGATOR SIGNATURE PAGE

Study Title: FANTASY–A Randomised, Double-Blind, 3-arm Parallel Study to Compare the Pharmacokinetics, Safety, Immunogenicity and Tolerability of MB05 (Proposed Palivizumab Biosimilar), EU-sourced Synagis® and US-sourced Synagis®, Administered as a Single Dose Intramuscular Injection in Healthy Volunteers.

Signature of Site Principal Investigator	***Date***
Printed Name of Site Principal Investigator	
Institution Name:	
By my signature, I agree to personally supervise the conduct of this study at my study site and to ensure its conduct is in compliance with the protocol, informed consent, ethics committee/competent authority procedures, instructions from mAbxience representatives, the Declaration of Helsinki, ICH Good Clinical Practice Guidelines, and local regulations governing the conduct of clinical studies.	

RATIONALE FOR CHANGES FROM PROTOCOL VERSION 1.1 TO VERSION 2.0

[redacted]

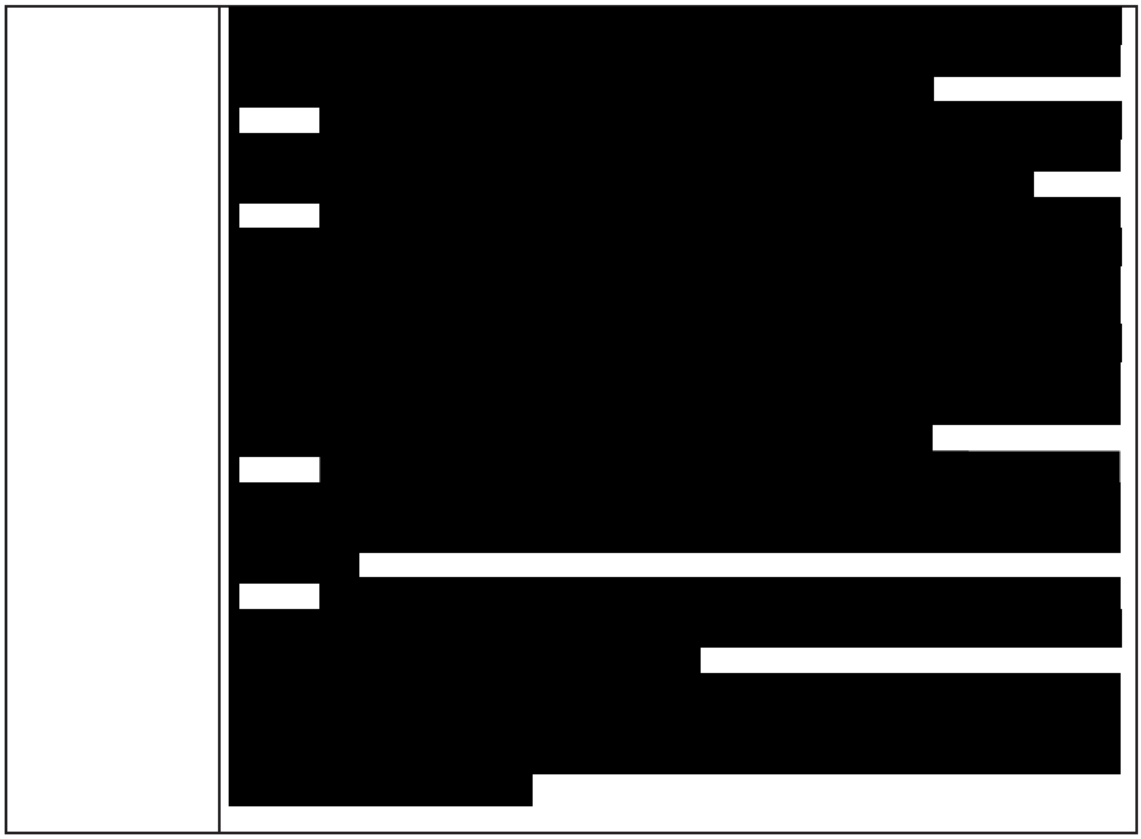
Protocol Section	Description of Changes from Final Protocol
APPENDIX 3: Clinical Laboratory Safety and Screening Assessments **Urine Drug Screen**	Previous text: [redacted] Amended Text: [redacted]
APPENDIX 3: Clinical Laboratory Safety and Screening Assessments **Serum Chemistry,**	Previous text: [redacted]

Including Liver Function	[redacted] Amended Text: [redacted]

RATIONALE FOR CHANGES FROM PROTOCOL VERSION 1.0 TO VERSION 1.1

[redacted]

Protocol Section	Description of Changes from Final Protocol
Section 6.3: Dose Stopping Rules	Previous text: [redacted]



1 PROTOCOL SYNOPSIS

Study Title	FANTASY–A Randomised, Double-Blind, 3-arm Parallel Study to Compare the Pharmacokinetics, Safety, Immunogenicity and Tolerability of MB05 (Proposed Palivizumab Biosimilar), EU-sourced Synagis® and US-sourced Synagis®, Administered as a Single Dose Intramuscular Injection in Healthy Volunteers.
Study Number	MB05-A-01-21
Phase	Phase I
Single/Multicentre:	This is a multicentre clinical trial (Australia/New Zealand).
Study Population	Healthy male and female volunteers, aged 18 to 55 years of age (inclusive) at the time of screening.
Study Treatment	MB05 (proposed palivizumab biosimilar)
Comparators	EU-Synagis® and US-Synagis®
Participant Number	Up to a maximum of 141 participants will be enrolled (47 participants per treatment arm). • Arm A: 3 mg/kg MB05 • Arm B: 3 mg/kg EU-Synagis® • Arm C: 3 mg/kg US-Synagis®
Route of Administration	Intramuscular injection (IM)
Number of doses per treatment	Single dose
Study Duration	The total maximum duration for participants is 130 days, inclusive of visit windows. This includes a screening period of up to 28 days, a treatment period of 1 day and a follow-up period through to 99 days (± 3 days) after treatment administration.
Study Confinement periods	Each enrolled participant will commence the confinement period on Day -1 (the day before dosing) and will remain in the clinic until they are discharged on Day 2. If participants experience any clinically significant adverse events (AEs) during the confinement period, they may remain in the clinical facility for further observation at the discretion of the Principal Investigator (PI) or delegate. Participants will be required to return to the clinic for 14 additional outpatient visits: Days 3, 4, 5, 6, 8, 15 (±1 day), 22 (±1 day), 29 (±1 day), 36 (±1 day), 43 (±1 day), 57 (±3 days), 71 (±3 days), 85 (±3 days), and Day 99 (± 3 days).

Study Objectives and Endpoints		
	Objectives	Endpoints
Primary	To establish the bioequivalence between MB05 and EU-Synagis®, between MB05 and US-Synagis® and between EU-Synagis® and US-Synagis® up to Day 99, in terms of: • Area under the serum concentration versus time curve from time zero to infinity (AUC_{0-inf}) • Maximum observed serum concentration (C_{max})	Bioequivalence between MB05 and EU-Synagis®, between MB05 and US-Synagis® and between EU-Synagis® and US-Synagis® will be determined for AUC_{0-inf} and C_{max}.
Secondary	To compare the pharmacokinetics (PK) of MB05 with EU- Synagis® and US-Synagis® following a single 3 mg/kg IM injection in healthy adult volunteers.	Additional PK parameters to be determined include (but are not limited to): • Time to C_{max} (T_{max}) • Apparent terminal elimination half-life ($t_{1/2}$) • Apparent volume of distribution (Vz/F) • Apparent total serum clearance (CL/F) • Area under the serum concentration versus time curve from time zero to time t (AUC_t)
	To assess the safety and tolerability of MB05, EU- Synagis® and US-Synagis®	Safety and tolerability endpoints include: • Incidence, type and severity of AEs • Changes from baseline in clinical laboratory results (haematology, serum chemistry, coagulation, and urinalysis) • Changes from baseline in vital signs parameters • Changes from baseline in physical examination findings • Change from baseline in body weight • Change from baseline in ECG parameters • Incidence, type and severity of injection site reactions.

	To assess the immunogenicity of MB05, EU- Synagis® and US-Synagis®	Immunogenicity endpoints include: • Incidence of anti-drug antibody (ADA) against MB05, US- and EU-Synagis®, including titres for ADA. • Incidence of neutralising antibody (nAb) against MB05, US- and EU-Synagis®,.

Inclusion Criteria	Healthy volunteers will be included in the study if they meet all of the following criteria at screening, and after check-in on Day -1 (prior to dose administration on Day 1): 1. Must have given written informed consent before any study-related activities are carried out and must be able to understand the full nature and purpose of the trial, including possible risks and adverse effects. 2. Adult male and female volunteers, 18 to 55 years of age (inclusive) at screening. 3. Body mass index (calculated) within the range of 18 to 30 kg/m^2 inclusive and total body weight between 50 and 95 kg, inclusive, at screening and check-in. 4. Medically healthy without clinically significant abnormalities, including: a. Physical examination without any clinically significant findings, in the opinion of the Investigator. b. Systolic blood pressure (BP) in the range of 90 to 145 mm Hg (inclusive) and diastolic BP in the range of 50 to 90 mm Hg (inclusive) after at least 5 minutes in the supine position. c. Pulse rate (PR) in the range of 40 to 100 beats/min (inclusive) after at least 5 minutes rest in a supine position. d. Normal body temperature between 35.1°C and 37.6°C (inclusive) (tympanic temperature). e. Triplicate 12-lead electrocardiogram (ECG), taken after the volunteer has been supine for at least 5 minutes, with a QT interval corrected using the Fridericia method (QTcF) ≤ 450 msec for males and ≤ 470 msec for females and no clinically significant abnormalities, in the opinion of the Investigator. f. Adequate bone marrow function as defined by absolute neutrophil count, platelet count and haemoglobin levels within normal ranges (per local laboratory standard). g. Adequate liver function as defined by: • Alanine aminotransferase (ALT) aspartate aminotransferase (AST), alkaline phosphatase (ALP) and bilirubin ≤ 1.5 x upper limit of normal (ULN).

Note: Bilirubin > 1.5 x ULN is acceptable if bilirubin is fractionated and direct bilirubin is < 35%.

- Albumin serum test within normal range (per local laboratory reference range).

h. Adequate coagulation, as defined by:

- Prothrombin time (PT)/International Normalised Ratio (INR), thrombin time (TT), and activated partial thromboplastin time (aPTT) ≤ 1.5 x ULN.

i. Adequate renal function, as defined by:

- Creatinine ≤ 1.5 x ULN or normal creatinine clearance levels as assessed by the investigator. *Note. Glomerular filtration rate can be used in place of creatinine or creatinine clearance.*

j. No other clinically significant findings in serum chemistry, haematology, coagulation and urinalysis examinations, in the opinion of the Investigator.

Note. The above assessments may be repeated once, if abnormal values were recorded in the first instance, at the discretion of the Investigator.

5. No prior history of chronic alcohol abuse or excessive alcohol intake, at the discretion of the PI, within 12 weeks prior to screening, and negative alcohol breath or urine test results (at screening and on Day -1). Excessive alcohol intake is defined as an average consumption of > 12 standard units of alcohol per week, or more than 4 standard drinks on > 3 days per week, where 1 standard drink is 10 g of pure alcohol and is equivalent to 285 mL beer [4.9% Alc./Vol], 100 mL wine [12% Alc./Vol], 30 mL spirit [40% Alc./Vol]).
6. No prior history of substance abuse or drug addiction within 12 months prior to first study drug administration and negative drug test results (at screening and on Day -1).
7. Female volunteers must:

a. Be of non-childbearing potential i.e., surgically sterilised (for example: hysterectomy, bilateral salpingectomy, bilateral oophorectomy at least 6 weeks before the Screening visit) or postmenopausal (where postmenopausal is defined as no menses for 12 months without an alternative medical cause and a follicle-stimulating hormone [FSH] level indicative of postmenopausal status per local laboratory definition), OR

b. If of childbearing potential:

- Must have a negative serum pregnancy test at the screening visit and a negative urine pregnancy test within 24 hours prior to dose administration on Day 1

	• Must not be breastfeeding, lactating or planning pregnancy during the study period • Must agree not to attempt to become pregnant • If not exclusively in same-sex relationships, must agree to use adequate contraception (which is defined as use of a condom by the male partner combined with the use of a highly effective method of contraception per APPENDIX 4) from 30 days prior to dosing until at least 190 days after the last dose of study drug. • Must agree not to donate ova for at least 190 days after the last dose of study drug. 8. Male volunteers, must agree not to donate sperm for at least 190 days after the last dose of study drug, and if engaging in sexual intercourse, must agree to: a. use a condom for at least 190 days after the first dose of study drug, PLUS b. when engaging in sexual intercourse with a female who may become pregnant, must agree to have the female use an acceptable form of contraception (refer to APPENDIX 4) from 30 days prior to dosing until at least 190 days after the last dose of study drug. 9. Have suitable venous access for blood sampling. 10. Be willing and able to comply with all study assessments and adhere to the protocol schedule and restrictions.
Exclusion Criteria	Healthy volunteers will be excluded from the study if there is evidence of any of the following at screening or any time after check-in on Day -1 (prior to dose administration on Day 1): 1. Prior exposure to Synagis® (palivizumab). 2. Have a history of hypersensitivity or allergic reactions (either spontaneous or following drug administration) to any drug compound or its excipients, food, or other substance. Minor (non-anaphylactic) reactions to food substances (non-excipients) may be permitted, at the discretion of the Investigator. 3. Significant history or clinical manifestation of any metabolic, allergic, dermatological, hepatic, renal, haematological, pulmonary, cardiovascular, gastrointestinal, neurological, respiratory, endocrine, or psychiatric disorder, deemed to be clinically relevant as determined by the Investigator (or designee). 4. Presence or evidence of recent sunburn, scar tissue, tattoo (more than 25% of body area), open sore or branding that, in the opinion of the Investigator, would interfere with interpretation of skin adverse reactions.

	5. Have a positive test result for hepatitis B surface antigen (HBsAg), hepatitis B core antibody (HBcAb), hepatitis C virus (HCV) or human immunodeficiency virus (HIV). *Screening only.* 6. Have a positive test result for COVID-19 (polymerase chain reaction [PCR] or antigen test) within 72 hours prior to dose administration. 7. If subject smokes, subject is unwilling to abstain from smoking for 7 days prior to admission and during the confinement period. 8. Positive serum pregnancy test for women of childbearing potential (WOCBP) at the screening visit or positive urine pregnancy test with confirmatory serum pregnancy test prior to dosing on Day 1. 9. Females who are breastfeeding or lactating. 10. Have a history of cancer including lymphoma, leukaemia and skin cancer (volunteers with surgically resected basal cell carcinoma or squamous cell carcinomas are permitted). 11. Have an illness within 30 days prior to screening, or prior to dosing, that is classed as clinically significant by the Investigator. 12. Any clinically significant infection, in the opinion of the Investigator, ongoing at screening or admission to the clinical unit. 13. Prior exposure to any investigational monoclonal antibody within 6 months or 5 half-lives of the previous drug (if known), whichever is longer, prior to study drug administration. 14. Have been dosed in another clinical study with an investigational drug (excluding monoclonal antibody) within 30 days or 5 half-lives of the investigational drug (whichever is longer) prior to the administration of the study drug or are currently participating in another clinical study of an investigational drug or intending to participate in another clinical study of an investigational drug before completion of all scheduled evaluations in this clinical study. 15. Have had major surgery within 30 days prior to screening or will have an operation between screening and the end of study visit. 16. Have donated > 100 mL blood or plasma within 4 weeks prior to the administration of the study drug. Participant must also agree to refrain from donating blood or blood products throughout the duration of the study. 17. Use of any prescription or over-the-counter medication (including herbal products, diet aids, and hormone supplements) within 10 days or 5 half-lives of the medication (whichever is longer) prior to the first study drug administration, which, in the opinion of the Investigator, could affect the outcome of the study. The following exceptions apply: a. Contraceptives for WOCBP. b. Paracetamol (up to a maximum of 4 doses of 500 mg per day, and no more than 3g per week).

	c. Ibuprofen (up to a maximum of 4 doses of 200 mg per day). 18. Has received (or plans to receive) a vaccine within the following timeframes: a. Live or attenuated vaccine within 3 months prior to dose administration on Day 1 or plans to receive a live or live attenuated vaccine during the study. b. Other vaccines (including COVID-19 vaccines) within 14 days prior to dose administration on Day 1 or plans to receive other vaccines within 14 days following dose administration on Day 1. 19. Any person who is an employee of an Investigator or Sponsor, or an immediate relative of an Investigator. 20. Any other condition or prior therapy that in the opinion of the Investigator would make the volunteer unsuitable for this study, including inability to cooperate fully with the requirements of the study protocol or likelihood of noncompliance with any study requirements.
Study Restrictions	The use of any prescription or over-the-counter medications (including herbal products, diet aids and hormone supplements) is prohibited within 10 days or at least 5 half-lives of the medication (whichever is longer) prior to the first administration of study drug and for the duration of the study, with the exception of medications used to manage AEs and contraceptives for WOCBP. Live and live attenuated vaccines are not permitted within 3 months prior to dose administration on Day 1 and throughout the duration of the study. Other vaccines (including COVID-19 vaccines) are not permitted within 14 days prior to dose administration on Day 1 and within 14 days following Day 1. Subjects are required to refrain from strenuous exercise from 7 days before check-in and within 7 days before non-residential visits and will otherwise maintain their normal level of physical activity during this time (i.e., will not begin a new exercise program nor participate in any unusually strenuous physical exertion). Other restrictions also apply, as described in the study protocol.
Overall Study Design Description	This is a multicentre, randomised, double-blind, 3-arm parallel group study. Up to a total of 141 participants are planned to be enrolled and randomised to receive a single dose of MB05, EU-Synagis® or US-Synagis with participants randomised to Arm A, B or C in equal proportions (1:1:1) as shown in Table S1. Randomisation will be stratified based on the subject's body weight (50 to <75 kg and ⩾75 to 95 kg) and gender (male and female). To achieve balance, the number of subjects enrolled in each stratum should be a multiple of 3, where possible. In Group 1, a total of 9 healthy volunteers will be enrolled and dosed with MB05, EU-Synagis® or US-Synagis® (1:1:1). Once all participants in

<table>
<tr><td></td><td>Group 1 have completed the Day 8 visit, a safety review committee (SRC) will meet to review all available safety data up to and including Day 8. No additional enrolment or dosing of the remaining participants should occur until the safety review is complete.

