Clinical Study Protocol

Protocol Title:	**Placebo-Controlled Proof of Concept Study to Investigate ANB020 Activity in Adult Patients with Peanut Allergy**
Protocol Number:	**ANB020-003**
Version:	**Amendment 5**
Date of Protocol:	**01 DEC 2017**
Product:	**ANB020**
IND No.:	**126765**
Study Phase	**II**
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Signatures

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[redacted] Signature 4th December 2017 Date

AnaptysBio Inc.

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Stanford University Medical Center

Sean N Parker Center for Allergy Research at Stanford University

SYNOPSIS

Name of Sponsor/Company:	AnaptysBio Inc.
Name of Finished Product:	Humanized immunoglobulin subtype G1/kappa (IgG1/kappa) monoclonal antibody
Name of Active Ingredient:	ANB020
Title of Study:	Placebo-Controlled Proof of Concept Study to Investigate ANB020 Activity in Adult Patients with Peanut Allergy
Protocol No:	ANB020-003
Study center:	Up to 3 centers in the US

Study duration: The expected duration of the study is approximately 66 days (Screening period of 21 days, Treatment period of 15 days, and Follow-up period of 30 days).	**Phase:** II

Objectives:

Primary:

- To assess the safety and tolerability of single dose administration of ANB020 in adult patients with peanut allergy.
- To measure the response of adult patients with peanut allergy on Day 14 following an oral blind placebo-controlled food challenge (BPCFC) threshold and cumulative peanut dose tolerated after administration of ANB020 or placebo compared to cumulative baseline peanut BPCFC.

Secondary:

- To compare the symptoms to peanut antigen challenge on Day 14 using the Oral Food Challenge (OFC) Symptoms Scoring Assessment Tool after administration of ANB020 or placebo compared to baseline peanut BPCFC symptoms.
- To describe the limited pharmacokinetics (PK) of ANB020 following a single, intravenous (IV) dose.

Exploratory:

- To assess the effect of ANB020 on circulating serum cytokines.
- To assess the effect of ANB020 on leukocytes within whole blood.
- To compare the immune response of ANB020 to placebo dosed patients in the ex vivo peanut antigen challenge. Stanford University Only
- To measure the response of adult patients with peanut allergy on Day 45 following an oral BPCFC threshold and cumulative peanut dose tolerated after administration of ANB020 or placebo compared to cumulative baseline peanut BPCFC.
- To compare the symptoms to peanut antigen challenge on Day 45 using the OFC Symptoms Scoring Assessment Tool after administration of ANB020 or placebo compared to baseline peanut BPCFC symptoms.

Methodology:

This will be a proof of concept study aiming to assess the safety and tolerability of ANB020 in adult patients with peanut allergy. This study will also investigate the effects of ANB020 or placebo in adult patients with peanut allergy following an oral BPCFC at 2 and 6 weeks post ANB020 or placebo administration. The effects of ANB020 on the immune response to peanut upon ex vivo peanut antigen challenge will be evaluated in Stanford University patients

Informed consent must be obtained prior to participation in the study. At the screening visit (7-21 days before Day 1), inclusion/exclusion criteria is assessed, each eligible patient will be administered a graded peanut and placebo oral food challenge (BPCFC) according to the PRACTALL consensus report. Vital signs, physical examination findings, and subjective symptoms during the BPCFC will be monitored per

PRACTALL guidelines using the OFC Symptom Scoring Assessment Tool. The oral challenge should be stopped when the patient develops clinically significant symptoms indicative of an allergic reaction as per the Investigator's assessment. The total cumulative dose of blinded peanut/placebo tolerated and dosing step/threshold reached prior to the reaction will be recorded. Patients will be observed in the study center until the Investigator determines that the patient is clinically stable and can be discharged. The oral food challenge (BPCFC) can be completed in 2 days if the Investigator feels that it is the best for patient's safety and convenience. Otherwise all patients will undergo the peanut challenge and placebo challenge on the same day. Blood samples collected from Stanford University patients for pharmacodynamic (PD) assessments (ex vivo whole blood peanut antigen challenge) will be collected to determine the intensity of response and establish a baseline value of peanut antigen induced immune activation. Medical history and various other safety assessments including laboratory and biomarker analysis (cytokines) will be performed.

On Day 1, the patients will return to the study center and the inclusion and exclusion criteria will be reviewed. Eligible patients will be randomized to receive one intravenous dose of either ANB020 (300 mg/100 mL) or placebo (0.9% sodium chloride [100 mL]) in a 3:1 ratio. Specific laboratory and safety assessments will be performed, and serial samples for PK analysis will be collected. Patients with any ongoing adverse events (AEs) or serious adverse events (SAEs) at the time of scheduled discharge from the study center should remain at the study center until the Investigator has determined that these events have been resolved or deemed as not clinically significant by the Investigator.

On Day 2 and Day 5, the patients will return to the study center and the samples for PK, biomarker analysis (cytokines), and whole blood for leukocytes will be collected and other safety assessments will be performed. In addition, whole blood samples from Stanford University patients for ex vivo peanut antigen challenge assay will be obtained to determine the peanut antigen induced activation.

On Day 14, the patients will return to the study center and the peanut and placebo oral food challenge (BPCFC) will be performed according to the PRACTALL guidelines. Symptoms will be monitored using the OFC Symptom Scoring Assessment Tool and other safety assessments will be performed. The oral challenge should be stopped when the patient develops clinically significant symptoms indicative of an allergic reaction as per the Investigator's assessment. The total cumulative dose of blinded peanut/placebo tolerated and dosing step/threshold reached prior to reaction will be recorded. Patients will be observed until the Investigator determines that the patient is clinically stable and can be discharged. The oral BPCFC (peanut challenge and placebo challenge) can be completed in 2 days (one challenge on Day 14 and the second challenge on Day 15) if the Investigator feels that it is the best for patient's safety and convenience. Otherwise all patients will undergo the challenges (peanut challenge and placebo challenge) on Day 14 itself.

On Day 15, patients will return to the study center and the laboratory and safety assessments will be performed. The oral food challenge will be continued on Day 15 if the patient has received only the placebo challenge on Day 14 and the blood samples scheduled on Day 15 will be collected on Day 16 (only applicable if the Investigator decides to complete the challenge in 2 days). After completing the oral food challenge (BPCFC), all patients will be in the follow-up period for 30 days. During the 30 days follow-up period, the patients will be contacted weekly via telephone by study staff to assess the patient's well-being.