Following approval by the SRC, Group 2 may be enrolled (n=132, randomised 1:1:1 MB05: EU-Synagis®: US-Synagis®).

Table S1. Number of Participants to be Enrolled per Group and Treatment Arm
<table>
<tr><th></th><th>Arm A</th><th>Arm B</th><th>Arm C</th></tr>
<tr><td></td><td>MB05</td><td>EU-Synagis®</td><td>US-Synagis®</td></tr>
<tr><td>Group 1</td><td>3</td><td>3</td><td>3</td></tr>
<tr><td colspan="4">SRC review of initial group</td></tr>
<tr><td>Group 2</td><td>44</td><td>44</td><td>44</td></tr>
</table></td></tr>
<tr><td colspan="2">Study Assessments</td></tr>
<tr><td>Screening and on-study Safety and Tolerability</td><td>Safety and Tolerability:

• Medical history, including prior medications.
• Evaluation of any on-study AEs and concomitant medication use
• Height and weight
• Physical examination
• Vital signs (supine systolic and diastolic BP, pulse rate (PR), respiratory rate (RR), body temperature)
• 12-lead ECGs
• Injection site reaction assessments
• Analysis of laboratory safety markers (including haematology, serum chemistry, coagulation and urinalysis) (refer to APPENDIX 3 for a full list of parameters to be evaluated).

Other Screening Laboratory Assessments include:

• HIV-1, HIV-2, HBsAg, HBcAb and HCV antibody testing.
• COVID-19 PCR or antigen testing
• Urine drugs of abuse screen (methamphetamines, opiates, cocaine, tetrahydrocannabinol, phencyclidine, benzodiazepines, barbiturates, methadone and amphetamines).
• Alcohol breath or urine test.
• Serum and urine human chorionic gonadotropin (hCG) pregnancy test (in women of childbearing potential).
• FSH testing (postmenopausal women).</td></tr>
<tr><td>Pharmacokinetics</td><td>Blood samples for PK analysis will be collected prior to dosing and at a number of timepoints post-dose (refer to APPENDIX 2). Serum concentrations of palivizumab will be determined at each timepoint and will be used to calculate PK parameters.</td></tr>
<tr><td>Immunogenicity</td><td>Blood samples for immunogenicity (ADA and nAb) will be collected prior to dosing and at a number of timepoints post-dose (refer to APPENDIX 2).</td></tr>
</table>

Statistical Analysis	
Safety and Tolerability	All randomised participants who received any amount of study treatment will be included in the safety analysis. Adverse events will be coded using Medical Dictionary for Regulatory Activities and grouped by system organ class and preferred term, classified from verbatim terms. The number and percentage of participants with treatment-emergent AEs (TEAEs) and serious TEAEs as well as the number of TEAEs and serious TEAEs will be summarized by system organ class and preferred term and tabulated for each treatment. Summaries by severity and relationship will also be presented. Observed values and changes from baseline in vital signs, ECGs parameters body weight and clinical laboratory parameters will be summarised at each protocol scheduled timepoint by treatment arm. Physical examination data will be listed. Injection site reactions will be summarised by reaction using frequency counts and percentage by treatment arm.
Pharmacokinetics	PK parameters will be determined using a non-compartmental analysis method. Bioequivalence between MB05 and EU-Synagis®, between MB05 and US-Synagis® and between EU-Synagis® and US-Synagis® will be established by analysis of variance for the PK parameters $AUC_{0\text{-}inf}$, and C_{max}.
Immunogenicity	ADA titres and changes from baseline will be presented by means of counts and percentages by treatment group and study visit. ADA titres and changes from baseline will be summarised by summarised by treatment group and study visit.

2 TABLE OF CONTENTS

3 LIST OF ABBREVIATION AND TERMS

ADA	Anti-drug antibody
ADL	Activities of daily living
AE	Adverse events
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
aPTT	Activated partial thromboplastin time
AST	Aspartate aminotransferase
BP	Blood pressure
BMI	Body mass index
CI	Confidence interval
CrCl	Creatinine clearance
CS	Clinically significant
CTCAE	Common terminology criteria for adverse events
CV	Coefficients of variation
EC	Ethics committee
ECG	Electrocardiogram
eCRF	Electronic case report form
EIU	Exposure occurred in utero
EMA	European Medicines agency
EoS	End of study
ER	Emergency room
ETV	Early Termination Visit
FDA	Food and Drug Administration
FSH	Follicle-stimulating hormone
GCP	Good Clinical Practice
GFR	Glomerular filtration rate
HBcAb	Hepatitis B core antibody
HBsAg	Hepatitis B surface antigen
hCG	Human chorionic gonadotropin
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HR	Heart rate
IB	Investigator's Brochure
ICH	International Council for Harmonisation
IM	Intramuscular
IMM	Independent medical monitor
INR	International Normalised Ratio

IP	Investigational product
ISF	Investigator Site File
LRT	Lower respiratory tract
MedDRA	Medical Dictionary for Regulator Activities
nAb	Neutralising antibody
NCI	National Cancer Institute
NCS	Not clinically significant
PCR	Polymerase chain reaction
PD	Pharmacodynamics
PI	Principal Investigator
PK	Pharmacokinetics
PR	Pulse rate
PT	Prothrombin time
QTcF	Corrected QT interval using the Fridericia method
RMP	Reference medicinal product
RR	Respiratory rate
RSV	Respiratory syncytial virus
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SMR	Sponsor medical representative
SoA	Schedule of assessments
SOC	System organ class
SRC	Safety review committee
SUSAR	Suspected unexpected serious adverse reaction
TEAE	Treatment-emergent adverse event
TOST	Two one-sided tests (of statistical significance)
TT	Thrombin time
ULN	Upper limit of normal
WHO	World Health Organisation
WOCBP	Women of childbearing potential

3.1 List of Pharmacokinetic Abbreviations and terms

AUC	Area under the concentration-time curve
AUC_{inf}	Area under the serum concentration versus time curve from zero to infinity
AUC_t	Area under the serum concentration versus time curve from time zero to time t
CL/F	Apparent total serum clearance of drug
C_{max}	Maximum observed serum concentration
k_{el}	Terminal elimination rate constant
$t_{1/2}$	Apparent terminal elimination half-life
T_{max}	Time to C_{max}
Vz/F	Apparent volume of distribution during terminal phase

4 INTRODUCTION

4.1 Background Information

Respiratory syncytial virus (RSV) is a major viral pathogen which causes serious respiratory illness in infants and children worldwide. Approximately 0.5% to 2.5% of all children infected with RSV are hospitalised with lower respiratory tract (LRT) infection, of which 50% to 90% represent cases of bronchiolitis and 5% to 40% are pneumonia. Peak hospitalisation rates occur in vulnerable infants aged 2 to 3 months (Collins and Melero., 2011). Overall, the World Health Organisation (WHO) estimates that RSV accounts for greater than 60% of acute respiratory infections in children globally and is responsible for more than 80% of LRT infections in infants aged <1 year (Piedimonte and Perez, 2014), with morbidity and mortality due to RSV infection highest in children with nosocomial infection and in those with underlying medical illnesses such as cardiac and chronic lung disease.

Palivizumab (Synagis®) is an anti-RSV monoclonal antibody administered intramuscularly for the prevention of severe RSV respiratory disease in high-risk infants and young children. Palivizumab, the active substance of Synagis®, is a humanised IgG1κ monoclonal antibody directed to an epitope in the A antigenic site of the fusion protein of RSV. It has potent neutralising and fusion-inhibitory activity against both RSV subtype A and B strains. Palivizumab acts by binding the RSV envelope fusion protein (RSV F) with specificity to an epitope in the A antigenic site of the F protein, inhibiting the entry of RSV into the cell and preventing infection. By blocking a critical step in the membrane fusion process, palivizumab acts to prevent cell to-cell fusion of RSV-infected cells.

Synagis® is therapeutically indicated for the prevention of serious LRT disease requiring hospitalisation caused by RSV in children at high risk for RSV disease.

4.2 Investigational Product and Mechanism of Action

MB05 is a medicinal product containing the same active substance: the monoclonal antibody palivizumab, developed by mAbxience as a biosimilar product to the originator reference medicinal product (RMP) Synagis® manufactured and marketed by AbbVie in Europe and USA. Synagis® is approved in multiple regions including the US, EU and Australia.

As described in the Investigator's Brochure (IB), MB05 and the RMP, Synagis® have been shown to be analytically similar in terms of the physicochemical (structure, conformation, post-translational modifications including charge variants and glycosylation profile and product purity), and biological attributes, using an exhaustive panel of state-of-the-art orthogonal and complementary analytical methods.

4.3 Non-clinical Safety, Toxicity and Pharmacokinetics

The evidence from the comprehensive analytical characterisation and comparability program performed using state of the art technology and orthogonal methods to compare structural and functional attributes has shown that MB05 drug product is similar to US- and EU-Synagis® in terms of primary structure, higher order structure and confirmational stability, post-

translational modifications (including charge variants and glycosylation profile), purity and biological properties.

The presence of trehalose in the formulation of MB05 (not present in US- or EU-Synagis®) is not expected to impact the clinical pharmacokinetic (PK) profile.

Detailed information is available in the MB05 IB.

4.4 Clinical Experience

This is a first-in-human study of the Synagis® biosimilar MB05. The reference product Synagis® was first approved by the US Food and Drug Administration (FDA) in 1998 and by the European Medicines agency (EMA) in 1999.

As a proposed biosimilar, the clinical experience with Synagis® (as described in the Synagis® summary of product characteristics) (most recent versions) is deemed applicable to MB05.

4.5 Rationale and Considerations for Proposed Clinical Use

MB05 is being developed as a potential biosimilar to Synagis® for all indications for which Synagis® is approved.

This study is designed to demonstrate PK similarity of the proposed biosimilar test product MB05 and the reference products EU- and US-Synagis®.

4.6 Justification for Dose Level

A single weight-adjusted dose of 3 mg/kg has been selected for this study to support PK and safety comparisons between MB05, EU- Synagis® and US- Synagis®. Publicly available data shows that palivizumab has linear PK relationship up to 15 mg/kg (Groothuis and Nishida, 2002). Based on this, the PK of palivizumab allows extrapolation from the 3 mg/kg intramuscular (IM) dose to the 15 mg/kg dose IM while minimising the risk for healthy volunteers and reducing the injection volume.

4.7 Risk Assessment and Guidance for Investigators

MB05 is an investigational drug. As with any investigational drug, unexpected clinically significant or serious adverse events (SAEs) may occur with the use of MB05. All participants treated with MB05 should be closely monitored by means of adverse events (AEs), vital signs, physical examinations, electrocardiogram (ECGs), and clinical laboratory tests.

As with any IM injection, palivizumab should be given with caution to patients with thrombocytopenia or any coagulation disorder. Accordingly, appropriate provisions have been made in the study eligibility criteria, and healthy volunteers must have adequate coagulation and bone marrow function at screening and prior to first dose, as determined by screening clinical laboratory safety blood tests.

Identified risks for MB05 are based on safety issues highlighted in the product labelling for palivizumab in sections “Warnings and Precautions” / “Special Warnings and Precautions for Use” and/or the “Adverse Reactions / Undesirable Effects”.

Based on data from clinical studies and post-marketing data for Synagis®, the most serious adverse reactions are anaphylaxis and other acute hypersensitivity reactions. Accordingly, participants will remain under the supervision of clinic staff for at least 24 hours following dose administration. Vital signs and other safety assessments will be performed at regular intervals during this time. Other adverse reactions occurring with Synagis® (reported in clinic studies and post-marketing reports in paediatric patients) include:

Very common (≥ 1 in 10):

- Rash
- Pyrexia

Common (≥ 1 to 10 in 100):

- Injection site reaction
- Apnoea

Uncommon (≥ 1/1,000 to < 1/100):

- Thrombocytopenia
- Convulsion
- Urticaria

The Warnings and Precautions sections of the Synagis® product information and the Synagis summary of product characteristics (latest versions) should be consulted for detailed recommendations on the identification, monitoring, and management of the risks that are associated with Synagis® and are likely to be associated with MB05.

Further information regarding MB05 is available in the IB.

5 STUDY OBJECTIVES

5.1 Primary

The primary objective of this study is to establish the bioequivalence between MB05 and EU-Synagis®, between MB05 and US-Synagis® and between EU-Synagis® and US-Synagis® up to Day 99, in terms of:

- Area under the serum concentration versus time curve from time zero to infinity ($AUC_{0\text{-}inf}$)
- Maximum observed serum concentration (C_{max})

5.2 Secondary

The secondary objectives of this study are to:

1. Compare the PK of MB05 with EU- Synagis® and US-Synagis® following a single 3 mg/kg IM injection in healthy adult volunteers.
2. To assess the safety and tolerability of MB05, EU- Synagis® and US-Synagis®
3. To assess the immunogenicity of MB05, EU-Synagis® and US-Synagis®

6 STUDY DESIGN AND ENDPOINTS

6.1 Overall Design Summary

This is a multicentre, randomised, double-blind, 3-arm parallel group study. Up to a total of 141 participants are planned to be enrolled and randomised to receive a single dose of MB05, EU-Synagis® or US-Synagis with participants randomised to Arm A, B or C in equal proportions (1:1:1) as shown in Table 1. Randomisation will be stratified based on the subject's body weight (50 to <75 kg and ⩾75 to 95 kg) and gender (male and female). To achieve balance, the number of subjects enrolled in each stratum should be a multiple of 3, where possible.

Participants will be enrolled across multiple sites in Australia and New Zealand.

In Group 1, a total of 9 participants will be enrolled and dosed with MB05, EU-Synagis® or US-Synagis® (1:1:1). Once all participants in Group 1 have completed the Day 8 visit, a safety review committee (SRC) will meet to review all available safety data from Group 1, up to and including Day 8. No additional enrolment or dosing of the remaining participants should occur until the safety review is complete.

Following approval by the SRC, Group 2 may be enrolled (n=132, randomised 1:1:1 MB05: EU-Synagis®: US-Synagis®).

Table 1. Number of Participants to be Enrolled per Group and Treatment Arm

	Arm A	**Arm B**	**Arm C**	***Total number of participants***
	MB05	EU-Synagis®	US-Synagis®	
Group 1	3	3	3	***9***
SRC review of Group 1				
Group 2	44	44	44	***132***
				141

6.2 Detailed Description of Study Design

The study schedule and procedures are identical for each group. Healthy volunteers will be screened between Day -28 and Day -2. Eligible participants will be admitted to the clinical facility the day prior to dosing (Day -1).

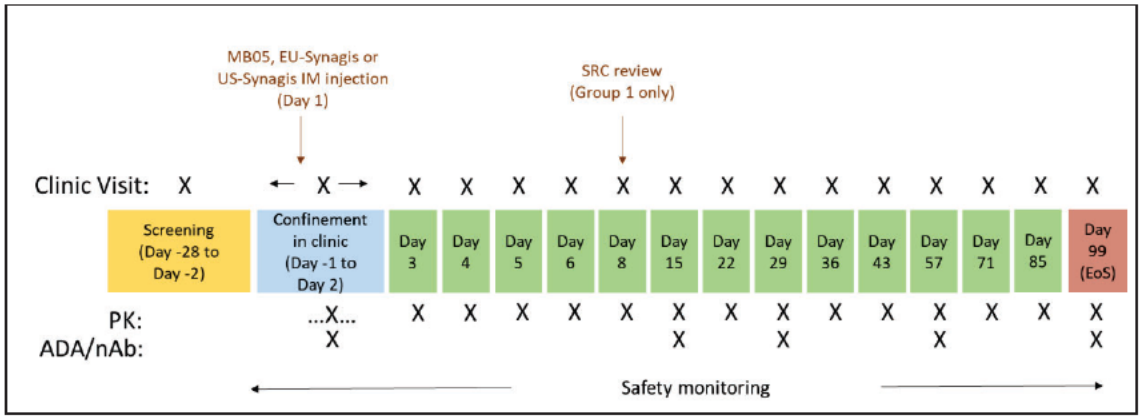
On Day 1, participants will be randomised to receive a single IM dose of 3 mg/kg MB05, EU-Synagis® or US-Synagis®. Participants will remain in the clinical site until all post-dose assessments have been completed on Day 2. If any participants experience any clinically significant AEs during the confinement period, they may remain at the clinical site for further observation at the discretion of the Principal Investigator (PI).

Participants will return to the clinical site on Days 3, 4, 5, 6, 8, 15 (± 1 day), 22 (± 1 day), 29 (± 1 day), 36 (± 1 day), 43 (± 1 day), 57 (± 3 days), 71 (± 3 days) and 85 (± 3 days) for follow-up assessments. The end of study (EOS) visit will be on Day 99 (± 3 days). Safety assessments (including safety laboratory blood and urinalysis sampling, vital signs assessments, body

weight determination ECG assessments, physical examination, and injection site reaction assessments) will be performed as indicated in the schedule of assessments (APPENDIX 1).

Additional blood samples will be collected for PK evaluations at each scheduled visit. Blood samples for analysis of anti-drug antibody (ADA), neutralising antibody (nAb). (Figure 1 and APPENDIX 1).

Figure 1. Summary of Key Procedures



Abbreviations: ADA = anti-drug antibody; IM = intramuscular; nAb = neutralising antibody; PK = pharmacokinetic; SRC = safety review committee. Notes: ...X.... indicates multiple samples collected.

Dosing will occur in a sequential manner. The decision to proceed to Group 2 group will be based on review of available blinded safety data from Group 1, up to and including Day 8, by the SRC.

At a minimum, the SRC will consist of the PI(s) who have enrolled participants, an independent medical monitor (IMM) and the Sponsor medical representative (SMR), however all Investigators involved in the study will be invited to attend the meeting, regardless of whether they have enrolled participants into Group 1. Other individuals (e.g., medical experts) may also be invited to participate and provide additional input into the review process, if required.

Following review of the data, the SRC will discuss the findings and recommend proceeding to Group 2 or terminating enrolment. There is no formal requirement for an SRC meeting in Group 2. Safety and tolerability will be reviewed in an ongoing manner during this part of the study.

6.3 Dose Stopping Rules

The decision to proceed to Group 2 will be made following evaluation of safety data from Group 1, up to and including Day 8 (i.e., clinical laboratory blood and urinalysis results, vital signs assessment, ECG assessments, physical examination findings and AE data) by the SRC. The clinical facility will provide the SRC with blinded safety data during the study.

Dosing will proceed until evaluation of all subjects has been completed or the trial is stopped by the SRC. Temporary suspension of further dosing may be decided by the SRC if any of the following criteria are fulfilled:

- One occurrence of an SAE assessed to be at least possibly related to the study drug and

that in the opinion of the SRC has a high likelihood to repeat in additional groups and would mean a significant risk to study participants

- Multiple occurrences of Hy's law criteria are met, as defined by at least 3-fold. elevations of serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) above the upper limit of normal (ULN), plus an elevation of serum total bilirubin > 2 times ULN without elevated serum alkaline phosphatase (ALP), and no other disease or condition can be found to explain the liver test abnormalities, and no other potential explanation in the opinion of the SRC can be a probable cause for this event, and in the opinion of the SRC study continuation would mean a significant risk to study participants
- If 2 or more participants experience the same or similar Grade III or higher AE which is possibly or probably related to the study drug, and according to SRC opinion study continuation would mean a significant risk to study participants
- Presence of any effects that are assessed as probably related to study drug that are, in the opinion of the SRC, medically relevant and may potentially endanger the welfare of study participants.

For any of the scenarios described above, the SRC will review all available safety data and will recommend if the group or the entire study should be terminated. No more healthy volunteers should be enrolled (or participants dosed) until this safety review is completed.

6.4 Dose Adjustments/Modifications/Delays

A single dose is planned for administration in this study. As such, dose adjustments, modifications or delays are not applicable.

6.5 Study Duration

The total maximum study duration for each participant is 130 days, inclusive of screening and visit windows.

6.6 Randomisation and Blinding

6.6.1 Randomisation and Allocation to Treatment Arm

All study participants who sign an informed consent form will receive a unique sequential number (i.e., a screening number). Randomisation will be stratified based on the subject's body weight (50 to <75 kg and ⩾75 to 95 kg) and gender (male and female).

Participants who are deemed eligible to be dosed will be assigned a randomisation number in accordance with the study randomisation schedule. Each participant will be assigned to one of the following study treatment arms in a 1:1:1 allocation ratio:

- Arm A: MB05
- Arm B: EU-Synagis®
- Arm C: US-Synagis®

The allocation to Arm A, B or C will be performed using a block randomisation algorithm, and the randomisation schedule will be maintained under controlled access. If required, sealed participant-specific code break envelopes will be produced by the Sponsor (or a Sponsor delegate) and will be retained at the clinical facility in a secure, accessible location.

The personnel involved in the dispensing of study treatments will be accountable for ensuring compliance to the study randomisation schedule. The unblinded study Monitor will review the randomisation schedule in comparison to the dispensing log in order to verify correct randomisation.

6.6.2 Blinding and Breaking Code

This is a double-blind study. Blinding of study drug assignment is critical to the integrity of this clinical trial. Those **blinded** to study drug assignment include:

- the Sponsor
- the PI
- the clinical study personnel participating in participants' care or clinical evaluations
- the study participants
- the Pharmacokineticist performing interim PK analysis (if performed)
- the study monitor(s)

Blinded safety data will be provided to the SRC so as not to reveal treatment assignment. Blinded personnel must not make any effort to determine which study drug therapy is being administered and are to remain blinded throughout the conduct of the study until the study database is locked and unblinding has been performed.

Those **unblinded** to study drug assignment include:

- the statisticians preparing the randomisation schedule
- the unblinded pharmacy personnel preparing the patient-specific doses

If a medical emergency occurs and a decision regarding the patient's condition/treatment requires knowledge of the treatment being administered, the study blind may be broken for the specific participant. If this occurs, the Investigator will immediately notify the Medical Monitor of the situation. In general, unblinding should only occur if management of the medical emergency would be different based on the subject having received investigational product. In the majority of cases, the management of a medical emergency would be the same whether or not investigational product was received by the subject. If this was the case, the investigational product allocation should not be unblinded. The date, time, and reason for un-blinding must be documented in the source document and in the appropriate section of the eCRF.

With the exception of emergency unblinding (as described above), unblinding may only take place following the notification and agreement of the Sponsor. Unless the clinical situation warrants emergency unblinding, the PI is strongly advised to discuss options with the SMR (or delegate) for this study, prior to any unblinding. The PI should contact the Sponsor to discuss the participant and circumstances requiring the unblinding. Should the Sponsor agree, the PI may acquire the treatment assignment information for the participant in question. The treatment assignment blind will be broken only for the specific participant under consideration. If the blind is broken for any reason and the PI was unable to contact the Sponsor before unblinding, the PI must notify the Sponsor as soon as possible. If code break envelopes are used, a record, including date, time, name, and signature of person opening the code break envelope and reason, must be made both on the opened envelope and in the participant's medical records. If an interactive web response system is used to break the blind, then the documentation received from the IWRS indicating the blind break must be retained in a secure manner in the participant's medical records. The Study Monitor should be informed promptly.

The Sponsor (mAbxience) retains the right to unblind the treatment allocation for SAEs that are unexpected and are suspected to be causally related to an investigational product and that potentially require expedited reporting to regulatory authorities.

The Sponsor (and any Sponsor nominee, e.g., Study Monitor(s)) will remain blinded to the participant assignment. Every effort will be made to restrict knowledge of the participant assignment to the PI only. The PI may discuss the circumstances and clinical status relating the participant without revealing the participant's study drug treatment assignment (unless important to the safety of participants remaining in the study). Any such discussions should be captured electronically (e.g., by email) and submitted to the Sponsor (or designee) for filing in the study Trial Master File.

6.7 Endpoints

6.7.1 Primary Endpoints

Bioequivalence between MB05 and EU-Synagis®, between MB05 and US-Synagis® and between EU-Synagis® and US-Synagis® will be determined for $AUC_{0\text{-}inf}$, and C_{max}.

6.7.2 Secondary Endpoints

Pharmacokinetics

Additional PK parameters to be determined include (but are not limited to):

- Time to C_{max} (T_{max})
- Apparent terminal elimination half-life ($t_{1/2}$)
- Apparent volume of distribution (Vz/F)
- Apparent total serum clearance (CL/F)
- Area under the serum concentration-time curve from time zero to time t (AUC_t)

Safety and Tolerability

Safety and tolerability endpoints include:

- Incidence, type and severity of AEs
- Changes from baseline in clinical laboratory results (haematology, serum chemistry, coagulation, and urinalysis)
- Changes from baseline in vital signs parameters
- Changes from baseline in body weight
- Changes from baseline in ECG parameters
- Changes from baseline in physical examination findings
- Incidence, type and severity of injection site reactions.

Immunogenicity

Immunogenicity endpoints include:

- Incidence of anti-drug antibody (ADA) against MB05, US- and EU-Synagis®, including titres for ADA.
- Incidence of neutralising antibody (nAb) against MB05, US- and EU-Synagis®.

7 PARTICIPANT SELECTION

7.1 Number of Participants

Up to a total of 141 participants will be enrolled as follows:

- Group 1 (n=9)
- Group 2 (n=132)

7.2 Inclusion Criteria

Healthy volunteers will be included in the study if they meet all of the following criteria at screening, and after check-in on Day -1 (prior to dose administration on Day 1):

1. Must have given written informed consent before any study-related activities are carried out and must be able to understand the full nature and purpose of the trial, including possible risks and adverse effects.
2. Adult male and female volunteers, 18 to 55 years of age (inclusive) at screening.
3. Body mass index (BMI, calculated) within the range of 18 to 30 kg/m^2 inclusive and total body weight between 50 and 95 kg, inclusive, at screening and check-in.
4. Medically healthy without clinically significant abnormalities, including:
    a. Physical examination without any clinically significant findings, in the opinion of the Investigator.
    b. Systolic blood pressure (BP) in the range of 90 to 145 mm Hg (inclusive) and diastolic BP in the range of 50 to 90 mm Hg (inclusive) after at least 5 minutes in the supine position.
    c. Pulse rate (PR) in the range of 40 to 100 beats/min (inclusive) after at least 5 minutes rest in a supine position.
    d. Normal body temperature between 35.1°C and 37.6°C (inclusive) (tympanic temperature).
    e. Triplicate 12-lead ECG, taken after the volunteer has been supine for at least 5 minutes, with a QT interval corrected using the Fridericia method (QTcF) $\leq$ 450 msec for males and $\leq$ 470 msec for females and no clinically significant abnormalities, in the opinion of the Investigator.
    f. Adequate bone marrow function as defined by absolute neutrophil count, platelet count and haemoglobin levels within normal ranges (per local laboratory standard).
    g. Adequate liver function as defined by:
        - ALT, AST, ALP and bilirubin $\leq$ 1.5 x ULN. *Note: Bilirubin > 1.5 x ULN is acceptable if bilirubin is fractionated and direct bilirubin is < 35%.*
        - Albumin serum test within normal range (per local laboratory reference range).
    h. Adequate coagulation, as defined by:

- Prothrombin time (PT) / International Normalised Ratio (INR), thrombin time (TT), and activated partial thromboplastin time (aPTT) ≤ 1.5 x ULN.

i. Adequate renal function, as defined by:

- Creatinine ≤ 1.5 x ULN or normal creatinine clearance levels as assessed by the investigator. *Note. Glomerular filtration rate (GFR) can be used in place of creatinine or creatinine clearance (CrCl).*

j. No other clinically significant findings in serum chemistry, haematology, coagulation and urinalysis examinations, in the opinion of the Investigator.

Note. The above assessments may be repeated once, if abnormal values were recorded in the first instance, at the discretion of the Investigator.

5. No prior history of chronic alcohol abuse or excessive alcohol intake, at the discretion of the PI, within 12 weeks prior to screening, and negative alcohol breath or urine test results (at screening and on Day -1). Excessive alcohol intake is defined as an average consumption of > 12 standard units of alcohol per week, or more than 4 standard drinks on > 3 days per week, where 1 standard drink is 10 g of pure alcohol and is equivalent to 285 mL beer [4.9% Alc./Vol], 100 mL wine [12% Alc./Vol], 30 mL spirit [40% Alc./Vol]).
6. No prior history of substance abuse or drug addiction within 12 months prior to first study drug administration and negative drugs of abuse test results (at screening and on Day -1).
7. Female volunteers must:

a. Be of non-childbearing potential i.e., surgically sterilised (for example: hysterectomy, bilateral salpingectomy, bilateral oophorectomy at least 6 weeks before the Screening visit) or postmenopausal (where postmenopausal is defined as no menses for 12 months without an alternative medical cause and a follicle-stimulating hormone [FSH] level indicative of postmenopausal status per local laboratory definition), OR

b. If of childbearing potential:

- Must have a negative serum pregnancy test at the screening visit and a negative urine pregnancy test within 24 hours prior to dose administration on Day 1
- Must not be breastfeeding, lactating or planning pregnancy during the study period
- Must agree not to attempt to become pregnant
- If not exclusively in same-sex relationships, must agree to use adequate contraception (which is defined as use of a condom by the male partner combined with the use of a highly effective method of contraception per APPENDIX 4) from 30 days prior to dosing until at least 190 days after the last dose of study drug.
- Must agree not to donate ova for at least 190 days after the last dose of study drug.

8. Male volunteers, must agree not to donate sperm for at least 190 days after the last dose of study drug, and if engaging in sexual intercourse, must agree to:
    a. use a condom for at least 190 days after the first dose of study drug, PLUS
    b. when engaging in sexual intercourse with a female who may become pregnant, must agree to have the female use an acceptable form of contraception (refer to APPENDIX 4) from 30 days prior to dosing until at least 190 days after the last dose of study drug.
9. Have suitable venous access for blood sampling.
10. Be willing and able to comply with all study assessments and adhere to the protocol schedule and restrictions.

7.3 Exclusion Criteria

Healthy volunteers will be excluded from the study if there is evidence of any of the following at screening or any time after check-in on Day -1 (prior to dose administration on Day 1):

1. Prior exposure to Synagis® (palivizumab).
2. Have a history of hypersensitivity or allergic reactions (either spontaneous or following drug administration) to any drug compound or its excipients, food, or other substance. Minor (non-anaphylactic) reactions to food substances (non-excipients) may be permitted, at the discretion of the Investigator.
3. Significant history or clinical manifestation of any metabolic, allergic, dermatological, hepatic, renal, haematological, pulmonary, cardiovascular, gastrointestinal, neurological, respiratory, endocrine, or psychiatric disorder, deemed to be clinically relevant as determined by the Investigator (or designee).
4. Presence or evidence of recent sunburn, scar tissue, tattoo (more than 25% of body area), open sore or branding that, in the opinion of the Investigator, would interfere with interpretation of skin adverse reactions.
5. Have a positive test result for hepatitis B surface antigen (HBsAg), hepatitis B core antibody (HBcAb), hepatitis C virus (HCV) or human immunodeficiency virus (HIV). *Screening only.*
6. Have a positive test result for COVID-19 (polymerase chain reaction [PCR] or antigen test) within 72 hours prior to dose administration.
7. If subject smokes, subject is unwilling to abstain from smoking 7 days prior to admission and during the confinement period.
8. Positive serum pregnancy test for women of childbearing potential (WOCBP) at the screening visit or positive urine pregnancy test with confirmatory serum pregnancy test prior to dosing on Day 1.
9. Females who are breastfeeding or lactating.
10. Have a history of cancer including lymphoma, leukaemia and skin cancer (volunteers with surgically resected basal cell carcinoma or squamous cell carcinomas are permitted).

11. Have an illness within 30 days prior to screening, or prior to dosing, that is classed as clinically significant by the Investigator.
12. Any clinically significant infection, in the opinion of the Investigator, ongoing at screening or admission to the clinical unit.
13. Prior exposure to any investigational monoclonal antibody within 6 months or 5 half-lives of the previous drug (if known), whichever is longer, prior to study drug administration.
14. Have been dosed in another clinical study with an investigational drug (excluding monoclonal antibody) within 30 days or 5 half-lives of the investigational drug (whichever is longer) prior to the administration of the study drug or are currently participating in another clinical study of an investigational drug or intending to participate in another clinical study of an investigational drug before completion of all scheduled evaluations in this clinical study.
15. Have had major surgery within 30 days prior to screening or will have an operation between screening and the EOS visit.
16. Have donated > 100 mL blood or plasma within 4 weeks prior to the administration of the study drug. Participant must also agree to refrain from donating blood or blood products throughout the duration of the study.
17. Use of any prescription or over-the-counter medication (including herbal products, diet aids, and hormone supplements) within 10 days or 5 half-lives of the medication (whichever is longer) prior to the first study drug administration, which, in the opinion of the Investigator, could affect the outcome of the study. The following exceptions apply:
    a. Contraceptives for WOCBP.
    b. Paracetamol (up to a maximum of 4 doses of 500 mg per day, and no more than 3g per week).
    c. Ibuprofen (up to a maximum of 4 doses of 200 mg per day).
18. Has received (or plans to receive) a vaccine within the following timeframes:
    a. Live or attenuated vaccine within 3 months prior to dose administration on Day 1 or plans to receive a live or live attenuated vaccine during the study.
    b. Other vaccines (including COVID-19 vaccines) within 14 days prior to dose administration on Day 1 or plans to receive other vaccines within 14 days following dose administration on Day 1.
19. Any person who is an employee of an Investigator or Sponsor, or an immediate relative of an Investigator.
20. Any other condition or prior therapy that in the opinion of the Investigator would make the volunteer unsuitable for this study, including inability to cooperate fully with the requirements of the study protocol or likelihood of noncompliance with any study requirements.