On Day 45, the patients will return to the study center for the End of Study (EOS) visit. If any objective reaction occurred at Day 14/15 the BPCFC (peanut and placebo oral food challenge) will not be required but may be performed at the discretion of the PI. If the Investigator decides to perform the challenge, the procedures will be the same as the Day 14/15 visit. The BPCFC will be performed according to the PRACTALL guidelines. Symptoms will be monitored using the OFC Symptom Scoring Assessment Tool and other safety assessments will be performed. The oral challenge should be stopped when the patient develops clinically significant symptoms indicative of an allergic reaction as per the Investigator's assessment. The total cumulative dose of blinded peanut/placebo tolerated and dosing step/threshold reached prior to reaction will be recorded. Patients will be observed until the Investigator determines that the patient is clinically stable and can be discharged. The oral BPCFC (peanut challenge and placebo challenge) can be completed in 2 days (one challenge on Day 45 and the second challenge on Day 46) if the Investigator feels that it is the best for patient's safety and convenience. Otherwise all patients will undergo the challenges (peanut challenge and placebo challenge) on Day 45/EOS visit itself. Other procedures scheduled for the EOS visit will also be performed on Day 45.

Planned number of patients:	20
Diagnosis and main criteria for inclusion:	Male or female patients (women of childbearing potential must be taking adequate contraceptive measures) aged >18 years with a confirmed clinical diagnosis of peanut allergy
Test product, dose and mode of administration:	ANB020 is a humanized immunoglobulin subtype G1/kappa (IgG1/kappa) monoclonal antibody that specifically neutralizes the biological effects of human interleukin-33 (hIL-33). A single dose of 300 mg ANB020 will be administered by IV infusion in polyvinyl chloride or polyolefin bags following dilution to a total volume of 100 mL with 0.9% sodium chloride.
Placebo, dose, and mode of administration:	A total dose of 100 mL of placebo (0.9% sodium chloride) will be administered IV on Day 1.

Criteria for evaluation:

Primary Safety and Tolerability Endpoints:

- Assessment of AEs/SAEs (potentially significant and clinically important AEs, SAEs, and AEs leading to withdrawal).
- Physical examinations.
- Vital signs.
- Clinical safety laboratory tests (hematology, biochemistry, and urinalysis).
- Electrocardiogram (ECG).

Primary Efficacy Endpoint:

- Difference in total cumulative tolerated peanut dose during BPCFC between baseline and post-treatment with ANB020 or placebo on Day 14.

Secondary Endpoints:

The following efficacy and PK parameters will be assessed under secondary endpoints.

Secondary Efficacy Endpoint

- Clinical scores of OFC Symptom Scoring Assessment Tool on Day 14.

Pharmacokinetic Endpoints:

A limited sampling strategy to collect samples of whole blood will be implemented for the determination of ANB020 in human serum for PK assessment. Where possible, the following PK parameters will be determined for ANB020 after a single IV infusion:

- Maximum observed concentration (C_{max}).
- Time to maximum observed concentration (t_{max}).

Exploratory Pharmacodynamic Endpoints:

- Serum cytokines will be evaluated including, but not be limited to, IL-4, IL-5, IL-9, IL-13, IL-33 and sST2.
- Differential white blood cell counts (WBC) in the whole blood will be measured to monitor circulating leukocyte populations.
- For the ex vivo peanut antigen challenge, the whole blood peanut response assay will measure the cytokine levels released from pathogenic T cells. (Stanford University Only)

Exploratory Efficacy Endpoints:

- Difference in total cumulative tolerated peanut dose during BPCFC between baseline and post-treatment with ANB020 or placebo on Day 45.
- Clinical scores of OFC Symptom Scoring Assessment Tool on Day 45.

Statistical methods:

A total of approximately 20 patients will be randomized in a 3:1 ratio to receive ANB020 or placebo.

For primary safety and tolerability, AEs, SAEs, vital signs, physical examinations, ECGs, and clinical laboratory assessments at specific time points will be evaluated. All safety data will be summarized descriptively. Number and percentage of AEs will be presented for each treatment by preferred term and system organ class of the current Medical Dictionary for Regulatory Authorities (MedDRA) dictionary. Individual listings of all SAEs and AEs leading to discontinuation from the investigational product (IP) will be summarized using the current MedDRA dictionary. Similar analyses will be performed for potentially significant and clinically important AEs.

For primary efficacy endpoint, total cumulative tolerated peanut dose on Day 14, and for secondary efficacy and exploratory endpoints, the OFC symptom scores (Day 14 and 45) and total cumulative tolerated peanut dose on Day 45 will be summarized using descriptive statistics.

Change from baseline on Day 14 for tolerated dose and OFC scores will be compared between ANB020 and placebo using analysis of covariance (ANCOVA) with treatment as fixed effect and baseline results as covariate. Treatment differences will be presented with corresponding p-values for the test of no difference and 95% confidence interval (CI). Mixed model for repeated measures will be used to estimate 95% CI for the difference between ANB020 and placebo on Day 45 for tolerated dose and OFC scores. This model will include treatment, visit, and treatment by visit interaction as fixed effect and baseline results as covariate. The data collected at baseline, Day 14, and Day 45 will be used in the model.

For exploratory endpoints, change from baseline will be evaluated where possible. Actual and change in data from baseline will be summarized descriptively for each treatment. Comparison between ANB020 and placebo will be performed using a mixed model for repeated measures with treatment, time point of measurement, and treatment by time point interaction as fixed effects, and baseline results as a covariate. Appropriate correlation matrix will be used. All tests of treatment effects will be conducted at a 2-sided alpha level of 0.05 or with 2-sided 95% CIs.

Summaries and listings of vital signs, hematology, clinical chemistry, urinalysis, and ECGs will be presented. Appropriate descriptive statistics will be summarized for the observed values at each scheduled assessment and for the corresponding change from baseline. Baseline will be the last assessment before administration of the IP.

The PK of ANB020 will be evaluated by assessment of drug concentrations in serum. ANB020 concentrations will be listed and summarized for each sampling time point using appropriate descriptive statistics. The PK parameters will be summarized using appropriate descriptive statistics.

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1.0 LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
AD	Atopic dermatitis
ADR	Adverse drug reaction
AE	Adverse event
ANCOVA	Analysis of covariance
BMI	Body mass index
BP	Blood pressure
CI	Confidence interval
C_{max}	Maximum observed concentration
CV	Coefficient of variation
BPCFC	Blind placebo-controlled food challenge
ECG	Electrocardiogram
eCRF	Electronic case report form
EDC	Electronic data capture
EpiPen	Epinephrine
EOS	End of Study
ET	Early Termination
FSH	Follicle stimulating hormone
GCP	Good Clinical Practice
gCV	Geometric coefficient of variation
GINA	Global Initiative for Asthma Assessment
Gmean	Geometric mean
GMP	Good Manufacturing Practice
hIL-33	Human interleukin-33
HR	Heart rate
ICF	Informed Consent Form
ICH	International Council for Harmonisation
ICU	Intensive care unit
IgE	Immunoglobulin E
IL	Interleukin