7.4 Participant Withdrawal Criteria

Participants will be advised that they are free to withdraw from the study at any time for any reason or, if necessary, the PI, or medically trained delegate, may discontinue a participant from the study according to (but not limited to) the following criteria:

- The need to take medication which may interfere with study measurements
- Intolerable/unacceptable AEs
- Major deviation or noncompliance with study protocol procedures, including (but not limited to):
  - Participant misses 3 consecutive visits, or a more than 5 non-consecutive visits*
- Lost to follow-up
- Participant unwilling to proceed and/or consent is withdrawn, or
- Withdrawal from the study if, in the PI's judgement, it is in the participant's best interest.

The reasons for discontinuation will be recorded in the electronic Case Report Form (eCRF) and included in the final clinical study report, along with any AEs and necessary medical treatment.

* Participants who miss 3 consecutive visits or more than 5 non-consecutive visits due to reasons beyond their control (for example, reasons related to the current COVID-19 pandemic) may not automatically be discontinued. In these instances, the decision to discontinue a participant will be at the discretion of the Sponsor and may depend on the impact of the missed visits on obtaining sufficient safety, PK and/or immunogenicity sampling timepoints to allow for full analysis.

If a participant withdraws or is withdrawn from the study, an attempt should be made to collect all remaining PK, safety, and immunogenicity samples scheduled for that day.

In the event that a participant is discontinued from the study due to a SAE, the PI, or medically trained nominee, will evaluate the urgency of the event. If the situation warrants, the PI, or medically trained nominee, will take appropriate diagnostic and therapeutic measures and make attempt to notify the SMR. If the situation is not an immediate emergency, the PI, or medically trained nominee, at the clinical study facility will attempt to contact the IMM and the SMR for consultation. No medical help, diagnosis, or advice will be withheld from the participant due to an inability to contact the contact the IMM or SMR. The participant will be encouraged to remain available for follow-up medical monitoring. The Sponsor will be notified as soon as possible of any participant withdrawals.

7.5 Participant Replacement

Final confirmation of eligibility will be checked prior to dose administration on Day 1.

Participants who withdraw consent from the study after randomisation, but prior to dose administration may be replaced.

Participants who are withdrawn for reasons outlined in Section 7.4 (or who withdraw consent from the study following dose administration but prior to completion of the nominal clinical conduct) for reasons other than occurrence of an SAE, may be replaced at the discretion of the

PI and following consultation with the Sponsor.

Any participants enrolled as replacements will be allocated to the same treatment arm in the group as the participant replaced. Reasonable efforts will be made to contact participants who are lost to follow-up. These efforts must be documented in the participant's file.

8 STUDY TREATMENTS

8.1 Identification and Description of Study Treatments

The study treatments that will be used in this study are outlined in Table 2. The Investigational Product (IP) (MB05) is a colourless to slightly yellow liquid with opalescence supplied as a solution for injection.

Table 2. Identity of Study Treatments

Product Information	Product Name		
	MB05	**EU-Synagis®**	**US-Synagis®**
Active ingredient	Palivizumab	Palivizumab	Palivizumab
Supplied as	Single use 1 mL vials (vials contain 100 mg/1 mL solution; plus overflow).		
Final Dosage form	Solution for IM injection		
Dose to be administered	3 mg/kg	3 mg/kg	3 mg/kg
Route of administration	IM		
Excipients	Trehalose dihydrate, glycine, histidine water for injection	Histidine, glycine, water for injection	Histidine, glycine, water for injection

Abbreviations: IM = intramuscular.

8.2 Storage and Stability

All study drugs (MB05, EU-Synagis® and US-Synagis®) must be stored between 2-8°C, protected from light and as according to the storage and expiration information provided on the label and as described in the study Pharmacy Manual. Vials and syringes must not be frozen or shaken.

For further information regarding stability of the drug product, please refer to the MB05 IB and product labels for EU- and US-Synagis®.

All study drugs must be stored in a secure area with access limited to the PI and authorised staff in accordance with country, state and regional laws. Refer to the directions for use in the study Pharmacy Manual for additional storage requirements.

8.3 Labelling

The final study doses to be administered to a participant will be labelled according to current

Good Manufacturing Practice guidelines for medicinal products as adopted in Australia and New Zealand.

The detail on the labels will include (but will not be limited to):

- The notation- '*For Clinical Trial Use Only*'
- Protocol number
- PI/site identification
- Trial participant number
- Name of Sponsor
- Route of administration
- Lot number
- Expiry date

The final labels will be produced in compliance with this protocol. Detailed instructions for the preparation, labelling and supply of MB05, EU- and US-Synagis® are described in the study Pharmacy Manual.

8.4 Investigational Product Handling

The PI (or delegate) must ensure that deliveries of study drug from the Sponsor (or designated supplier) are correctly received by a responsible person, that all receipts of study drug shipments are recorded on the appropriate drug accountability forms prepared by the designated pharmacy and that the study drugs are stored in a secure area under the recommended storage conditions. It is also the responsibility of the PI (or delegate) to ensure that the integrity of packaging not be jeopardised prior to dispensing. Only participants enrolled in the study may receive the study drugs, in accordance with all applicable regulatory requirements.

Only authorised and trained site staff may dispense and administer the study drugs. An authorised and trained staff member from the designated pharmacy, will dispense the study drugs according to predefined drug dispensing requirements. The pharmacy staff member will be responsible for dispensing study drug in accordance with the randomisation schedule. Individual doses will be dispensed by the designated staff member on the morning of dosing and recorded in the appropriate dispensing and drug accountability records. The dispensing will be verified by a second authorised staff member. The date and time of dose preparation and release will be maintained to support administration of the investigational products within the predefined use period. A study Pharmacy Manual will be prepared to define the procedures for dispensing.

The designated pharmacy will dispense the study drug to the clinical facility and the clinical facility staff will administer the study drug only to participants included in this study following the procedures set out in this study protocol. Administration of study drugs will be recorded in the appropriate drug accountability records and the eCRF. Administration of study drug will be verified by a second staff member. Each participant will be given only the study drug preparation carrying his/her study number.

8.5 Accountability of Study Drug Supplies

All material supplied is for use only in this clinical study and should not be used for any other purpose.

The PI is responsible for study drug accountability, reconciliation, and record maintenance at the clinical facility. In accordance with all applicable regulatory requirements, the PI or designated trained site staff must maintain study drug accountability records throughout the course of the study. This person will document the amount of study drug received by the pharmacy and the amount dispensed to, administered to, and returned by participants, if applicable. The shipment/receipt records as well as records of dispensing, administration and return will be verified by a second member of the site staff. The PI (or designated trained site staff) is responsible for assuring the retrieval of all left-over study drug supplies following administration to participants.

A Study Monitor will perform initial and ongoing study drug accountability. The study drug inventory and accountability/dispensing records must be available for inspection by the Study Monitor during the study. Used containers of the study drug will be retained and sequestered per participant and cohort and made available to the Study Monitor during study drug reconciliation.

8.6 Destruction of Study Drug

When requested in writing by the Sponsor and following drug accountability and reconciliation, unused study drug supplies may be returned to the Sponsor or destroyed by the PI (or delegate), provided destruction does not expose humans to risks from the study drugs. Records shall be maintained of the return or destruction of the study drug materials. These records must show the identification and quantity of each unit returned or disposed, the method of destruction (taking into account the requirements of local law), and the person who returned or disposed of the study drug materials. Such records must be submitted to the Sponsor.

9 ADMINISTRATION OF STUDY TREATMENTS

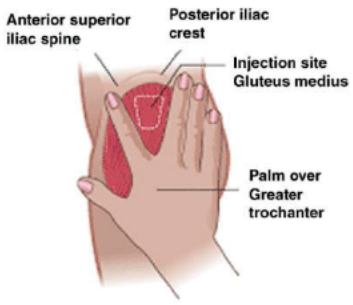
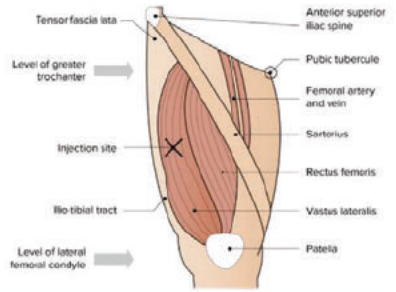
Delegated blinded study site personnel will administer the study treatment to each participant. All study treatment will be administered as per the randomisation schedule. A second blinded staff member will witness the study drug administration.

Each participant will receive a single IM administration of MB05, EU- or US-Synagis®, via a syringe using manual injection.

Participants will be dosed while in a supine or semi-supine position, and administration of the IP will be performed in the clinical unit by an appropriately qualified staff member who is trained on the procedure(s) of administering each of the study treatments. The IM injection will be administered into the ventrogluteal muscle of the hip (preferred site) or vastus lateralis of the thigh (secondary site) (Figure 2). The injection should never be given into an area where the skin is tender, bruised, red or hard. In addition, the skin at the injection site should be free of blemishes, scars, heavy hair, veins, moles, skin conditions, sores or tattoos that have the potential to interfere with the detection of local reactions

Subjects are required to refrain from strenuous exercise for at least 72 hours post-dose.

Figure 2. Anatomical Markers Used to Identify the Ventrogluteal Muscle and Vastus Lateralis of the Thigh Injection Sites

Ventrogluteal Muscle [1]	Vastus Lateralis of the Thigh [2]
	

[1] Soliman et al., 2018

[2] Australian Technical Advisory Group on Immunisation (ATAGI), Australian Immunisation Handbook, 2018.

The skin at the site of injection will be disinfected, and the skin gently stretched around the injection site.

Insert the needle at a 90-degree angle using a dart-like action and depress the plunger slowly at a rate of approximately 1 mL / 10 seconds. Wait for 10 seconds to allow the drug to diffuse into the tissue and then quickly withdraw the needle.

Before injecting, the plunger will be pulled back to check that the position of the needle tip is not intravascular. In the event that blood is observed in the syringe, the IP must not be injected and the needle must be withdrawn. In this instance, the withdrawn dose must be quarantined, another syringe dispensed, and the injection administered at another site. The replacement syringe dispensed will be the same treatment arm as with quarantined dose.

Participants will be instructed not to rub the area after injection.

Refer to the Pharmacy Manual for further details regarding administration of study treatments for this study.

10 CONCOMITANT MEDICATIONS AND OTHER RESTRICTIONS

Compliance to these restrictions will be assessed prior to first dosing and throughout the duration of the study.

10.1 Concomitant Medications

The use of concomitant medication during the study is prohibited, with the exception of medications used to manage AEs and contraceptives for WOCBP.

Participants will be instructed not to take any prescription or over-the-counter medication (including herbal products, diet aids, and hormone supplements) within 10 days or 5 half-lives of the medication (whichever is longer) prior to the first study drug administration (contraceptives, paracetamol and ibuprofen are permitted as defined in the study exclusion

criteria).

Paracetamol and Ibuprofen will be allowed for the treatment of headache or other pain at all other times during the study (doses and amounts per PI discretion).

If the need for concomitant medication arises to treat an AE, the Investigator should make decisions based on the participant's specific clinical factors.

Any concomitant medication that is taken by or administered to a participant during the course of the study must be recorded in the eCRF. The entry must include dose, regimen, route, indication and dates of use.

10.2 Vaccinations

Live or live-attenuated vaccines are not permitted within 3 months prior to dose administration on Day 1, or during the study.

Other vaccines (including COVID-19 vaccines) are not permitted within 14 days prior to dose administration on Day 1 or within 14 days following dose administration on Day 1.

10.3 Contraception

Female participants of childbearing potential, with a fertile male sexual partner, must use an acceptable method of contraception (APPENDIX 4) from 30 days prior to dosing until at least 190 days after the last dose of study drug.

Male participants, when engaging in any sexual intercourse must agree to use a condom for at least 190 days after the first dose of study drug. In addition, when engaging in sexual intercourse with a female who may become pregnant must agree to have the female use an acceptable form of contraception (APPENDIX 4) 30 days prior to dosing until at least 190 days after the last dose of study drug.

10.4 Caffeine, Tobacco and Alcohol

Participants will be instructed to abstain from consuming caffeine and/or xanthene products (e.g., coffee, tea, chocolate, and caffeine-containing sodas, colas) or alcohol for at least 24 hours prior to Day -1, and while confined to the clinical facility.

All subjects are required to abstain from smoking for 7 days prior to admission and during the confinement period.

Participants must have a negative result in a urine drug test and alcohol breath or urine test at screening and check-in (Day -1) and abstain from recreational drug use throughout the study.

10.5 Fasting Restrictions

Participants will be required to fast for at least 8 hours (water is permitted) prior to collection of clinical laboratory safety blood samples (except in the instance of an Early Termination Visit [ETV]).

10.6 Other Study Restrictions

The consumption of any foods containing poppy seeds should be avoided within 48 hours prior to screening and within 48 hours prior to admission to the clinical centre on Day -1.

Donation of >100 mL of blood or plasma is excluded within 4 weeks prior to the administration of study drug. Donation of blood products (except for sampling required for this study) or receiving blood products is not permitted throughout the period of participation in this study.

Subjects are required to refrain from strenuous exercise from 7 days before Check-in and within 7 days before non-residential visits and will otherwise maintain their normal level of physical activity during this time (i.e., will not begin a new exercise program nor participate in any unusually strenuous physical exertion). Subjects are also required to refrain from strenuous exercise for at least 72 hours post-dose on Day 1.

11 STUDY PROCEDURES

For the exact timing of each procedure, please refer to the schedule of assessments (APPENDIX 1).

Clinical staff are required to perform assessments at the nominated timepoints within the time windows indicated in this protocol. Actual times of procedures for each participant may vary depending on scheduling and will be recorded in the eCRF. In the event of multiple procedures scheduled at the same time, the order (where possible) will be vital signs, 12-lead ECG, PK sampling, ADA/nAb sampling, safety laboratory sampling.

Any abnormal or out of range test results obtained at the screening visit or after check-in on Day -1 prior to dose administration, may be repeated at the Investigator's discretion, to confirm eligibility.

11.1 Background Screening Assessments

11.1.1 Informed Consent

Before performing any study-related procedures, the PI (or delegate) will obtain written informed consent from participants.

11.1.2 Medical History

Medical history including pre-existing conditions, allergies, prior significant illnesses, and surgical history will be recorded. Medical history will also include alcohol consumption and smoking history.

In addition, demographic data, including gender, age, race and ethnicity will be recorded.

11.1.3 Concomitant Medications

Any non-study medication or therapy that is taken by or administered to a participant during the study will be recorded. The medication/therapy name as well as dose, dose regimen, route of administration, indication and dates of use will be noted, as applicable.

11.1.4 Body Height and Weight

Body height (centimetres) and weight (kilograms) will be measured in light clothing without shoes. Height should be measured on a wall-mounted stadiometer. Body mass index (BMI) will be calculated from the height recorded at screening.

11.1.5 Concomitant Medication Assessments

Concomitant medication usage will be monitored and recorded throughout the study.

11.1.6 Pregnancy Test

Women of childbearing potential (WOCBP) will have a serum human chorionic gonadotropin (hCG) pregnancy test at screening to determine their eligibility for participation in this study and at the EOS/ETV to confirm no exposure occurred in utero (EIU). A urine hCG pregnancy test will also be conducted at several timepoints during the study as indicated in the Schedule of Assessments (SoA). If a urine test is positive, pregnancy will be confirmed by a serum hCG test.

During their participation in this study, subjects must be instructed to notify the clinical site if they or their partner becomes pregnant.

11.1.7 Follicle-Stimulating Hormone Levels

Follicle-stimulating hormone (FSH) levels will be measured in postmenopausal women to confirm postmenopausal status at screening.

11.1.8 Alcohol Breath or Urine Test, and Urine Drug Screen

An alcohol breath or urine* test and urine drugs of abuse screen will be performed during screening and upon check-in. Refer to APPENDIX 3 for a list of illicit drugs screened in this study.

** Sites may choose whether to perform an alcohol breath or urine test, in line with site requirements (e.g. a breath test may not be considered appropriate at some sites due to the current COVID-19 pandemic). Where possible, sites should use the same technique (i.e. alcohol breath test or urine alcohol test) throughout the duration of the study.*

11.1.9 Serology Screening

HIV-1, HIV-2, HBsAg, HBcAb and HCV antibody testing will be performed at the screening visit. Subjects will be counselled if any tests return a positive result. Subjects who return a positive test result for HBsAg, HBcAb, HCV or HIV at the screening visit will not be eligible to participate in the study.

11.1.10COVID-19 Screening

A COVID-19 PCR test must be performed (and a negative result obtained) within 72 hours of dose administration on Day 1.

A COVID-19 PCR or antigen test may also be performed at any stage during the study (including at screening), if clinically indicated and/or as required by local and/or site regulations.

Participants with a positive result will not be allowed to continue in the study until evidence of a subsequent negative test is obtained.

11.2 Safety and Tolerability Assessments

11.2.1 Adverse Events

Adverse events will be recorded as described in Section 12.

11.2.2 Physical Examination

Full physical examinations will include, at a minimum, assessment of the following: general appearance; head; ears; eyes; nose and throat; neck (including thyroid and lymph nodes); respiratory system; cardiovascular system; gastrointestinal system; renal system (percussion); neurological condition; musculoskeletal system, skin and any other focused assessments suggested by the presence of specific symptoms.

Symptom-directed physical examinations will include focused assessments suggested by the presence of specific symptoms.

All physical examinations will be conducted by a licensed physician within the time windows specified in the SoA. Physical examinations may be performed at various unscheduled timepoints if deemed necessary by the PI. All clinically significant (CS) findings will be recorded as AEs.