IP	Investigational product
IRB	Institutional Review Board
IV	Intravenous(ly)
LLOQ	Lower limit of quantification
mAb	Monoclonal antibody
MAD	Multiple ascending dose
MedDRA	Medical Dictionary for Regulatory Activities
n	Sample size or number of observations
OFC	Oral Food Challenge
PD	Pharmacodynamic
PI	Principal Investigator
PK	Pharmacokinetic
SAE	Serious adverse event
SAD	Single ascending dose
SAP	Statistical analysis plan
SAS	Statistical analysis system
SC	Subcutaneous
SD	Standard deviation
SOP	Standard operating procedure
SST	Serum separator tube
ST2	Surface receptor 2
$t_{1/2}$	Terminal half-life
TEAE	Treatment emergent adverse event
Th2	T helper-2
t_{max}	Time to maximum observed concentration
U.S.	United States
WBC	White blood cell

2.0 INTRODUCTION

ANB020 is a first-in-class, anti-interleukin-33 therapeutic antibody to treat T helper-2 (Th2) cell driven inflammatory diseases with underlying interleukin-33 (IL-33) dysregulation. ANB020 is a humanized immunoglobulin subtype G1/kappa (IgG1/kappa) monoclonal antibody (mAb) that specifically neutralizes the biological effects of human IL-33 (hIL-33). Interleukin-33, a member of the IL-1 superfamily,[1] is a multifunctional cytokine that plays an important role in Th2-mediated cellular immunity and in the pathogenesis of atopic diseases.[2,3] ANB020 binds to and inhibits the interaction of IL-33 with its specific cell-surface receptor (ST2) thereby blocking IL-33-driven downstream signalling and subsequent cellular responses. It is being developed for the treatment of atopic diseases such as asthma, food allergies, and atopic dermatitis (AD).

2.1 Background Information

Worldwide, the prevalence of peanut allergy is quite variable with the highest rates (1-2% in adults) being observed in western countries, more specifically the United States (U.S.), United Kingdom, Canada and Australia.[4] Peanut allergy was once rare, but it is now the leading cause of fatal food-allergic reactions.[5] It tends to present at a median age of 14-24 months and continues through to adulthood. [6]For many patients, reactions become more severe on subsequent exposure. Unlike allergies to cow's milk and egg and similar to allergies to fish, shell fish and tree nuts, allergy to peanuts rarely resolves spontaneously.[4] Compared to other food allergies, peanuts cause particularly severe reactions, including a high risk of anaphylactic shock which in extreme cases, can cause death of some peanut allergy patients. Moreover, in some cases only a very small dose (0.1-1 mg) is required to cause a systemic reaction.[4]

As for all atopic disorders, high levels of immunoglobulin E (IgE), and peanut protein-specific IgE, have been described in peanut allergy patients. Current therapy involves education around the avoidance of peanuts in foods, which can be problematic given the wide and frequently hidden use of peanut as a food ingredient, and prompt recognition and treatment of anaphylactic reactions as soon as they occur. The only effective treatment for anaphylaxis is intramuscular epinephrine (EpiPen) administration, whilst oxygen, nebulized albuterol, systemic corticosteroids and histamine H1 and/or H2 receptor antagonists can help alleviate secondary symptoms. Therefore, many immunotherapeutic approaches, mainly based on antigen-specific (i.e., peanut) desensitization, are being explored to find an effective treatment for this life-threatening allergy. In this context, a recent study has shown the benefit of introducing peanuts to the diet early in life which may prevent the onset of allergy,[7] however for those with an established peanut allergy, there is an urgent need for novel and effective treatments.

Interleukin-33 serum levels are significantly increased in patients pre-disposed to allergic diseases who suffer from anaphylactic reactions, suggesting that IL-33 is a contributory factor in

the induction of anaphylaxis[8 9], thus IL-33 is now considered to be a key mediator in the development of allergic disorders via the activation of not only acquired immunity, but also innate immunity.[10] As ANB020 targets IL-33, it may offer a novel and effective treatment for peanut allergy patients.

Non-clinical studies

ANB020 is being developed by AnaptysBio Inc. as a lead drug candidate and exhibits strong inhibitory activity for human as well as cynomolgus monkey IL-33. Non-clinical data obtained from studies with ANB020 in primary human and cynomolgus monkey cells and from in vivo non-human primate studies demonstrated that:

- ANB020 shows reactivity with human and cynomolgus monkey IL-33 (dissociation constant of 1 pM versus 37 pM, respectively), but not with mouse or rat IL-33.
- In primary human and cynomolgus monkey cell populations, from peripheral blood mononuclear cells and human whole blood, ANB020 inhibited IL-33-induced interferon-gamma production. In human basophils, ANB020 also inhibited IL-33-induced IL-5 production. The IC50 was approximately 1-2 nM.
- The observed serum half-life ($t_{1/2}$) of ANB020 in cynomolgus monkeys was 160 hours after a single intravenous (IV) dose administration, and 187 hours after a single subcutaneous (SC) dose administration at 10 mg/kg, consistent with the anticipated pharmacokinetic (PK) characteristics for a human IgG1 scaffold mAb in the monkey.
- A multiple-dose, Good Laboratory Practice-compliant toxicology and toxicokinetics study (4-week duration with an 8-week recovery phase) has been conducted with ANB020 administered by SC and IV injection to cynomolgus monkeys. This study produced no significant test article-related effects and established a No Observed Adverse Effect Level of 50 mg/kg.

These data, together with non-clinical safety data generated, supported a strong scientific rationale for advancing ANB020 into clinical development.

Clinical studies

A first-in-man Phase I single ascending dose (SAD) and multiple ascending dose (MAD) study (ANB020-001) in healthy subjects is being performed. The SAD part of the study has been completed. In total, 64 subjects were enrolled. Dosed cohorts included 10, 40, 100, and 300 mg SC and 40, 100, 300, and 750 mg IV (n=32 SC route, n=32 IV route). No change in vital signs (blood pressure [BP], heart rate [HR], electrocardiogram [ECG], or body temperature) was noted. Hematology parameters, such as erythrocytes, white blood cell (WBC) and platelet

counts, were all within the normal range and did not show any modification or trend related to ANB020 administration. Serum chemistry results were also all in the normal range. A total of 81% subjects in the placebo group and 79% subjects in the ANB020 group had at least one treatment-emergent adverse event (TEAE) during the study. The most commonly reported treatment emergent adverse events (TEAEs) were of mild to moderate intensity and by preferred term were upper respiratory infection (50% versus 48% in placebo and ANB020 group, respectively) and headache (32% versus 27% in placebo and ANB020 group, respectively). One serious adverse event (SAE) of decreased neutrophils was reported in the 750 mg dose group which resolved without sequelae prior to study completion. No other observations of decreased neutrophils were observed. No dose dependent AEs were reported. The PK data from the study has been utilized to determine route and dose to be used in this study. The PK data generated indicates that a linear PK profile is observed upon ANB020 administration regardless of the route. The predicted ANB020 $t_{1/2}$ is approximately 14 days. Results from emergent data will serve as the basis for the route of administration of ANB020 in future studies.

2.2 Rationale

This proof of concept study is intended to explore the activity of ANB020 in adult patients with peanut allergy.