11.2.3 Vital Signs

Vital signs assessments will include systolic and diastolic BP, pulse rate (PR), body temperature (tympanic), and respiratory rate (RR). Participants should be resting in a supine position for at least 5 minutes prior to and during vital signs measurements. Clinical staff are required to perform vital sign assessments at the nominated timepoints within the time windows indicated in the SoA.

Abnormal vital signs assessments that are not clinically significant (NCS) will be repeated at the PI's discretion. Abnormal vital signs assessments that are CS will be repeated. All CS findings will be recorded as AEs.

11.2.4 12-Lead Safety ECG

Twelve-lead safety ECGs for on-site interpretation (including but not limited to the measurements of ventricular HR, PR interval, QRS duration, QT interval and QTcF) will be performed at the timepoints and windows indicated in the SoA. The screening and Day -1 ECGs to confirm eligibility will be performed in triplicate, with each replicate separated by at least 1 minute and the full set of triplicates completed within 5 minutes. The average of the triplicate readings for each parameter will be used to determine eligibility.

All other ECGs will be single readings. If any of the single ECG measurements is out of normal range, it will be repeated in triplicate (within 5 minutes, with each reading separated by at least 1 minute). If the "re-check" triplicate's average is still above these parameters, then the PI shall be notified for a decision on further action.

Each ECG will be conducted in a supine position after the participant has been resting for at least 5 minutes in a quiet setting without distractions (e.g., television, cell phones).

All ECGs will be interpreted, signed and dated by the PI, or qualified designee. The ECGs will be classified as normal, abnormal NCS, or abnormal CS. In addition, ECG parameters of ventricular HR, PR interval, QRS duration, QT interval and QTcF will be noted on the eCRF. All CS findings will be recorded as AEs.

Abnormal ECGs that are NCS may be repeated at the PI's discretion. Abnormal ECGs that are CS will be repeated. In the case of evidence of bad quality (e.g., muscle tremor) of the tracing, an ECG will be repeated.

All repeat assessments will be performed in triplicate.

11.2.5 Clinical Laboratory Safety Tests

Blood samples for haematology, serum chemistry, coagulation and urine samples for urinalysis will be collected at selected time points throughout the study as defined in the SoA. All samples should be collected within the windows indicated within the SoA. Tests for any CS results may be repeated at PI (or delegated medical officer) discretion. Clinically significant results obtained at screening may be repeated once at any time during the screening window.

Participants will be required to fast for at least 8 hours (water is permitted) prior to each clinical laboratory blood sample collection timepoint (except in the instance of an ETV).

Parameters to be evaluated at each specified timepoint are listed in APPENDIX 3.

All clinical laboratory safety assessments will be assessed by a certified local laboratory, using that laboratory's normal ranges. The PI (or delegate) must review the laboratory report, document this review, and record any CS changes occurring during the study in the AE section of the eCRF.

During the study, all out of range (abnormal) laboratory values must be evaluated and commented on by the PI (or delegate) for CS. Laboratory safety test results will be classified as normal, abnormal NCS, or abnormal CS.

In the event of an unexplained, CS abnormal laboratory test result, the test should be repeated and followed up until it has returned to the normal range and/or an adequate explanation of the abnormality is found. Abnormal laboratory test results that are NCS will be repeated at the PI's discretion. All CS findings will be recorded as AEs.

11.2.6 Injection Site Assessments

Prior to injection on Day 1, the region to be injected will be marked and examined, and findings from this examination will be documented.

The skin at the injection site should be free of blemishes, scars, heavy hair, veins, moles, skin conditions, sores or tattoos that have the potential to interfere with the detection of local reactions.

Following injection on Day 1, the Investigator or trained and delegated site staff will review

the participant at a number of timepoints post-dose (refer APPENDIX 1) to inspect the injection sites for evidence of local reactions, defined as an area of pain, tenderness, erythema/redness, swelling/induration, or other e.g., haemorrhage, haematoma and pruritus.

11.3 Pharmacokinetic and Immunogenicity Assessments

11.3.1 Pharmacokinetics

Blood samples (up to 10 mL per sample) will be collected for analysis of palivizumab concentrations and determination of PK parameters in serum.

Blood samples will be processed with the resultant serum divided into aliquots and placed into labelled serum storage tubes. Instructions for collecting and processing serum samples for PK will be provided in the study Laboratory Manual.

Serum samples will be assayed by validated bioanalytical methods, which are specific for the measurement of the analytes relevant to this study. The method validation conducted by the appointed bioanalytical laboratory will address (at a minimum) method accuracy, precision, reproducibility, specificity, recovery and sample stability, and other parameters as appropriate. The method validation report may be appended to the final clinical study report, if requested by the Sponsor.

11.3.2 Immunogenicity

Blood samples (up to 10 mL per sample) will be collected to determine the incidence of ADAs and nAbs against MB05, EU- and US-Synagis®.

Instructions for collecting and processing serum samples for ADA/nAb determination will be provided in the study Laboratory Manual.

11.4 Total Blood Sample Collection Volume

Blood samples for clinical safety labs, PK analysis and immunogenicity will be collected from each participant throughout the study. The blood sample collection volumes estimated per participant are provided in Table 3, below.

If additional blood sampling or an increased blood volume per sample is required, the maximum blood volume collected from each participant will not exceed 650 mL over the 14-15-week period. Additional blood (over and above the limit specified above) may be collected from any of the study participants if required for safety reasons.

Table 3. Approximate Blood Sample Volumes Collected Per Participant

Sample Type (volume/sample)	Volume Per Sample	Number of Samples to be Collected	Total Volume to be Collected
Haematology	4 mL	9	36 mL
Serum Chemistry [a]	9 mL	9	81 mL
Coagulation	3 mL	9	27 mL
PK	10 mL	18	180 mL
ADA/nAb	10 mL	5	50 mL
Study Total			**374 mL**

[a] *Also includes serum pregnancy, FSH testing and viral serology at screening.*

Abbreviations: ADA = anti-drug antibody; nAb = neutralising antibody; PK = pharmacokinetics.

12 ASSESSMENT AND MANAGEMENT OF ADVERSE EVENTS

12.1 Adverse Event Definition

An **AE** is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal (investigational or non-investigational) product, whether or not related to that medicinal (investigational or non-investigational) product (based on International Council for Harmonisation [ICH] definition)

Any AE where a causal relationship with the study treatment is at least a reasonable possibility (i.e., possibly/probably or definitely related), is referred to as an **Adverse Drug Reaction**.

An **SAE** is any AE that, at any dose:

- Results in death.
- Is life-threatening (The term 'life-threatening' in the definition of 'serious' refers to an event/reaction in which the participant was at risk of death at the time of the event/reaction; it does not refer to an event/reaction which hypothetically might have caused death, if it were more severe).
- Requires inpatient hospitalisation or prolongation of an existing hospitalisation (only hospitalisations that are longer than expected based on Investigator judgement, will be considered prolonged hospitalisations).
- Results in persistent or significant disability/incapacity (an AE that results in a substantial disruption of a person's ability to conduct normal life functions).
- Is a congenital anomaly/birth defect (A congenital anomaly/birth defect that occurs in the offspring of a participant exposed to the study treatment).

Medical and scientific judgement should be exercised in deciding whether other situations should be considered serious, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but might jeopardise the participant or might require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also be considered serious. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation, or development of drug dependency or drug abuse.

A **Suspected Unexpected Serious Adverse Reaction (SUSAR)**:

- Is serious.
- There is a least a reasonable possibility of a causal relationship between the event and the study treatment.
- Is considered unexpected (i.e., the event is not listed in the IB or is not listed at the specificity or severity that has been observed). For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the IB referred only to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the IB listed

only cerebral vascular accidents. "Unexpected" as used in this definition, also refers to AEs that are mentioned in the IB as occurring with a class of drugs or are anticipated from the pharmacological properties of the drug but are not specifically mentioned as occurring with the particular drug under investigation.

Abnormal laboratory findings (e.g., serum chemistry, haematology, coagulation and urinalysis) **or other abnormal assessments** (e.g., ECGs, vital signs) that are judged by the PI as clinically significant will be recorded as AEs or SAEs if they meet the definitions stated above. Clinically significant abnormal laboratory findings or other abnormal assessments that are detected during the study or are present at baseline and significantly worsen following the start of the study will be reported as AEs or SAEs. The PI will exercise his or her medical and scientific judgement in deciding whether an abnormal laboratory finding or other abnormal assessment is clinically significant.

12.1.1 Injection Site Reaction Assessments

Injection site reactions may include:

- Pain
- Tenderness
- Erythema/redness
- Swelling/ induration
- Other (e.g., haemorrhage, haematoma and pruritus)

Injection site reactions will be graded as per the FDA Guidance for Industry document entitled *Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials* (2007) as presented in Table 4.

Table 4. Grading for Injection Site Reactions

Local Reaction to Injectable Product	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life-Threatening (Grade 4)
Pain	Does not interfere with activity	Repeated use of nonnarcotic pain reliever > 24 hours or interferes with activity	Any use of narcotic pain reliever or prevents daily activity	Emergency room (ER) visit or hospitalisation
Tenderness	Mild discomfort to touch	Discomfort with movement	Significant discomfort at rest	ER visit or hospitalisation
Erythema/Redness*	2.5 – 5 cm	5.1 – 10 cm	> 10 cm	Necrosis or exfoliative dermatitis
Induration/Swelling**	2.5 – 5 cm and does not interfere with activity	5.1 – 10 cm or interferes with activity	> 10 cm or prevents daily activity	Necrosis

* In addition to grading the measured local reaction at the greatest single diameter, the measurement should be recorded as a continuous variable.
** Induration/Swelling should be evaluated and graded using the functional scale as well as the actual measurement.

Injection site reaction types not meeting the above definitions (e.g., haemorrhage, haematoma, pruritis), will be graded according to the National Cancer Institute Common Terminology Criteria for AEs (NCI-CTCAE, Version 5.0) 5-point scale, as described in Section 12.2.1

below.

All injection site reactions will also be recorded as AEs, with the overall severity of the injection site reaction graded according to NCI-CTCAE criteria, Version 5.0.

12.2 Evaluating AEs and SAEs

12.2.1 Assessment of Severity

The Investigator will assess the severity for each AE and SAE reported during the study. The assessment will be based on the Investigator's clinical judgement. The intensity of each AE and SAE will be graded using the NCI-CTCAE, Version 5.0) 5-point scale (Table 5):

Table 5. NCI-CTCAE v5.0 5-Point Scale for Grading the Intensity of Each AE and SAE

Grade		Definition
I	Mild	Asymptomatic or mild symptoms: clinical or diagnostic observations only; intervention not indicated.
II	Moderation	Minimal, local or non-invasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL).
III	Severe	Severe or medically significant but not immediately life-threatening: hospitalisation or prolongation of hospitalisation indicated; disabling; limiting self-care ADL.
IV	Life-threatening	Life-threatening consequences, urgent intervention indicated.
V	Death	Death related to AE.

If an AE has multiple aspects, the aspect with the highest severity will be graded. Any change to the severity of an AE will be recorded as a comment in the eCRF.

The term severe is a measure of severity. Thus, a severe AE is not necessarily serious. For example, itching for several days may be rated as severe, but may not be clinically serious.

12.2.2 Assessment of Causality

The Investigator will make an assessment as to the relationship between a study treatment and the occurrence of each AE/SAE. The Investigator will use clinical judgement to determine whether or not the AE/SAE is causally related to the study treatment(s). Alternative causes, such as natural history of an underlying medical condition, concomitant therapy, other risk factors, and the temporal relationship of the event to the study treatment will be considered and investigated. The Investigator will also consult the IB (or the product information sheet in instances where the study treatment is an approved agent) in the determination of his/her assessment.

The causal relationship of the study treatment to an AE will be rated according to the following 5-point scale (Table 6):

Table 6. Relationship of the Study Treatment to an AE (definitions)

Causal Relationship	Definition
Unrelated	Clearly and incontrovertibly due only to extraneous causes, and does not meet criteria listed under unlikely, possible or probable.
Unlikely	Does not follow a reasonable temporal sequence from administration; may have been produced by the participant's clinical state or by environmental factors or other therapies administered.
Possibly	Follows a reasonable temporal sequence from administration of the study treatment; may have been produced by the participant's clinical state or by environmental factors or other therapies administered.
Probably	Clear temporal association with improvement on cessation of study treatment. Reappears upon rechallenge if rechallenge occurs) or follows a known pattern of response to the study treatment.
Definitely	Cannot be reasonably explained by an alternative explanation, e.g., concomitant drug(s), concomitant disease(s). The relationship in time is very suggestive.

The causality assessment is one of the criteria used when determining regulatory reporting requirements, therefore, the Investigator must make an assessment of causality based on all available information for every event prior to transmission of the SAE form to the Sponsor. The Investigator may change his/her opinion regarding causality in light of follow-up information and amend the SAE form and the eCRF accordingly.

12.2.3 Action Taken and Outcome

For all AEs reported, the actions taken and outcomes must be specified and documented in the eCRF and appropriate form(s) (where required) as described in the eCRF completion guidelines.

Actions taken may include any of the following:

- No action
- Medication required
- Termination of a concomitant medication
- Change of the dose of a concomitant medication
- Hospitalisation or prolongation of hospitalisation (please complete SAE Form)
- Other (please specify)

The following terms and definitions are used in assessing the final outcome of an AE (Table 7):

Table 7. Terms and Definitions Used in Assessing the Final Outcome of an AE

Term	Definition
Recovered	The participant has fully recovered, or by medical or surgical treatment the condition has returned to the level observed at the first trial-related activity after the participant signed the informed consent.
Recovering	The condition is improving and the participant is expected to recover from the event.
Recovered with sequelae	The participant has recovered from the condition, but with lasting effect due to a disease, injury, treatment or procedure. If a sequelae meets an SAE criterion, the AE must be reported as an SAE.
Not recovered	The condition of the participant has not improved and the symptoms are unchanged, or the outcome is not known at the time of reporting.
Fatal	This term is only applicable if the participant died from a condition related to the reported AE. Outcomes of other reported AEs in a participant before he/she died should be assessed as "recovered", "recovering", "recovered with sequelae" or "not recovered". An AE with fatal outcome must be reported as an SAE.
Unknown	This term is only applicable if the participant is lost to follow-up.

12.3 Procedures and Time Period for Detecting Adverse Events

The Investigator (or designee) is responsible for detection, recording and reporting of events that meet the criteria and definition of AEs.

As a consistent method of soliciting AEs, the participant shall be asked a non-leading question such as: "How do you feel"?

Detection and recording of study-related AEs and SAEs extends from the signing of the consent form until completion of the last study-related procedure (including follow-up for safety assessments).

Any pre-existing conditions or signs and/or symptoms present in a volunteer prior to any involvement in the study (i.e., before informed consent) should be recorded as medical history. Any change in health status that is reported or observed after informed consent but prior to starting study treatment and is deemed by the study Investigator to be "not related" to study procedures, will be documented as medical history. In addition, any change in health status, which is reported after informed consent by the volunteer, but started prior to informed consent and did not worsen, will be documented as medical history. Any worsening of a pre-existing condition that occurs following informed consent will be recorded as an AE.

A post-study AE/SAE is defined as any event that occurs outside of the nominal AE/SAE study

detection period. Investigators are not obligated to actively seek AE/SAE in former study participants. However, if the Investigator learns of any SAE, including a death, at any time after a participant has completed the study and he/she considers the event reasonably related to the study treatment, the Investigator will promptly notify the Sponsor.

Participants must be provided with an "Emergency Wallet Card" indicating the name of the study treatment, the study number, the Investigator's name and an emergency contact number.

12.4 Recording of AEs and SAEs

All AEs, regardless of seriousness, severity, or presumed relationship to study treatment, must be recorded using medical terminology in the eCRF and/or other sources. Whenever possible, diagnoses should be given when signs and symptoms are due to a common aetiology (e.g., cough, runny nose, sneezing, sore throat, and head congestion may be reported as "upper respiratory infection"). Investigators must record in the eCRF the date of onset of the event, their opinion concerning the relationship of the event to the study treatment, severity of the event, whether the event is serious or nonserious, actions taken to manage the event, the outcome of the event, and date of resolution where applicable.

Any change to the severity of an AE must be recorded as a comment in the eCRF.

12.5 Reporting of SAEs and SUSARs

The Investigator must notify the study Sponsor Safety Department and Sponsor designated safety officer within 24 hours of becoming aware of the occurrence of an SAE. Information regarding SAEs will be transmitted to the Sponsor Safety Department using an SAE form as described in the study SAE Report Form Completion Guidelines.

The SAE form must be completed and signed by a member of the investigational staff and transmitted to the Sponsor Safety Department and Sponsor designated safety officer (Table 8). Any new or updated clinical information on the SAE will be recorded on a new SAE form and sent to the Sponsor Safety Department within 24 hours of the information being available. The initial and follow-up reports of an SAE should be transmitted by email. Receipt of the SAE form must be confirmed by each recipient.

Table 8. Contact Details for Transmission of SAE Reporting Forms to the Sponsor and Sponsor Designated Safety Officer.

Sponsor contact details for SAE reporting	Phone: 0034 917711590 Email: pharmacovigilance@mabxience.com
Sponsor designated safety officer details for SAE reporting	Name: Pilar Garzon / Alexander Leonov / Elena Bercu Phone: +61 478 034 138 Email: safety@avancecro.com

The Investigator must report SAEs to the ethics committee (EC) that approved the protocol unless otherwise required and documented by the EC.