Food allergy, especially peanut allergy, can lead to severe reactions and death in healthy individuals. The current standard of care is food allergen avoidance with availability of EpiPen for emergency treatment of anaphylaxis resulting from accidental ingestions.[11] Although patients with food allergies go to great lengths to avoid their allergens, accidental ingestions from cross-contamination, mislabelled ingredients or lapses in vigilance do occur.

There is no approved treatment for the prevention of food allergy reactions at this time. Currently various forms of food-specific immunotherapy are under investigation for the prevention of reactions to the treated food allergen. This therapy is food allergen specific and side effects to treatment are common. Many patients have limited or no response to therapy.[12]

Monoclonal antibodies interfering with the atopic pathways involved in food allergy reactions have the potential to be non-food specific with fewer side effects. Clinical trials with anti-IgE mAbs have demonstrated some benefit for the prevention of food allergy reactions; however, not all patients respond to treatment and most responses are partial. There has been interest in moving ‘higher’ in the atopic cytokine cascade to improve the response by inhibition of an increased number of downstream mediators. Interleukin-33 has been implicated in atopic pathways involved in food allergy. Research suggests that IL-33 is one of the initial mediators triggering atopic cytokine cascades. Interleukin-33 has also been involved in the magnification of the intensity of anaphylactic response. Furthermore IL-33 is considered to be the key cytokine setting and sustaining pathogenic (peanut specific) T cells. Therefore, IL-33 inhibition might

provide a novel and wide spectrum strategy to benefit patients with peanut, and possibly other food allergy. Data on the effect of an anti-IL33 mAb on the resulting atopic immune response in food allergy may provide important clues for potential treatment or preventative strategies.

2.3 Hypothesis

This is an exploratory study and no hypothesis testing will be examined.

2.4 Risk-Benefit Assessment

A patient with peanut allergy may or may not benefit from participating in this study. However, based upon the inhibition of IL-33 by the investigational product (IP) and pre-clinical study results, patients with peanut allergy may benefit. Participation in this study may help develop important scientific knowledge that could contribute to the development of a new medication and better comprehensive treatment of patients who suffer from AD, asthma, and food allergies.

ANB020 has been extensively tested in animals, and was found to be safe and well tolerated in a Phase I SAD study (ANB020-001) in healthy subjects. In animal studies, there were no ANB020 related adverse events (AEs) or abnormal ECG findings and the administration of ANB020 had no effect on hematology, coagulation, clinical chemistry, or urinalysis test results. In the SAD study, 64 healthy subjects were enrolled and dosed. The doses implemented in the SAD study were 10, 40, 100, and 300 mg SC and 40, 100, 300, 750 mg IV. No change in vital signs (BP, HR, ECG, or body temperature) was noted. Hematology parameters, such as erythrocytes, WBC, and platelet counts, were all within the normal range except for one subject in the 750 mg dose group. All others did not show any modification or trend related to ANB020 administration. Serum chemistry results were also all in the normal range. The most commonly reported TEAEs were upper respiratory tract infection (50% versus 48% in placebo and ANB020 group, respectively) and headache (32% versus 27% in placebo and ANB020 group, respectively) of mild to moderate intensity. No AEs were deemed by the Principal Investigator (PI) to be related to ANB020. Of all the AEs reported across all dose groups, 44% were reported as possibly related and 36% were reported as unrelated. One SAE of decreased neutrophils was reported in the 750 mg dose group which resolved without sequelae prior to study completion. No other observations of decreased neutrophils were observed. No dose dependent AEs were reported.

Although nothing in the testing of ANB020 to date indicates that an allergic reaction is likely; a reaction to any drug is possible. Some symptoms of allergic reactions are rash, wheezing or difficulty breathing, dizziness or fainting (also a possible outcome of a drop in BP), swelling around the mouth, throat or eyes, a fast pulse, or sweating.

As ANB020 is a mAb, based on clinical studies with other mAbs, study participants may experience symptoms of an apparent allergic reaction to the drug, also known as 'cytokine release syndrome'. The symptoms of this vary dramatically but can include:

- Mild to moderate fever, chills, headache, nausea, and vomiting.
- Moderate to severe symptoms such as edema, hypotension, and pulmonary infiltrates (e.g., blood and mucus in the lung).

3.0 STUDY OBJECTIVES

3.1 Primary Objectives

The primary objectives of the study are as follows:

- To assess the safety and tolerability of single dose administration of ANB020 in adult patients with peanut allergy.
- To measure the response of adult patients with peanut allergy on Day 14 following an oral blind placebo-controlled food challenge (BPCFC) threshold and total cumulative peanut dose tolerated after administration of ANB020 or placebo compared to cumulative baseline BPCFC.

3.2 Secondary Objectives

The secondary objectives of the study are as follows:

- To compare the symptoms to peanut antigen challenge on Day 14 using the Oral Food Challenge (OFC) Symptoms Scoring Assessment Tool after administration of ANB020 or placebo compared to baseline peanut BPCFC symptoms.
- To describe the limited PK of ANB020 following a single, IV dose.

3.3 Exploratory Objectives

- To assess the effect of ANB020 on circulating serum cytokines.
- To assess the effect of ANB020 on leukocytes within whole blood.
- To compare the immune response of ANB020 to placebo dosed patients in the ex vivo peanut antigen challenge. (Stanford University Only)
- To measure the response of adult patients with peanut allergy on Day 45 following an oral BPCFC threshold and cumulative peanut dose tolerated after administration of ANB020 or placebo compared to cumulative baseline peanut BPCFC.
- To compare the symptoms to peanut antigen challenge on Day 45 using the OFC Symptoms Scoring Assessment Tool after administration of ANB020 or placebo compared to baseline peanut BPCFC symptoms.

4.0 INVESTIGATIONAL PLAN

4.1 Summary of Study Design

This is a Phase II, double-blind, placebo-controlled, proof of concept study to assess the safety and tolerability of ANB020 in adult patients with peanut allergy. This study will also investigate the effects of ANB020 or placebo in adult peanut allergic patients following an oral BPCFC at 2 and 6 weeks post ANB020 or placebo administration. The effects of ANB020 on the immune response to peanut upon ex vivo peanut antigen challenge will be evaluated in Stanford University patients only.

Informed consent must be obtained prior to participation in the study. At the screening visit (7-21 days before Day 1), inclusion/exclusion criteria is assessed, each eligible patient will be administered a graded peanut and placebo oral food challenge (BPCFC) according to the PRACTALL consensus report (See Section 6.1.1). Vital signs, physical examination findings, and subjective symptoms during the BPCFC will be monitored per PRACTALL guidelines using the OFC Symptom Scoring Assessment Tool (See Section 6.1.2). The oral challenge should be stopped when the patient develops clinically significant symptoms indicative of an allergic reaction as per the Investigator's assessment. The total cumulative dose of blinded peanut/placebo tolerated during the dosing threshold challenge will be recorded. Patients will be observed until the Investigator determines that the patient is clinically stable and can be discharged. The oral food challenge can be completed in 2 days if the Investigator feels that it is the best for patient's safety and convenience. Otherwise all patients will undergo the peanut challenge and placebo challenge on the same day. If the Investigator is planning to complete the challenge (BPCFC) in 2 days, he or she needs to follow the procedures and assessments pertaining to the challenge on both the days as detailed in Section 6.1.1, 6.1.2, and 7.1.3. Blood samples collected from Stanford University patients for pharmacodynamic (PD) assessments (ex vivo whole blood peanut antigen challenge) will be collected at screening (prior to BPCFC) to determine the intensity of the response and establish a baseline value of peanut antigen induced immune activation. Medical history and various other safety assessments including laboratory and biomarker analysis (cytokines) will be performed.