It is the responsibility of the Sponsor to determine whether a reported SAE fits the classification of a SUSAR. The Investigator's opinion regarding the assessment of expectedness (if provided)

and causality will be taken into account in the Sponsor's determination of the SAE as a SUSAR. The causality assessment given by the Investigator cannot be downgraded by the Sponsor.

SAEs (including SUSARs) will be reported to competent authorities in accordance with national requirements. The Sponsor assumes responsibility for appropriate reporting of SAEs (including SUSARs) to the regulatory authorities.

12.6 Follow-up of AEs and SAEs

Following initial observation of an AE/SAE, the Investigator is required to proactively follow progress of the relevant participant. Any information obtained in relation to the status of the AE/SAE and the condition of the participant must be appropriately documented in the eCRF or in a follow-up SAE form.

All AEs and SAEs documented at a previous visit/contact and are designated as ongoing, will be reviewed at subsequent visits/contacts. Adverse events/SAEs that have not resolved by the end of the study, or that have not resolved upon discontinuation of the participant's involvement in the study, must be followed until any of the following occurs:

- The event resolves
- The event stabilises
- The event returns to baseline if a baseline value is available
- The event can be attributed to agents other than the study treatment or to factors unrelated to study conduct
- It becomes unlikely that any additional information can be obtained (participant or health care practitioner refusal to provide additional information, lost to follow-up after demonstration of due diligence with follow-up efforts)

The Investigator will ensure that AE/SAE follow-up includes any supplemental investigations as may be indicated to elucidate the nature and/or causality of the event. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals.

The Sponsor may request that the Investigator perform or arrange for the conduct of supplemental measurements and/or evaluations to elucidate as fully as possible the nature and/or causality of the SAE. If a participant dies during participation in the study or during a recognised follow-up period, the Sponsor will be provided with a copy of any post-mortem findings, including histopathology.

New or updated information will be recorded on a new SAE form and sent to the Sponsor.

Due to the coronavirus SARS-COV-2 (COVID-19) pandemic, Investigators must also ensure compliance with local governing legislation and reporting requirements associated with COVID-19 infections.

12.7 Exposure *In Utero* Management and Reporting

In instances of pregnancies or suspected pregnancies identified or reported for any female participant (or male participant's female partner), including a positive pregnancy test regardless of age, during participation in this study, the pregnant female participant (or the male

participant's female partner) will be advised to notify her healthcare provider.

The Investigator will notify the Sponsor and designated study safety officer of this event and document the pregnancy on the EIU form as described in the study Pregnancy/EIU Report Form Completion Guidelines.

The Investigator shall obtain informed consent from the pregnant female participant (or male participant's female partner) in order to allow him/her to review relevant medical records and conduct follow-up throughout the gestational period and on the infant following delivery. The Investigator shall follow-up newborn infants that have been exposed to study treatment *in utero* for a minimum of 12 months. Upon discovery of any congenital anomalies (or neonatal deaths) the Investigator shall submit a follow-up report to the Sponsor (and study safety officer) using an SAE Form (as per study Safety Reporting Plan) including information regarding the status of the newborn. A miscarriage or abortion shall also be reported by the Investigator to the study Safety Officer (and the Sponsor) using an SAE Form.

12.8 Safety Review Committee

The decision to enrol Group 2 will be made following the evaluation of all available safety data by the SRC up to and including Day 8 of Group 1 (details described in the study SRC Charter). There are no other formal requirements for an SRC meeting, however safety and tolerability data will be continually reviewed and an ad-hoc SRC meeting may be called at any time, if requested by the Investigator (in consultation with the study Sponsor).

At a minimum, the SRC will consist of the Investigator(s) who have enrolled patients in the current group, an IMM and the SMR, however all Investigators involved in the study will be invited to attend each SRC review meeting, regardless of whether they have enrolled participants into the group. Other individuals (e.g., medical experts) may be invited to participate at the discretion of the SRC to provide additional input into the review process if required.

All decisions will be made by agreement between the Investigator(s) and the SMR.

13 STATISTICS AND DATA ANALYSIS

Detailed methodology for summaries and statistical analyses of the data collected will be documented in a separate Statistical Analysis Plan (SAP) and will be finalised before database lock. Any changes to the methods described in the final SAP will be described and justified as needed in the clinical study report (CSR).

This section describes the general framework to be used for the analysis and presentation of data in this study. The information described in this section may be revised during the study to accommodate protocol amendments and to make changes to adapt to unexpected issues in study execution and data that could affect planned analyses. All available data will be included in data listings. Data tabulations will be performed for specific analysis populations.

13.1 Sample Size Considerations

Up to a total number of 141 healthy subjects (male and female) are planned to be enrolled in

the study. Subjects who meet the entry criteria will be randomised to receive a single dose of MB05, EU-sourced Synagis® or US-sourced Synagis® in a 1:1:1 fashion. Randomisation will be stratified based on the subject's body weight (50 to <75 kg and ⩾75 to 95 kg) and gender (male and female). To achieve balance, the number of subjects enrolled in each stratum should be a multiple of 3, where possible.

The reported coefficients of variation (CVs) for AUC and C_{max} for Synagis® vary between 0.25 and 0.35. Based on a worst-case CV of 0.35 (Robbie et al., 2012), alpha of 0.05 (i.e., utilising a two-sided 90% CI around the mean difference) and a true hypothesised ratio for the mean difference of 0.95, a total of 141 subjects (47 subjects per arm respectively), 1:1:1 ratio) will provide approximately 85% power to demonstrate bioequivalence of MB05 with EU-sourced Synagis® and US-sourced Synagis®. Assuming a 5% dropout, a total of 132 evaluable subjects (44 subjects per arm) are sufficient for this measure.

13.2 Interim Analysis

A blinded interim analysis may be performed when 50% of the PK profiles are available in correlation with safety data to evaluate potential drug-related events. In this instance, blinded PK data would serve as preliminary assessment of the achievement of the therapeutic threshold for palivizumab (40 µg/ml) This analysis of the PK in healthy adult volunteers, together with analytical comparability, may preliminarily inform about clinical extrapolation to the paediatric population.

13.3 Analysis Populations

For the purpose of analysis, the following populations are defined for this protocol. The final definition of each population will be presented in the SAP.

Population	Description
Safety	The safety population will include all randomised participants who received any amount of study treatment and will be summarised according to the treatment actually received, if this differs from that to which the participant was randomised to. The safety population will be used for the summaries of all safety, baseline and demographic data.
Pharmacokinetic	The PK population will include all randomised participants where there is sufficient data for reliable estimates of C_{max} (as determined by the study Pharmacokineticist). Participants with dosing or PK sampling deviations that could potentially affect the PK profile will also be excluded from the PK population, at the discretion of the study Pharmacokineticist. The PK population will be used for the summaries of all PK data.
Immunogenicity	The immunogenicity population will include all randomised participants who receive any amount of study treatment and who have at least 1 evaluable immunogenicity parameter post-dose and

Population	Description
	will be summarised according to the treatment actually received, if this differs from that to which the participant was randomised. The immunogenicity population will be used for the summaries of all immunogenicity data.

13.4 Demographic and Baseline Data

Demographic data (eg. gender, age, race, ethnicity, and BMI) will be summarized for all participants in the Safety population using descriptive statistics (mean, standard deviation [SD], median, minimum, and maximum) and presented by treatment. Medical history will be listed for the Safety population.

Screening serology results (HIV-1, HIV-2, HBsAg, HBcAb, HCV) and COVID-19 (PCR or antigen) results will be listed only.

Concomitant medications taken after the start of study treatment will be summarised for the Safety population. Prior and concomitant medications will be coded using the latest version of the WHO Drug Dictionary, and summarised by drug class, generic name and treatment group. The recorded start/stop dates will be used to identify when a concomitant medication was taken during the study. Prior medications will be listed only.

13.5 Safety/Tolerability Data

All participants in the Safety population will be included in the safety and tolerability analysis. Baseline for analysis of physical examination, vital signs, and clinical laboratory data will be defined as the last evaluation done before administration of study drug for each participant.

Safety evaluations will be based on the incidence, severity and relationship of AEs and changes from baseline in body weight, physical examination findings, vital signs, clinical laboratory, and ECG results and injection site reactions.

Abnormalities in clinical laboratory parameters, and vital signs, will be based on predefined normal ranges and will be tabulated by treatment showing participant counts and percentages.

13.5.1 Adverse Event Data

The verbatim terms used in the eCRF by investigators to identify AEs will be coded using the current version of the Medical Dictionary for Regulatory Activities (MedDRA) by system organ class (SOC) and preferred term, classified from verbatim terms. The number and percentage of participants with treatment-emergent AEs (TEAEs) and serious TEAEs as well as the number of TEAEs and serious TEAEs will be summarized by SOC and preferred term and tabulated for each treatment. Summaries by severity and relationship will also be presented. The percentage of participants who discontinued treatment due to a TEAE will be summarized and tabulated for each treatment. The duration of AEs will be determined and included in the listings only.

13.5.2 Clinical Laboratory Data

Clinical laboratory data will be summarized by the laboratory parameter. Normal reference ranges and abnormal results will be used in the summary of laboratory data. Individual abnormal results will be flagged as being "Low" or "High." Observed values and changes from baseline for continuous clinical laboratory parameters will be summarized at each scheduled timepoint using descriptive statistics (n, mean, SD, median, minimum, and maximum) and tabulated for each treatment. Categorical clinical laboratory data will be summarized at each scheduled timepoint using participant counts and percentages and tabulated by treatment. This includes the number and percentage of participants with any CS laboratory abnormalities. A listing of participants with any laboratory results outside the reference ranges and deemed CS will be provided.

13.5.3 Vital Signs

Observed values and changes from baseline for vital signs will be summarized at each scheduled timepoint using descriptive statistics (n, mean, SD, median, minimum, and maximum) and tabulated for each treatment.

13.5.4 Physical Examination Data

Physical examination findings will be listed only.

13.5.5 Electrocardiogram Data

The following ECG parameters will be measured: ventricular HR, PR interval, QRS duration, QT interval and QTcF. Observed ECG values and their changes from baseline will be presented in tabular format and summarised using descriptive statistics (n, mean, SD, median, minimum, and maximum) by timepoint. The baseline value will be the average of the triplicate measurements taken at Day -1.

13.5.6 Injection Site Reactions

All individual injection site results will be presented in data listings. Frequency of severity will be summarised by reaction type (pain, tenderness, erythema/redness and swelling/induration, or other), assessment timepoint and treatment.

13.6 Pharmacokinetic Data

13.6.1 Serum Concentration Data

Serum palivizumab concentrations will be listed for each subject and summarized with descriptive statistics (N, mean, SD, CV, median, minimum, maximum and geometric mean) by treatment and nominal PK sampling time point.

Individual subject and arithmetic mean (per treatment) palivizumab concentration-time profiles will be plotted with the concentration axis displayed on linear and logarithmic scales.

13.6.2 Serum Pharmacokinetic Parameters and Bioequivalence Analysis

Serum palivizumab concentrations from samples collected at specific timepoints following IM administration of each study treatment will be used to calculate PK parameters using non-

compartmental analysis methods. The following PK parameters will be determined:

C_{max}	Maximum observed serum concentration obtained directly from the concentration versus time data.
T_{max}	Time to maximum observed concentration, taken directly from the data. If the maximum serum concentration occurs at more than one time point, the first is chosen.
k_{el}	Terminal elimination rate constant obtained from the slope of the line, fitted by linear least squares regression through the terminal points of the logarithmic concentration-time profiles.
$AUC_{0\text{-}inf}$	Area under the serum concentration versus time curve from time zero to infinity, calculated as ($AUC_{0\text{–}tlast} + C_t/ k_{el}$), where C_t is the last quantifiable concentration.
AUC_t	Area under the serum concentration-time curve from time zero to time t
$t_{½}$	Apparent terminal half-life, calculated as $t_{½} = \ln (2)/ k_{el}$.
CL/F	Apparent total serum clearance of drug after IM administration, where F is the fraction of drug absorbed, calculated as (Dose / $AUC_{0\text{-}inf}$).
Vz/F	Apparent volume of distribution during terminal phase after IM administration, calculated as ($CL/F / k_{el}$).

PK parameters for each participant will be listed and summarised by treatment using descriptive statistics.

Bioequivalence between MB05 and EU-Synagis®, between MB05 and US-Synagis® and between EU-Synagis® and US-Synagis® will be investigated for $AUC_{0\text{-}inf}$ and C_{max} by analysis of variance using log-transformed PK parameter values. Bioequivalence will be assessed by calculating the 90% CIs for the ratio of the least squares geometric means for each pairwise comparison and each PK parameter. Bioequivalence will be concluded where the 90% CIs for the ratio of least squares geometric means are contained within the range 80.00% to 125.00%. For each pairwise treatment comparison and each PK parameter, this corresponds to undertaking two one-sided tests (TOST) of significance each at the 5% level.

Additional details of PK analysis will be provided in the study SAP.

13.7 Immunogenicity Data

Data for immunogenicity endpoints will be listed for all participants.

Incidence of ADAs will be presented by means of counts and percentages by treatment group and study visit. ADA titres and changes from baseline will be summarised by treatment group and study visit.

Incidence of nAbs will be presented by means of counts and percentages by treatment group and study visit.

Immunogenicity analyses will be based on the Immunogenicity population.

14 DATA HANDLING AND RECORD KEEPING

14.1 Privacy of Personal Data

In order to maintain participant privacy, all eCRFs, study treatment accountability records, study reports and communications will identify the participant by only their assigned participant study number. The PI will grant monitor(s) and auditor(s) from the Sponsor (or designee) and regulatory authorities access to the participant's original medical records for verification of data gathered on the eCRF and for the purposes of auditing the data collection process. The participant's confidentiality will be maintained at all times and will not be made publicly available to the extent permitted by the applicable laws and regulations.

14.2 Screening/Enrolment Logs and Privacy

The PI is required to complete a participant enrolment log to permit reference to each participant during and after the study. Any log identifying study participant identity will be treated as confidential and will be filed by the PI (or delegate) in the Investigator Site File (ISF). This document will be reviewed by the Study Monitor for completeness. To ensure participant confidentiality, if such a log is required to be distributed to the Sponsor, it must first have any personal details (e.g., name, initials, date of birth) redacted.

The PI must also complete a volunteer screening log, which reports on all volunteers who were assessed to determine eligibility for inclusion in the study.

14.3 Source Documentation

Source documentation must be prepared and available to capture at a minimum the following aspects and parameters:

- Adherence to protocol procedures
- Participant study reference number(s)
- Informed consent procedures
- Eligibility assessments
- Protocol specified schedules and assessments
- Dates of visits
- Safety observations including reporting and follow-up of AEs
- Drug receipt/dispensing/return records
- Study treatment administration information
- Date of participant completion
- Withdrawal from the study (including reason)

Specific items required as source documents will be reviewed with the PI before the study.

The author of an entry in the source documents must be identifiable. Worksheets may be used for the capture of some data to facilitate completion of the eCRF. Any such worksheets will become part of the participants' source documentation.

Following the ICH Good Clinical Practice (GCP) guidelines, direct access to source

documentation and medical records must be allowed for the purpose of verifying that the data recorded in the eCRF are consistent with the original source data.

14.4 Electronic Case Report Form

An eCRF entry must be completed for each subject who is successfully enrolled (received at least one dose of study drug). For reasons of confidentiality, the name and initials of the subject should not appear in the eCRF. All eCRF entries, corrections, and alterations must be made by the Investigator or other authorised study site personnel.

Data entry into the eCRF will be conducted throughout study conduct according to the Sponsor's (or designee) instructions and reviewed by the Sponsor (or designee) to determine their acceptability. If necessary, eCRF queries will be raised by the Sponsor (or designee) relating to eCRF data entries. The Investigator or authorised study site staff must address all eCRF queries raised.

14.5 Recordkeeping and Retention of Records

In compliance with the ICH GCP guidelines, the Investigator/Institution will maintain all source documents that support the data collected from each subject, as well as all study documents as specified in ICH GCP Section 8, Essential Documents for the Conduct of a Clinical Trial. The Investigator/Institution will take measures to prevent accidental or premature destruction of these documents.

Following closure of the study, the PI (or delegate) must maintain all site study records in a safe and secure location. The records must be maintained to allow easy and timely retrieval, when needed (e.g., audit or inspection) and whenever feasible, to allow any subsequent review of data in conjunction with assessment of the facility, supporting systems and staff. When permitted by local laws/regulations or institutional policy, some or all of these records can be maintained in a format other than hard copy (e.g., microfiche, scanned, electronic); however, caution needs to be exercised before such action is taken. The PI must assure that all reproductions are legible and are a true and accurate copy of the original and meet accessibility and retrieval standards, including re-generating a hard copy, if required. Furthermore, the PI must ensure there is an acceptable back-up of these reproductions and that an acceptable quality control process exists for making these reproductions.

The Sponsor will inform the PI (or delegate) of the time period for retaining these records to comply with all applicable regulatory requirements. The minimum retention time will meet the strictest standard applicable to that site for the study, as dictated by any institutional requirements or local laws or regulations, or Sponsor standards/procedures; otherwise, the retention period will default to 25 years.

It is the responsibility of the Sponsor to inform the Investigator/Institution as to when these documents no longer need to be retained.

If the responsible Investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who will accept the responsibility. The Sponsor must be notified in writing of the name and address of

the new custodian.

Under no circumstance shall the Investigator relocate or dispose of any study documents before having obtained written approval from the Sponsor.

If it becomes necessary for the Sponsor or the appropriate Regulatory Authority to review any documentation relating to this study, the Investigator must permit access to all study documentation.

The material to be stored shall include, but is not limited to, the following:

- Signed and dated copy of the final study protocol and any amendments
- Signed and dated letter of ethics committee approval, relevant regulatory authority approval, letter of constitution of the ethics committee and copies of any other correspondence relevant to the study with the ethics committee and relevant regulatory authorities
- The ethics committee approved informed consent form
- Current *curriculum vitae* (signed and dated) of the PI and co-workers with major responsibilities in the trial
- Site Signature and Delegation of Responsibility Log
- Financial Disclosure Form(s)
- Blank eCRF
- Signed participant informed consent forms
- Laboratory reference ranges (signed and dated)
- The final clinical study report
- Clinical raw data including the Source Data Forms, all clinical laboratory report forms, participant eCRF, drug accountability forms, and dispensing records, etc.

15 ETHICS AND REGULATORY COMPLIANCE

15.1 Investigator Responsibilities

The Investigator agrees to conduct the clinical study in accordance with the protocol, current ICH guidelines for GCP, and applicable regulatory and legal requirements. Good clinical practice is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human participants. Compliance with this standard provides public assurance that the rights, safety, and wellbeing of study participants are protected, consistent with the principles that originated in the Declaration of Helsinki, and that the clinical study data are credible.

15.2 Ethics Committee and Regulatory Authority Approval

This study protocol and any amendment(s) must be submitted to the appropriate ethics committee(s)/relevant competent authority in each respective country, as required. The Sponsor (or designee) is responsible for regulatory submissions. This clinical study may not be initiated until all local regulatory requirements are met.

Before the start of the study, a written favourable opinion or approval must be received from the ethics committee/relevant competent authority. To achieve this, the Investigator or the Sponsor will submit to the ethics committee and regulatory authorities, as required by local

regulations, current and complete copies of relevant documents.

The written favourable opinion or approval must be dated and must clearly identify the documents reviewed, which should include the final protocol and any amendments, the informed consent form, applicable recruiting materials, and any participant compensation program.

During the study, the Investigator or Sponsor (or designee), as required, will submit the following for ethics committee review or opinion/approval:

1. Revisions or updates of documents previously submitted to the ethics committee, and
2. Relevant new information or documents, as required:

    a. Summaries of the status of the study (at least annually or at intervals stipulated in guidelines of the ethics committee).

    b. Reports of AEs that are serious, unlisted, and associated with the investigational drug.

    c. Deviations from or changes to the study protocol to eliminate immediate hazards to the participants.

When and where required by local regulations, before implementation of any change, study protocol amendments and revised documents must receive ethics committee favourable opinion or approval.

The ethics committee will be given official notification of the study completion.

15.3 Informed Consent

Each potential participant must give written consent according to local requirements after receiving a full explanation of the nature of the study. The consent form must be signed before performance of any study-related activity. The consent form that is used must be approved by both the Sponsor and by the reviewing ethics committee (and regulatory authorities where applicable). The informed consent process and form should be in accordance with principles that originated in the Declaration of Helsinki, current ICH GCP guidelines, applicable regulatory requirements, and Sponsor policy.

Before a potential participant's entry into the study, the Investigator or an authorised member of the clinical staff must explain to the potential participant the aims, methods, and potential hazards of the study, and any discomfort it may entail. The potential participants will be informed that their participation is voluntary and that they may withdraw consent to participate at any time. They will be informed that choosing not to participate will not affect the care a participant will receive.

Finally, potential participants will be informed that their records may be accessed by health authorities and/or clinical study personnel that have been authorised to do so by the Sponsor without violating the confidentiality of the participant, to the extent permitted by the applicable law(s) or regulations. By signing the informed consent form the potential participant is authorising such access.

Potential participants will be given sufficient time to read the informed consent form in a language that they understand and the opportunity to ask questions. After this explanation and

before entry into the study, consent should be appropriately recorded by means of the potential participant's personally dated signature. After the consent is obtained, a copy of the informed consent form must be given to the participant. The original consent form will be filed in the Investigator Site File.

15.4 Emergency Contact with Principal Investigator

Suitable arrangements will be made for participants to make contact with the PI or medically trained nominee in the event of an emergency.

15.5 Pandemic Preparedness

Clinical sites should have in place procedures and strategies to accommodate the current COVID-19 pandemic (or other pandemics as appropriate), in accordance with local requirements. Such procedures should include requirements in relation to criteria such as:

- Attendance (e.g., who is permitted to be on-site during a pandemic, limitations, records of attendance, plans for suppliers and deliveries).
- Physical layout (e.g., physical distancing requirements and signage).
- Flexibility (e.g., procedures for scaling, ability to respond to outbreak).
- Support for remote interactions with Sponsors and study teams (e.g., communication including infrastructure).
- The local environment (e.g., contact with local Health Authorities, ability to access up-to-date pandemic information).
- Any other relevant criteria.

15.6 Notification of General Practitioner

It is the responsibility of the PI or nominee, to notify, where applicable and in accordance with local state and country specific requirements, the participant's general practitioner of the participant's participation in the trial. This notification should be by sending a letter stating the nature of the trial, treatments, expected benefits or AEs and concomitant drugs to be avoided. The consent of the participant should be sought prior to contacting their general practitioner.

15.7 Clinical Laboratory Certification and Reference Ranges

Before the initiation of this study, the PI, or nominee, will obtain a copy of the certification form, with certification number and expiration date for all clinical laboratories used in the study. Reference ranges for each clinical laboratory test used in this study will be obtained from the appropriate laboratory, which will perform the test for the study.

15.8 Study Completion/Site Closure

The study is considered completed at the last contact of the last participant involved in the study. The final data from the investigational site will be sent to the Sponsor (or designee) in the time frame specified in the Clinical Trial Agreement. Investigational sites will be closed upon study completion. An investigational site is considered closed when all required documents and study supplies have been collected and a site closure visit has been performed by the Sponsor (or delegate).

15.9 End of Study and Regulatory Notification

At the end of the study, the ethics committee and any relevant Regulatory Authorities will be notified by the Sponsor (or delegate) according to applicable local regulatory requirements.

16 QUALITY CONTROL AND ASSURANCE

16.1 Study Monitoring

The Sponsor is responsible for assuring the proper conduct of the study with regard to protocol adherence and validity of the data recorded in the eCRF.

During the course of the trial, the Sponsor (or designee) will visit the trial site and/or perform remote monitoring at regular intervals. The PI must make themselves available to the Study Monitor during an on-site (or remote) monitoring visit to enable discussion on any arising issues relating to the study. The purpose of the monitoring (on-site or remote) is to ensure that the eCRF is completed correctly, the protocol is being adhered to, the source data are verified and drug accountability is performed.

The PI agrees to allow the Study Monitor direct access to relevant source documents (original documents, data and records). Direct access includes permission to examine, analyse, verify and reproduce any record(s) and report(s) that are important to evaluation of the clinical trial. The PI also agrees to allocate his/her time and the time of his/her staff to the Monitor to discuss findings and any relevant issues.

Participant confidentiality must be maintained during any monitoring activities conducted by the Sponsor (or delegate).

In accordance with applicable regulations and ICH GCP, Avance Clinical (contracted by the study Sponsor, mAbxience), will be responsible for assigning a Study Monitor who will contact the site to organise an on-site (or remote) visit prior to participant enrolment to review the protocol and data collection procedures with site staff. In addition, the assigned Study Monitor will periodically contact the site, including conducting on-site (or remote) visits. The extent, nature and frequency of on-site visits will be based on such considerations as the study objectives and/or endpoints, the purpose of the study, study design complexity, and enrolment rate.

During these site visits, the Study Monitor will:

- Check the progress of the study;
- Review study data collected;
- Conduct source document verification;
- Identify any issues and address their resolution;
- Check study treatment accountability records;
- Review biological samples collected for the study and ensure that they are labelled and stored correctly;
- Verify that:
    - The data are authentic, accurate and complete;

- Safety and rights of participants are being protected;
- Study is conducted in accordance with the currently approved protocol (and any amendments), ICH GCP and all applicable regulatory requirements.

At study closure, a Study Monitor will conduct the following activities in conjunction with the PI or site staff as appropriate:

- Ensure that all data queries have been resolved;
- Conduct final accountability and reconciliation for study treatment supplies including inventory and final disposition (e.g., destruction, shipping to repository, etc.).
- Review of site study records for completeness.

Because the study is blinded, an unblinded study monitor will be assigned to visit the site pharmacy during the study and at study completion, to review the randomisation schedule in comparison to the dispensing log in order to verify correct randomisation of the study treatments.

16.2 Quality Assurance and Quality Control

To ensure compliance with ICH GCP and all applicable regulatory requirements, the Sponsor (or a designated third party), may conduct a quality assurance audit of the study site. Regulatory agencies may also conduct a regulatory inspection of this study. Such audits/inspections can occur at any time during or after completion of the study. If an audit or inspection occurs, the PI and institution agree to notify the Sponsor as soon as possible following awareness of an impending regulatory inspection. The Investigator and Institution agree to allow the auditor/inspector direct access to all relevant documents and allocate his/her time and the time of his/her staff to the auditor/inspector to discuss findings and any relevant issues.

The Sponsor (or delegate) will perform the quality assurance and quality control activities for this study; however, responsibility for the accuracy, completeness, and reliability of the study data presented to the Sponsor lies with the PI (and delegate(s)) generating the data.

Prior to the study initiation, the Sponsor (or delegate) will explain the protocol, the IB, and eCRF to the PI and the site staff involved in this study. In addition, the assigned Study Monitor will be available to explain applicable regulations and to answer any questions regarding the conduct of the study.

16.3 Data Quality Control

Steps to be taken to ensure the accuracy and reliability of data include the selection of qualified Investigators and appropriate study centres, review of protocol procedures with the PI and associated personnel before the study, and periodic monitoring visits by the Sponsor (or delegate). Written instructions will be provided for collection, preparation, and shipment of biological samples collected for the purposes of this study. Electronic CRF completion training will be conducted with study personnel before the start of the study. The Study Monitor will review electronic data for accuracy and completeness during on-site (or remote) monitoring visits and any discrepancies will be resolved with the PI or designee, as appropriate. The data will be entered into the clinical study eCRF and verified for accuracy.

17 FINANCING AND INSURANCE

Financial aspects of the study are addressed in a separate clinical study agreement.

The PI and/or study site (as appropriate) is required to have adequate current insurance to cover claims for negligence and/or malpractice.

The Sponsor will provide insurance coverage for the clinical study as required by national regulations. The Sponsor will be subscribed to an insurance policy covering, in its terms and provisions, its legal liability for injuries caused to participating persons and arising out of this research performed strictly in accordance with the study protocol as well as with applicable law and professional standards prior to commencement of the study.

18 STUDY PROTOCOL GUIDELINES

18.1 Protocol Deviations and Violations

A minor protocol deviation is an accidental or unintentional change to, or noncompliance with this study protocol that does not increase risk or decrease benefit or does not have a significant effect on the participant's rights, safety or welfare; and/or on the integrity of the data. No deviations to the protocol are permitted, except in instances when an emergency occurs that requires a departure from the protocol for an individual. The nature and reasons for the protocol deviation will be recorded in the participant's eCRF and reported at the end of the study in the clinical study report.

A major protocol deviation is an accidental or unintentional change to, or noncompliance with the EC approved protocol (without prior Sponsor and EC approval), which increases risk or decreases benefit, affects the participant's rights, safety, or welfare, or the integrity of the data. Should a major protocol deviation occur, the Sponsor must be informed as soon as possible. Reporting of major protocol deviations to the EC and in accordance with applicable regulatory authority mandates is a PI responsibility.

The nature and reasons for the protocol deviation will be recorded in the CTMS and reported at the end of the study in the clinical study report.

18.2 Protocol Waivers

Protocol waivers will not be granted by the Sponsor in this study.

18.3 Protocol Amendments

Protocol revisions of typographical errors, clarifications of confusing wording, and other minor modifications including but not limited to name, address, and contact information changes that have no impact on the safety of the participant or the science of the study will be classed as **administrative amendments**. Administrative amendments will be submitted to the EC for information only. The local sponsor (or designee) will ensure that ethics committee/competent authority acknowledgement of administrative changes to the protocol is received and filed.

In all other instances, an amendment to the protocol will be classed as a **substantial**

amendment and will be submitted to the EC for approval and the appropriate regulatory authorities, as applicable. Any substantial amendment to the protocol will be implemented in the conduct of the trial only after approval has been received from EC.

19 INTELLECTUAL PROPERTY, CONFIDENTIALITY AND PUBLICATIONS

19.1 Ownership

All information provided by the Sponsor and all data and information generated by the clinical facility staff as part of the study (other than a participant's medical records), are the sole property of the Sponsor.

All rights, title and interests in any inventions, know-how or other intellectual or industrial property rights which are conceived or reduced to practice by clinical facility staff during the course of or as a result of the study are the sole property of the Sponsor and are hereby assigned to mAbxience.

If a written contract for the conduct of the study which includes ownership provisions inconsistent with this statement is executed between the Sponsor and the clinical facility, that contract's ownership provisions shall apply rather than this statement.

19.2 Confidentiality

All information provided by the Sponsor and all data and information generated by the clinical facility as part of the study will be kept confidential by the PI and other site staff. The PI or other site personnel will not use this information and data for any purpose other than conducting the study. These restrictions do not apply to:

1. Information which becomes publicly available through no fault of the PI or site staff.
2. Information which it is necessary to disclose in confidence to an EC solely for the evaluation of the study.
3. Information which it is necessary to disclose in order to provide appropriate medical care to a study participant, or
4. Study results which may be published as described in the Publication Policy (Section 19.3).

If a written contract for the conduct of the study, which includes confidentiality provisions inconsistent with this statement, is executed, that contract's confidentiality provisions shall apply rather than this statement.

19.3 Data Protection

All personal data received for any reason in relation to the study will be treated in accordance with the objectives and provisions of all applicable laws and regulations relating to data protection and privacy. The Sponsor and PI will process personal data only to the extent, in the manner, and while necessary to provide services for the study, and take reasonable steps to protect the personal data it holds from misuse, interference, and loss, and from unauthorised access, modification, or disclosure.

19.4 Publication Policy

The Sponsor may publish the results of this study at an appropriate time. No publication of the results shall take place without the express consent of the global Sponsor. Publication of the trial results includes but is not limited to conference presentations, scientific conference abstracts or posters, scientific manuscripts, instructional materials or any such public disclosures of the study results generated by the clinical site.

Participant confidentiality shall be maintained and must not be disclosed in any proposed publication materials.

20 REFERENCES

Australian Technical Advisory Group on Immunisation (ATAGI). Australian Immunisation Handbook, Australian Government Department of Health, Canberra, 2018, immunisationhandbook.health.gov.au

Collins PL, Melero JA. Progress in understanding and controlling respiratory syncytial virus: still crazy after all these years. Virus Res. 2011 Dec;162(1-2):80-99.

Groothuis JR, Nishida H. Prevention of respiratory syncytial virus infections in high-risk infants by monoclonal antibody (palivizumab). Pediatr Int. 2002 Jun;44(3):235-41.

Piedimonte G, Perez MK. Respiratory syncytial virus infection and bronchiolitis. Pediatr Rev. 2014 Dec;35(12):519-30. Erratum in: Pediatr Rev. 2015 Feb;36(2):85.

Robbie GJ, Zhao L, Mondick J, Losonsky G, Roskos LK. Population pharmacokinetics of palivizumab, a humanized anti-respiratory syncytial virus monoclonal antibody, in adults and children. Antimicrob Agents Chemother. 2012 Sep;56(9):4927-36. Erratum in: Antimicrob Agents Chemother. 2012 Oct;56(10):5431.

Soliman E, Ranjan S, Xu T, Gee C, Harker A, Barrera A, Geddes J. A narrative review of the success of intramuscular gluteal injections and its impact in psychiatry. Biodes Manuf. 2018;1(3):161-170.

21 APPENDICES

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21.1 APPENDIX 1. Overall Schedule of Assessments

Please note. The schedule of assessments appears over 2 pages.