On Day 1, the patients will return to the study center and the assessment for inclusion and exclusion criteria will be reviewed. Eligible patients will be randomized to receive one intravenous dose of either ANB020 (300 mg/100 mL) or placebo (0.9% sodium chloride [100 mL]) in a 3:1 ratio. Specific laboratory and safety assessments will be performed. Serial samples for PK analysis will be collected according to Section 18.0. Patients with any ongoing AEs or SAEs at the time of scheduled discharge from the study center should remain at the study center until the Investigator has determined that these events have been resolved or deemed as not clinically significant by the Investigator.

On Day 2 and Day 5, the patients will return to the study center and the samples for PK, biomarker analysis (cytokines), and whole blood for leukocytes will be collected, and other safety assessments will be performed. In addition, whole blood samples from Stanford University patients for ex vivo peanut antigen challenge assay will be obtained to determine the peanut antigen induced activation.

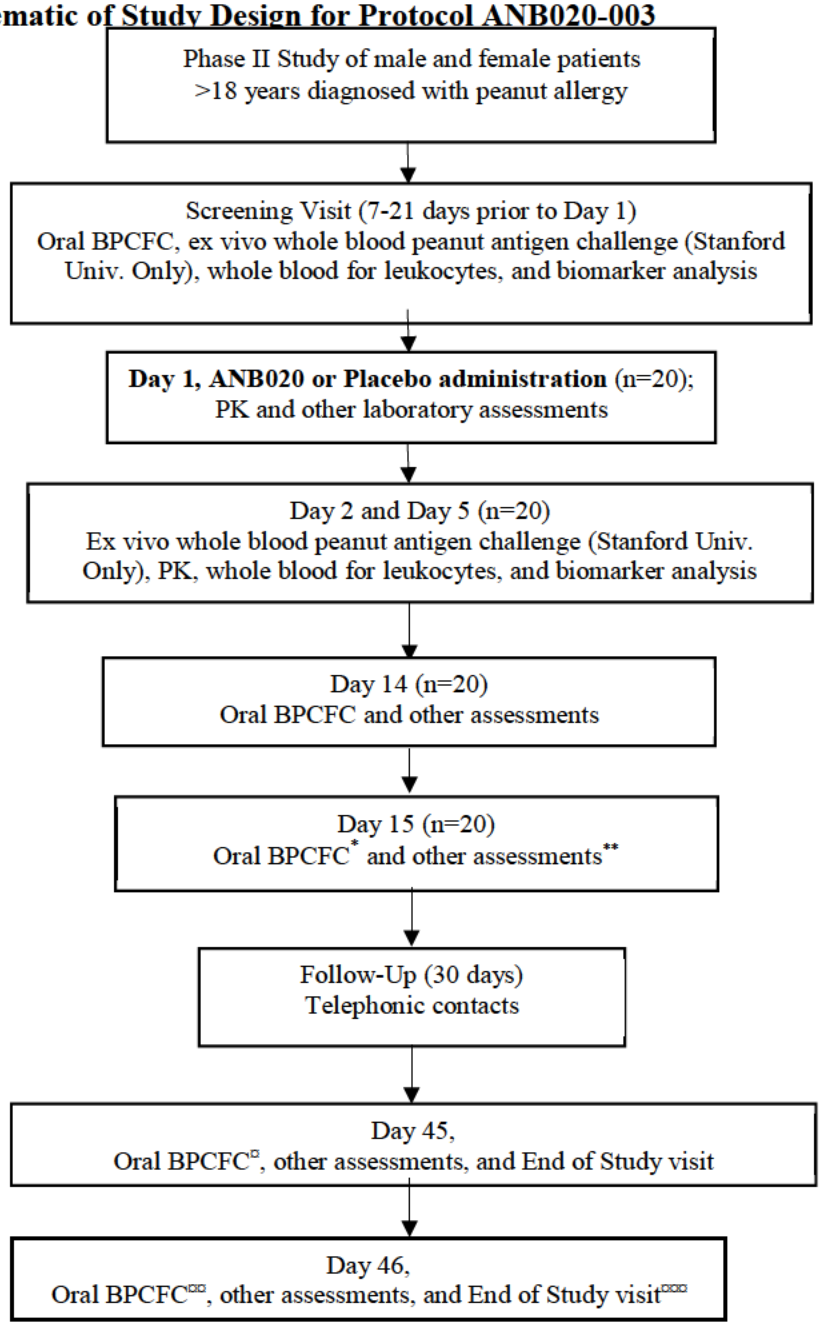
On Day 14, the patients will return to the study center and the oral BPCFC will be administered. Symptoms will be monitored using the OFC Symptom Scoring Assessment Tool and other safety assessments will be performed. The oral challenge should be stopped when the patient develops clinically significant symptoms indicative of an allergic reaction as per the Investigator's assessment. The total cumulative dose of blinded peanut/placebo tolerated and dosing step/threshold reached prior to reaction will be recorded. Patients will be observed until the Investigator determines that the patient is clinically stable and can be discharged. The oral BPCFC (peanut challenge and placebo challenge) can be completed in 2 days (one challenge on Day 14 and the second challenge on Day 15) if the Investigator feels that it is the best for patient's safety and convenience. Otherwise all patients will undergo the challenges (peanut challenge and placebo challenge) on Day 14 itself.

On Day 15, patients will visit the study center and the laboratory and safety assessments will be performed. The oral food challenge will be continued on Day 15 if the patient has received only the placebo challenge on Day 14 and the blood samples scheduled on Day 15 will be collected on Day 16 (only applicable if the Investigator decides to complete the challenge in 2 days). The Investigator must follow the procedures and assessments pertaining to the challenge on both Day 14 and Day 15 as detailed in Section 6.1.1, 6.1.2, and 7.1.3. After completing the oral food challenge, all patients will be in the follow-up period for 30 days. During the 30 days follow-up period, the patients will be contacted weekly via telephone by study staff to assess the patient's well-being.

On Day 45, the patients will return to the study center for the End of Study (EOS) visit. If any objective reaction occurred at Day 14/15, the BPCFC (peanut and placebo oral food challenge) will not be required but may be performed at the discretion of the Investigator. If the Investigator decides to perform the challenge, the procedures will be the same as the Day 14/15 visit. The BPCFC may be performed on Day 45 according to the PRACTALL guidelines. Symptoms will be monitored using the OFC Symptom Scoring Assessment Tool and other safety assessments will be performed. The oral challenge should be stopped when the patient develops clinically significant symptoms indicative of an allergic reaction as per the Investigator's assessment. The total cumulative dose of blinded peanut/placebo tolerated and dosing step/threshold reached prior to reaction will be recorded. Patients will be observed until the Investigator determines that the patient is clinically stable and can be discharged. The oral BPCFC (peanut challenge and placebo challenge) can be completed in 2 days (one challenge on

Day 45 and the second challenge on Day 46) if the Investigator feels that it is the best for patient's safety and convenience. Otherwise all patients will undergo the challenges (peanut challenge and placebo challenge) on Day 45 (EOS visit) itself. Other procedures scheduled for the EOS visit will also be performed on Day 45.The study design is presented in Figure 4.1 and the Schedule of Events is presented in Table 4.1.

Figure 4.1 Schematic of Study Design for Protocol ANB020-003



Abbreviations: BPCFC = Blind placebo-controlled food challenge; PK = pharmacokinetics; n = sample size
*Oral BPCFC will be continued on Day 15 if the patient has received only the placebo challenge on Day 14.
**If the BPCFC continued on Day 15, the blood samples scheduled on Day 15 will be collected on Day 16.
¤If objective reaction occurs on Day 14/15, the Oral BPCFC will not be required but may be performed at the discretion of the Investigator
¤¤Oral BPCFC will be continued on Day 46 if the patient has received the placebo challenge Day 45/EOS visit.
¤¤¤If the BPCFC continued on Day 46, all assessments related to the BPCFC will be performed on Day 46. Concomitant medications and adverse events will also be recorded on Day 46. All laboratory/diagnostic tests scheduled for the EOS visit will be performed on Day 45. (See Table 4.1).

Table 4.1 Schedule of Events

Assessment Days	Screening *7-21 days prior to Day1*	Day 1	Day 2	Day 5	Day 14	Day 15	Follow-Up(30 days) Weekly Telephonic Contacts	EOS Day 45	EOS Day 46 [n]	ET[f,p]
General Assessments										
Informed Consent	X[q]	X[a]								
Medical History/Demographics	X									
Inclusion/Exclusion Criteria	X	X								
Oral Peanut Food Challenge (BPCFC)	X				X	X[i,k]		X[l]	X[i,o]	
Stanford University Only: Ex vivo Peanut Challenge Assay (whole blood)[e]	X		X	X						
Skin Prick Test and ImmunoCAP Testing	X[h]									
Safety Assessments										
Physical Examination[b]	X				X	X[j]		X	X[j]	X
Safety Laboratory[c]	X	X	X		X			X		X
Vital Signs[b]	X	X	X	X	X	X		X	X[j]	X
Spirometry or Peak Flow for Patients with History of Asthma[i]	X				X	X[i,j]		X[i]	X[i,j]	
Urinalysis	X	X	X		X			X		X
Serum Pregnancy Test (WOCBP Only)	X	X			X			X		X
FSH [m]	X[l]									
12-Lead ECG	X							X		X
Concomitant Medications	X	X	X	X	X	X	X	X	X[j]	X
Adverse Events	X	X	X	X	X	X	X	X	X[j]	X
Clinical Observations										
Clinician and Patient Reported Outcomes (OFC Symptom Scoring Assessment Tool)	X				X	X[j]		X	X[j]	
PK/Biomarker Assessments										
Samples for PK[d]		X	X	X		X[k]		X		X
Serum Sampling for Biomarkers Cytokines[e] (IL-33, IL-4, IL-5, IL-9, IL-13, sST2)	X		X	X		X[k]				
Whole Blood for Leukocytes[e]	X[g]		X[g]	X		X[k]		X[g]		X[g]
IP administration										
Administration of ANB020 or Placebo		X								

Abbreviations: BPCFC = Blind placebo-controlled food challenge; ECG = electrocardiogram; EOS: End of Study; ET = Early Termination; FSH = follicle stimulating hormone; IL = interleukin; IP = investigational product; OFC = Oral Food Challenge; PK = pharmacokinetics; WOCBP = Women of childbearing potential

a Confirm informed consent and continued willingness to participate.

b See Section 6.1.1 and 7.1.3 for the instructions to record vital signs, physical examination, and clinical evaluations using the OFC Symptom Scoring Assessment Tool during BPCFC.

c See Table 7.1 for safety laboratory details (Virology, Quantiferon Gold® test, and drugs of abuse to be performed at screening only).

d See Section 18.0 (Appendix 2) for schedule of PK collection time points.

e See Section 18.0 (Appendix 2) for schedule of peanut challenge assay, biomarker cytokines, and whole blood for leukocytes collection time points. During screening the samples for ex vivo peanut antigen challenge, whole blood for leukocytes, and serum samples for cytokines should be collected prior to administration of BPCFC. If necessary, the sample for ex vivo peanut antigen challenge can be collected on Day 1(instead of Screening), prior to dosing. **Ex vivo Peanut challenge is for Stanford University only.**

f ET visit will include all procedures to be done at EOS visit as well as any procedures that should be done at the next regularly scheduled visit. ET visit will be performed if the patient discontinues the study before EOS visit. If the patient completes all study visits and return to study center for EOS visit on Day 45, ET visit will not be applicable.

g Leukocytes will be obtained as part of hematology safety laboratory panel at screening, Day 2, and Day 45/ET. On Day 5 and Day 15, whole blood samples for leukocytes will be collected separately as there is no safety laboratory assessment on Day 5 and Day 15.

h Only conduct skin prick test and ImmunoCAP testing if these tests had not been performed within 8 weeks before screening.

i For patients with a history of asthma, spirometry or peak flow will be obtained before starting the initial placebo challenge and again before starting the initial peanut challenge . See Section 6.1.1.

j Only applicable if the Investigator decides to complete the oral food challenge in 2 days. See Section 6.1.1 and 7.1.3 for the instructions to record vital signs, physical examination, and clinical evaluations using the OFC Symptom Scoring Assessment Tool during BPCFC.

k If the Investigator decides to complete the BPCFC on Day 15, the blood samples for leukocytes (whole blood), biomarker analysis (cytokines), and PK analysis should be collected on the following day (Day 16). The patient's vital signs, adverse events, if any, and concomitant medications will also be recorded on Day 16.

l If any objective reaction occurred at Day 14/15, the BPCFC (peanut and placebo oral food challenge) will not be required but may be performed at the discretion of the Investigator

m The FSH levels will be obtained only on postmenopausal patients defined as aged over 45 years with at least 1 year of amenorrhea. Blood samples to determine the FSH levels will be obtained only at screening.

n If the Investigator decides to complete the oral food challenge over two days, please refer to Day 46 and appropriate footnotes for guidance.

o If the BPCFC is continued on Day 46, all assessments related to the BPCFC will be performed on Day 46. Concomitant medications and adverse events will also be recorded on Day 46. All laboratory/diagnostic tests scheduled for the EOS visit will be performed on day 45.