STUDY TIME SCHEDULE▼																				
STUDY PERIOD►	Screen	Confinement					Follow-up													EOS/ETV
STUDY DAY►	-28 to -2	-1	1			2	3	4	5	6	8	15	22	29	36	43	57	71	85	99
			Pre-dose	Dose	Post-dose															
VISIT WINDOW (± DAYS)												1	1	1	1	1	3	3	3	3
VISIT & FOLLOW-UP SCHEDULE▼																				
CLINIC CONFINEMENT►		X																		
OUTPATIENT CLINIC VISIT►	X						X	X	X	X	X	X	X	X	X	X	X	X	X	X
SCHEDULE OF ASSESSMENTS▼																				
Background Screening Assessments																				
Informed Consent	X																			
Eligibility Criteria	X	X [1]																		
Demographics	X																			
Medical History	X	X [1]																		
Height	X																			
Body Weight[2]	X	X																		X
Calculation of BMI [3]	X	X																		
Concomitant Medication Assessment [4]	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy Test (Serum) [5]	X																			X
Pregnancy Test (Urine) [6]		X																		
Follicle-Stimulating Hormone [7]	X																			
Alcohol Breath or Urine Test [24]	X	X																		
Urine Drug Screen	X	X																		
Serology Screen [8]	X																			
COVID-19 Screening [9]	X																			
Safety and Tolerability Assessments																				
Adverse Events [10]	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical Examination (Full) [11]	X																			X

STUDY TIME SCHEDULE▼																				
STUDY PERIOD►	Screen	Confinement					Follow-up													EOS/ETV
STUDY DAY►	-28 to -2	-1	1			2	3	4	5	6	8	15	22	29	36	43	57	71	85	99
			Pre-dose	Dose	Post-dose															
VISIT WINDOW (± DAYS)												1	1	1	1	1	3	3	3	3
VISIT & FOLLOW-UP SCHEDULE▼																				
CLINIC CONFINEMENT►		X																		
OUTPATIENT CLINIC VISIT►	X						X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical Examination (Symptom-directed) [12]		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Vital Signs (BP, PR, RR, Temp) [13]	X	X	X		..X..	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
12-Lead ECG [14]	X	X	X		X															X
Clinical Laboratory Safety Tests (Blood) (Coagulation, Serum Chemistry, Haematology) [15]	X	X				X		X			X	X		X			X		X	X
Safety Laboratory Tests (Urinalysis) [16]	X	X				X		X			X	X								X
Injection Site Reaction Assessment [17]			X		..X..	X	X	X	X	X										X [23]
Pharmacokinetic, Pharmacodynamic and Immunogenicity Assessments																				
Blood sampling (PK) [18]			X		..X..	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Blood sampling (ADA/nAb)) [19]			X									X		X			X			X
Other																				
Dose Administration [20]				X																
Randomisation [21]		X																		
Check-in		X																		
Check-out [22]						X														

Notes: ..X.. indicates multiple assessments are to be performed on this day.
Abbreviations (includes footnotes): ADA = anti-drug antibody; BMI = body mass index; BP = blood pressure; COVID-19 = coronavirus disease 2019; ECG = electrocardiogram; EOS = end of study; ETV = early termination visit; HBcAb = hepatitis B core antibody; HBsAg = hepatitis B surface antigen; HCV = hepatitis C virus; HIV = human immunodeficiency virus; nAb = neutralising antibody; PCR = polymerase chain reaction; PK = pharmacokinetics; PR = pulse rate; RR = respiratory rate; Temp = temperature.

Notes: Overall Schedule of Assessments

1	Medical history to be reviewed and eligibility to be confirmed prior to dose administration on Day 1.
2	Weight to be measured in light clothing, without shoes.
3	BMI to be calculated using the height value recorded at screening.
4	Concomitant medication usage to be reviewed by study staff at each scheduled visit.
5	Women of childbearing potential only.
6	Women of childbearing potential only. If the urine test is positive, pregnancy will be confirmed by a serum pregnancy test.
7	For women identifying as postmenopausal at screening only.
8	HIV 1/2, HbsAg, HBcAb and HCV testing. Participants to be counselled if tests return positive result.
9	A COVID-19 PCR or antigen test must be performed (and a negative result obtained) within 72 hours of dose administration. A COVID-19 PCR or antigen test may also be performed at any stage during the study (including at screening) if clinically indicated, and/or as required by local and/or site regulations. Participants with a positive result will not be allowed to continue in the study until evidence of a subsequent negative test result is obtained.
10	Assessment to be performed throughout study conduct.
11	Full physical examination to include, at a minimum, assessment of the following: general appearance; head; ears; eyes; nose and throat; neck (including thyroid and lymph nodes); respiratory system; cardiovascular system; gastrointestinal system; renal system (percussion); neurological condition; musculoskeletal system, skin and any other focused assessments suggested by the presence of specific symptoms.
12	Symptom-directed physical examination only. On Day 1, symptom-directed physical examination to be performed pre-dose (any time prior to dose administration on the day) and at 8 hours (± 2 hours) post-dose.
13	Participants should be resting in a supine position for at least 5 minutes prior to and during vital signs measurements. Abnormal vital signs assessments that are not clinically significant will be repeated at the Investigator's discretion. Abnormal vital signs assessments that are clinically significant will be repeated. All clinically significant findings will be recorded as AEs. On Day 1, vital sign assessments are to be performed prior to dosing (within 1 hour prior to injection), and 30 mins (± 10 min), 1 hour (±10 min), 4 hours (± 30 min), 8 hours (± 30 min) and 12 hours (±30 min) post-dose. On Days 2 and 3, vital sign assessments are to be performed at 24 hours (± 1 hour) and 48 hours (± 5 hours) post-start of injection, respectively. All other vital signs assessments may be taken at any time during the scheduled visit.
14	Screening and Day -1 ECGs will be performed in triplicate (each reading separated by at least 1 minute and completed within 5 minutes). The average value for the triplicate will be utilised for confirmation of eligibility. All other readings will be single measurements. Each ECG will be conducted in a supine position after the participant has been resting for at least 5

	minutes in a quiet setting without distractions (e.g., television, cell phones). In case of evident bad quality (e.g., muscle tremor) of the tracing, the ECG will be repeated. On Day 1, the ECG is to be performed prior to dosing (within 1 hour prior to injection) and 4 hours (±30 minutes) post-dose. After dosing, additional ECGs may be performed for participant safety at the discretion of the PI (or delegate), especially if a participant meets QTcF repeat criteria or if QTcF has not returned to baseline.
15	Participants are required to fast for a minimum of 8 hours prior to each safety laboratory blood sample collection timepoint (water is permitted), except in the instance of an ETV. Blood samples collected on Day 2 are to be collected at 24 hours (± 1 hour) post-Day 1 injection. Safety laboratory blood samples scheduled for all other visits may be taken at any time during the scheduled visit.
16	The urine sample scheduled for Day 2 is to be collected at 24 hours (± 2 hours) post-Day 1 injection. Urinalysis samples scheduled for all other visits may be taken at any time during the scheduled visit.
17	Prior to injection on Day 1, the region that is to be injected will be marked and examined, and findings from this examination will be documented. On Day 1, the Investigator or trained and delegated site staff will review the participant at 30- and 60-minutes post-dosing (both ± 10 min) and inspect injection site for evidence of local reactions, defined as an area of pain, tenderness, erythema/redness, swelling/induration, or other e.g. haemorrhage, haematoma and pruritus. Injection site reaction assessments on all other days may be performed at any time on the day of the scheduled visit. All injection site reactions will be reported as adverse events.
18	Approximately 10 mL per sample of whole blood will be collected for pharmacokinetic analysis. Blood samples are to be collected at the timepoints and windows indicated in APPENDIX 2.
19	Approximately 10 mL per sample of whole blood will be collected for immunogenicity (ADA, nAb) analysis. Blood samples are to be collected at the timepoints and windows indicated in APPENDIX 2.
20	A single IM injection of MB05, EU-Synagis® or US-Synagis® to be administered on Day 1, into the ventrogluteal muscle of the hip (preferred site) or vastus lateralis of the thigh (secondary site). The dose will be administered by an appropriately trained member of staff, per protocol. Subjects are required to refrain from strenuous exercise for at least 72 hours post-dose.
21	Randomisation to be performed prior to injection, after confirmation of eligibility on Day 1.
22	Participants will be discharged following completion of scheduled assessments on Day 2. If participants experience any clinically significant AEs during the confinement period, they may remain in the clinical facility for further observation at the discretion of the PI (or delegate).
23	To be assessed in the instance of an early termination visit only (and only if early termination occurs prior to Day 6).
24	Sites may choose whether to perform an alcohol breath or urine test, in line with site requirements (e.g. a breath test may not be considered appropriate at some sites due to the current COVID-19 pandemic). Where possible, sites should use the same technique (i.e. alcohol breath test or urine alcohol test) throughout the duration of the study.

21.2 APPENDIX 2: Pharmacokinetic and Immunogenicity Blood Sampling Timepoints and Windows

Visit (Day)	Visit window	Timepoint	Timepoint window	PK	ADA/nAb
Day 1		pre-dose	*Within 60 minutes prior to dosing*	✓	✓
		4 hr post-dose	±15 min	✓	
		12 hr post-dose	±15 min	✓	
Day 2		24 hr post-dose	± 1 hour	✓	
Day 3		48 hr post-dose	± 5 hours	✓	
Day 4		72 hr post-dose	± 5 hours	✓	
Day 5		96 hr post-dose	± 5 hours	✓	
Day 6		120 hr post-dose	± 5 hours	✓	
Day 8		168 hr post-dose	± 5 hours	✓	
Day 15	± 1 day			✓	✓
Day 22	± 1 day			✓	
Day 29	± 1 day			✓	✓
Day 36	± 1 day			✓	
Day 43	± 1 day			✓	
Day 57	± 3 days			✓	✓
Day 71	± 3 days			✓	
Day 85	± 3 days			✓	
Day 99 EOS/ETV	± 3 days			✓	✓
Total number of samples:				**18**	**5**

Abbreviations: EOS = end of study; ETV = early termination visit; PK = pharmacokinetics; ADA = anti-drug antibody; nAb = neutralising antibody; hr = hour; min = minute.

21.3 APPENDIX 3: Clinical Laboratory Safety and Screening Assessments

Haematology	**Serum Chemistry, Including Liver Function**	**Coagulation**	**Urinalysis [1]**
Haemoglobin Haematocrit Thrombocyte count (platelets) Reticulocyte count White blood cell (WBC) count with differential: Neutrophil count Eosinophil count Basophil count Lymphocyte count Monocyte count	Sodium Potassium Chloride Bicarbonate Phosphate Calcium Glucose Amylase Lipase Uric acid Albumin Protein LDH Creatine kinase Creatinine or creatinine clearance (Cockroft/Gault) Urea ALP ALT AST GGT Total bilirubin (total and direct) Total cholesterol, HDL LDL Triglycerides. Magnesium	PT INR aPTT TT/TCT	pH Specific gravity Glucose Protein Ketones Bilirubin Blood Nitrites Urobilinogen, Leukocyte esterase *[1] Urine sediment microscopy will be conducted in the instance of abnormal urinalysis findings for blood and leukocyte esterase.*
Serology	**Urine Drug Screen**	**Pregnancy Test**	**Follicle-Stimulating Hormone**
HIV HBsAg HBcAb HCV COVID-19 (PCR or antigen test)	Methamphetamines Opiates Cocaine THC Phencyclidine Benzodiazepines Barbiturates Methadone Amphetamines	Urine hCG Serum hCG [2] *[2] If the urine hCG is positive, pregnancy will be confirmed by a serum hCG test*	Serum FSH

Abbreviations: ALP = alkaline phosphatase; ALT = alanine aminotransferase; aPTT = activated partial prothrombin time; AST = aspartate aminotransferase; FSH= follicle stimulating hormone; GGT = gamma-glutamyl transferase; HBcAb = Hepatitis B core antibody; HBsAg = Hepatitis B surface antigen; hCG = human chorionic gonadotropin; HCV = hepatitis C virus; HCV = hepatitis C virus; HDL = high-density lipoprotein; HIV = Human Immunodeficiency Virus; INR = international normalised ratio; LDH = lactate dehydrogenase; LDL = low-density lipoprotein; PCR = polymerase chain reaction; PT = prothrombin time; RBC = red blood cell; THC = tetrahydrocannabinol; TCT = thrombin clotting time; TT = thrombin time; WBC = white blood cell.

21.4 APPENDIX 4: Highly Effective Methods of Birth Control

Highly effective forms of birth control are those with a failure rate less than 1% per year when used consistently and correctly, and include:

For female participants or female partners of male participants:

- Established use of oral, injected or implanted hormonal methods of contraception
- Placement of an intrauterine device (IUD) or intrauterine system (IUS)
- Sterilised male partner (with appropriate post-vasectomy documentation of the absence of sperm in the ejaculate)
- True abstinence: When this is in line with their preferred and usual lifestyle.
- Surgical sterilization.

Examples of non-acceptable methods of contraception include:

- Condoms alone or double barrier
- Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation)
- Withdrawal
- Spermicide (as it is not approved as a method of contraception in Australia).

21.5 APPENDIX 5. Clinical Conduct Schedule and Guidelines

The following describes the assessments to be performed at each scheduled clinic visit. This section should be read in conjunction with the overall schedule of assessments. Where timepoints are given, please refer to the schedule of assessments footnotes for allowable windows.

21.5.1 Screening, Selection and Consent

Healthy subjects will be screened between Day -28 and -2.

Informed consent will be obtained following provision of the Informed Consent Form at screening and prior to any study procedures being performed. Subjects will have to meet all eligibility criteria before being enrolled in the study.

The following assessments/procedures will be performed at the screening visit:

- Provision of signed informed consent by the study subject
- Subject evaluation against study eligibility criteria
- Collection of demographics
- Collection of medical history information
- Measurement of height and body weight (determination of body mass index [BMI])
- Review of prior medication(s)
- Pregnancy test (serum; female subjects of childbearing potential only)
- Follicle-stimulating hormone blood test (for women identifying as post-menopausal only, to confirm postmenopausal status)
- Alcohol breath or urine test
- Urine drug screen
- Viral serology tests
- COVID-19 PCR or antigen test (to be performed within 72 hours prior to dose administration on Day 1)
- Full physical examination
- Measurement of vital signs
- Acquisition of 12-lead electrocardiogram (ECG) measurements (triplicate)
- Clinical laboratory tests (haematology, serum chemistry coagulation and urinalysis)
- Record adverse events (AEs) (only after signing informed consent)

21.5.2 Day -1 (Check-in)

Eligible participants will present at the clinical facility on Day -1 (the day before dosing) and will be confined until Day 2. On arrival at the clinical facility on Day -1, the PI, or delegate, will meet with participants to explain all study procedures and encourage participants to ask any questions. All participants shall undergo a check-in procedure during which questions will be asked regarding protocol compliance and safety monitoring.

A review of medical history and documentation of the study eligibility criteria, for all participants considered for the study and subsequently included or excluded, is to be completed by the PI, or medically qualified delegate. Documentation of screening failure details may be recorded using eligibility screening forms or a participant screen failure log.

The following assessments will also be performed:

- Body weight (calculation of BMI using the height recorded at screening)
- Record prior and concomitant medications
- Urine pregnancy test (for females of childbearing potential only)
- Alcohol breath or urine test
- Urine drug screen
- Record any AEs
- Physical examination (if required)
- Vital signs
- 12-lead ECG (triplicate)
- Clinical laboratory tests (haematology, serum chemistry, coagulation and urinalysis) (do not need to be repeated if screening clinical laboratory tests were collected within 7 days of check-in)
- COVID-19 PCR or antigen test (if not performed earlier).
- Randomisation (can be performed anytime following confirmation of eligibility criteria, prior to dose administration on Day 1)

21.5.3 Days 1

The following assessments will be performed on Day 1 **prior to dose administration**:

- Final confirmation of eligibility (if required)
- Review of medical history (if required)
- Record concomitant medications
- Record pre-dose AEs
- Physical examination (if required)
- Vital signs
- 12-lead ECG (single)
- Mark injection site, document examination findings
- Blood sample for PK
- Blood sample for ADA/nAb

The following assessments will occur **after dose administration** on Day 1:

- Record concomitant medications
- Record AEs
- Physical examination if required)
- Vital signs: 30 min plus 1, 4, 8 and 12 hours post-dose
- 12-lead ECG (single): 4 hours post-dose
- Injection site reaction assessment: 30 min and 1 hour post-dose
- Blood sample for PK: 4 and 12 hours post-dose

21.5.4 Day 2

The following assessments will be performed on Day 2:

- Record concomitant medications
- Record AEs

- Physical examination (if required)
- Vital signs: 24 hours post-dose
- 12-lead ECG: 24 hours post-dose
- Injection site reaction assessment
- Blood sample for PK: 24 hours post-dose
- Clinical laboratory tests (haematology, serum chemistry, coagulation and urinalysis)

Participants will be discharged from the clinic after completion of the above assessments.

21.5.5 Days 3, 4, 5, 6, 8, 15 (±1 day), 22 (±1 day), 29 (±1 day), 36 (±1 day), 43 (±1 day), 57 (±3 days), 71 (±3 days) and 85 (±3 days)

Participants will be required to attend the clinic for outpatient visits on each day. The following assessments will be performed at **each visit**:

- Record concomitant medications
- Record AEs
- Physical examination (if required)
- Vital signs
- Clinical laboratory tests (haematology, coagulation and serum chemistry) on:
  - Days 4, 8, 15, 29, 57 and 85 only
- Clinical laboratory tests (urinalysis) on:
  - Days 4, 8, and 15 only
- Injection site reaction assessment (Days 3, 4, 5 and 6 only)
- Blood sample for PK on:
  - Day 3: 48 hours post-dose
  - Days 4 (72 hours post-dose), 5 (96 hours post-dose), 6 (120 hours post-dose), 8 (168 hours post-dose), 15, 22, 29, 36, 43, 57, 71 and 85 (any time during the visit)
- Blood sample for ADA/nAb on:
  - Days 15, 29 and 57

21.5.6 End of Study (Day 99 ± 3 days)

The following assessments will be performed at the end of study visit:

- Body weight
- Record concomitant medications
- Serum pregnancy test (for females of childbearing potential only)
- Record AEs
- Full physical examination
- Vital signs
- 12-lead ECG (single)
- Clinical laboratory tests (haematology, serum chemistry, coagulation and urinalysis)
- Blood sample for PK
- Blood sample for ADA/nAb

21.5.7 Early Termination Visit

The following procedures will be performed if a participant terminates from the study prior to the end of study visit:

- Body weight
- Record concomitant medications
- Serum pregnancy test (for females of childbearing potential only)
- Record AEs
- Full physical examination
- Vital signs
- 12-lead ECG (single)
- Clinical laboratory tests (haematology, serum chemistry, coagulation and urinalysis)
- Injection site reaction assessment (if participant withdraws/is withdrawn prior to Day 6 only)
- Blood sample for PK
- Blood sample for ADA/nAb