P If the patient's ET visit is between Day 35 to 45, and the termination is for non-medical reasons, the BPCFC will be administered during the ET visit. If the ET visit is before Day 35, the BPCFC will not be repeated.

q Informed consent must be obtained prior to participation in the study.

4.2 Discussion of Study Design

ANB020 is a first-in-class, anti-IL-33 therapeutic antibody developed by AnaptysBio, to treat Th2 cell driven inflammatory diseases with underlying IL-33 dysregulation. Preliminary evidence of this compound's significant PD activity in terms of cytokine modulation has been demonstrated in non-clinical and clinical studies, justifying its further development in patients with AD. Emergent data of the Phase I study (ANB020-001) in healthy subjects are the basis for the dose and IV route of administration of ANB020. The 300 mg IV dose was found to be safe and well tolerated in healthy subjects. The SAD part of the study has been completed but the MAD part of the study is ongoing. In the SAD part of the study, 64 subjects were enrolled and dosed. The doses implemented in the SAD study were 10, 40, 100, and 300 mg SC and 40, 100, 300, and 750 mg IV. No change in vital signs (BP, HR, ECG, or body temperature) was noted. Hematology parameters, such as erythrocytes, WBC and platelet counts, were all within the normal range except for one subject in the 750 mg dose group. All others did not show any modification or trend related to ANB020 administration. Serum chemistry results were also all in the normal range. The most commonly reported TEAEs were upper respiratory tract infection (50% versus 48% in placebo and ANB020 group, respectively) and headache (32% versus 27% in placebo and ANB020 group, respectively) of mild to moderate intensity. No AEs were deemed by the PI to be related to ANB020. Of all the AEs reported across all dose groups, 44% were reported as possibly related and 36% were reported as unrelated. One SAE of decreased neutrophils was reported in the 750 mg dose group which resolved without sequelae prior to study completion. No other observations of decreased neutrophils were observed. No dose dependent AEs were reported.

The dose of ANB020 selected for this study 300 mg/100 mL (IV) has provided complete inhibition of IL-33 induced cytokine release (ex vivo) up to 43 days and has been administered safely in study ANB020-001.

Patients with food allergy must consistently avoid food allergens including that which is often not readily apparent from visual inspection (cross-contamination during preparation or serving of food), to prevent potentially life threatening reactions. These avoidance measures significantly affect their quality of life. There are no currently approved treatments to prevent reactions from accidental ingestions. The use of targeted immune modulators such as ANB020 may be able to reduce the Th2 specific inflammatory cascade that trigger the clinical symptoms of a reaction. Other monoclonal Th2 immune modulators such as anti-IgE have shown promising but inconsistent results in clinical studies.

This is a proof of concept study[13] aiming to assess the effects of ANB020 compared to placebo in patients with peanut allergy and provide evidence that the hypothesized mechanisms is

affected by the IP and that the effect on the mechanism leads to a desired short-term clinical outcome such as increased tolerance to food peanut antigen challenge.

This study uses a screening BPCFC to provide a baseline for the assessments performed after ANB020 or placebo administration. Patients will receive active ANB020 or placebo in a 3:1 ratio on Day 1. On Day 14 and on Day 45, the oral BPCFC will be administered again. The BPCFC may be split into 2 days if the Investigator feels that that it is the best for patient's safety and convenience. Patients will be followed after ANB020 administration for PK, PD, and safety assessments from a single dose.

4.3 Selection of Study Population

Eligibility criteria for this study have been carefully considered to ensure the safety of the patients included in the study and that the results of the study can be used. It is imperative that patients fully meet all of the inclusion criteria and none of the exclusion criteria.

4.3.1 Inclusion Criteria

Patients will be enrolled in the study only if they meet all of the following criteria:

- Male and female patients with age >18 years and able to give informed consent.
- Patients with a confirmed clinically allergic response to peanut.
- Positive clinical reaction observed during the peanut oral food challenge and no clinical reaction observed during the placebo challenge.
- Positive peanut allergy skin prick test >3 mm of the negative control and detectable serum peanut-specific IgE levels (>0.35 kU/L) by ImmunoCAP testing. Skin prick test and ImmunoCAP testing will be conducted only if these tests had not been performed within 8 weeks before screening.
- Body mass index (BMI) of 18 to 36 kg/m^2 (inclusive) and total body weight >50 kg (110 lb). BMI = weight (kg)/(height [m^2]).
- Willing and able to comply with the study protocol requirements.
- Have the ability to read and understand the study procedures and have the ability to communicate meaningfully with the Investigator and staff.
- Women of childbearing potential, must have a negative serum pregnancy test at screening and Day 1, and be surgically sterile or using an acceptable method of contraception throughout the study and for 15 weeks after the last administration of IP. Postmenopausal patients defined as (1) aged over 45 years with at least 1 year of amenorrhea and levels of

follicle stimulating hormone (FSH) over 20 IU/L at screening or (2) aged over 50 years with at least 1 year of amenorrhea.

- Male patients must be willing to use effective methods of contraception during the entire study period and for 15 weeks after the last administration of IP (See Section 4.3.4).

4.3.2 Exclusion Criteria

Patients will not be enrolled in the study if they meet any of the exclusion criteria:

- Have concomitant dermatological or medical condition(s) which may interfere with the Investigator's ability to evaluate the patient's response to the IP.
- Have experienced severe life-threatening anaphylactic reactions to peanuts within 6 months before screening (i.e., requiring an intensive care unit (ICU) admission).
- Positive clinical reaction observed during the placebo oral food challenge.
- Participation in any interventional study for the treatment of peanut and/or food allergies in the 12 months before screening.
- Have received any IP or been part of any interventional clinical study within a period of 3 months or 5 half-lives (whichever is longer) before screening.
- Have received systemic corticosteroids, nonsteroidal, immunosuppressant, or immunomodulating drugs treatments within 2 weeks before screening.
- Use of beta blockers, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, or calcium channel blockers within 2 weeks before screening.
- History of ischemic cardiovascular diseases.
- Use of biologics such as omalizumab within 6 months before screening or subject is in build-up phase of allergen immunotherapy (excluding peanut) and has not reached maintenance dose.
- Have received antibiotic treatment within 1 week before screening.
- Have a history of hypersensitivity or allergic reactions following infusions of human blood or blood components.
- Have a history of hypersensitivity or allergic reactions to polysorbate 80 a component of ANB020 formulation or the inactive ingredients (excipients).
- If female, are pregnant or lactating, or intend to become pregnant during the study period.

- Current diagnosis of asthma requiring Global Initiative for Asthma Assessment (GINA) Step 4 or higher treatment or asthma partially controlled or uncontrolled according to GINA classifications[14] in the last three months before screening (Appendix I).
- History of a life threatening asthma attack within 1 year before screening (example: requiring an ICU admission, intubation with mechanical ventilation).
- Other significant medical conditions that in the opinion of the PI, prevent participation in the study
- History of drug, alcohol or other substance abuse, or other factors limiting the ability to cooperate and to comply with the study protocol.
- Have any other physical, mental, or medical conditions which, in the opinion of the Investigator, make study participation inadvisable or could confound study assessments.
- Receipt of a live attenuated vaccine within 4 weeks before screening.
- Planned surgery during the study or 30 days before screening.

4.3.3 Disease Diagnostic Criteria

Adult patients (age >18 years) with a confirmed clinical peanut allergy with a positive skin prick test >3 mm compared to the negative control and detectable serum IgE antibodies to peanuts (>0.35 kU/L).

4.3.4 Patient Restrictions

The following restrictions may affect patient participation in this study:

- Availability to attend visits according to the protocol.
- Concomitant medication restrictions as described in Section 5.8 and medications that should be avoided prior to BPCFC as shown in Appendix III.
- Women of childbearing potential must use a double-barrier method of contraception during the study (45 days) and for 15 weeks after the last administration of IP. Male patients must use effective methods of contraception (total abstinence or condom with spermicide) during the study and for at least 15 weeks after the last administration of IP. For woman of childbearing potential, abstinence alone is not an acceptable method of contraception.
- Restricted alcohol intake (<28 units per week) (1 unit of alcohol is equivalent to 8 ounces of beer, 4 ounces of wine, or 1 ounce of spirits).
- Strenuous exercise should be avoided up to 72 hours before planned study visits.

4.3.5 Patient Withdrawal

All patients are free to withdraw from participation in the study at any time, for any reason, specified or unspecified, and without prejudice to further treatment. The inclusion and exclusion criteria are to be followed explicitly. If a patient who does not meet the criteria is inadvertently enrolled, that patient should be withdrawn from the study. AnaptysBio and QuintilesIMS must be contacted, and if the patient has received ANB020 or placebo, the patient must be followed up until EOS (Day 45) for any AEs and/or SAEs.

In addition, the patients will be withdrawn from the study under the following circumstances:

- Prior to IP administration, the Investigator decides that the patient should be withdrawn or is at risk. If this decision is made because of an AE or a clinically significant laboratory value, the IP should not be administered and appropriate measures are to be taken. AnaptysBio and/or QuintilesIMS is to be notified immediately.
- The patient is unwilling to continue in the study.
- Lack of compliance with protocol.
- The Investigator or AnaptysBio, for any reason, stops the study.
- If a female patient becomes pregnant.
- New information suggests taking part in the study may not be in the participant's best interest.

Patients who discontinue the study early will have early termination (ET) procedures performed as shown in Table 4.1. Patients who are randomized and dosed with ANB020 or placebo and discontinued from the study after Day 14 will not be replaced. All patients who discontinue the study prior to completing the Day 14 study assessments will be replaced.

5.0 STUDY TREATMENTS

5.1 Treatments Administered

ANB020 is a humanized IgG1/kappa mAb and was selected from a panel of mouse mAb humanized by complementarity-determining region-grafting, optimized and matured via mammalian cell display and somatic hyper mutation using AnaptysBio's (SHM)-XEL^{TM} system to achieve a desired functional inhibitory potency.

ANB020 will be administered to patients by IV infusion in polyvinyl chloride or polyolefin bags following dilution to a total volume of 100 mL with sterile normal saline (0.9% NaCl). Placebo will be administered by IV infusion as 100 mL sterile normal saline (0.9% NaCl). Infusions will be administered over 1 hour.

5.2 Identity of Investigational Product

ANB020 is manufactured by Patheon of Greeneville, NC., U.S. under Good Manufacturing Practice (GMP) regulations. ANB020 is provided as a sterile clear solution in a glass vial for IV infusion and contains no preservatives.

ANB020 vials must be refrigerated at 2°C to 8°C (36°F to 46°F) until the day of use. ANB020 vials may be stored at room temperature (>8°C to 25°C [46°F to 77°F]) in the undiluted and/or diluted state for up to 8 hours. The vials should remain in the bulk cartons during storage and until use to provide protection from light. Vial contents should not be frozen or shaken. They are intended for single-use only; therefore, any remaining solution should be discarded.

The placebo contains no active drug and will be sterile normal saline (0.9% NaCl) for injection. The placebo will be procured from the pharmacy stock supply.

Table 5.1 provides an outline of the dosing schedule for the study.

Table 5.1 Dosing Schedule

Investigational product	Dosage form and strength	Manufacturer
ANB020	IV infusion: 300 mg/100 mL once on Day 1	Patheon

Abbreviation: IV = intravenous

5.3 Packaging and Labelling

Labels will be prepared in accordance with GMP and local regulatory guidelines.

All IPs should be kept in a secure place under appropriate storage conditions. The IP label on the packaging specifies the appropriate storage.

5.4 Method of Assigning Patients to Treatment Group

This is a randomized, double-blind, placebo-controlled study. On Day 1, after verification that all inclusion and no exclusion criteria have been met, the patients will be randomized in a 3:1 ratio to ANB020 or placebo. As patients become eligible they will be assigned sequential randomization numbers which will be used to assign the allocated treatment based on a randomization schedule. The Sponsor, Investigator, and patients will be blinded to treatment assignment of ANB020 or placebo. QuintilesIMS biostatistician will be responsible for providing randomization assignment list to the unblinded pharmacist.

5.5 Selection of Doses in the Study

A single IV infusion of 300 mg/100 mL of ANB020 or 100 mL placebo (0.9% sodium chloride) will be administered.

The dose of ANB020 selected for this study has provided complete inhibition of IL-33 induced cytokine release and has been administered safely in study ANB020-001.

5.6 Selection and Timing of Dose for Each Patient

Patients will receive a single dose of ANB020 or placebo administered under supervision at the study center. The infusion will be administered at the rate of 100 mL per hour via a Baxter infusion solutions set (FNC2110; prime volume 16 mL) or equivalent followed by a 16 mL IV saline flush, at the same infusion rate, to ensure that no residual drug remains in the infusion line. No in-line filter is to be used. The ANB020 or placebo infusion may be slowed or interrupted for patients experiencing infusion-related AEs.

5.7 Blinding

5.7.1 Blinding

This is a randomized, double-blind, placebo-controlled study with limited access to the randomization code. The IP and placebo will be identical in physical appearance. The Sponsor, Investigator, and patients will be blinded to treatment assignment of ANB020 or placebo. The unblinded pharmacy staff will be provided the randomization assignments to prepare the assigned IP for each patient.

5.7.2 Unblinding

The investigator is responsible for ensuring treatment-blinding information is maintained for all subjects. The investigator or his/her designee is responsible for ensuring that disclosure envelopes that contain the treatment code are stored safely, that their location is known, and that

access is readily available to the relevant staff in case of an emergency. Unblinding codes will be stored at the site by the unblinded pharmacist in case of a medical emergency.

Unblinding of treatment assignment during the study is discouraged and should occur only if it is absolutely necessary to know what treatment the subject received. If the investigator deems identification of the study drug is necessary for the purpose of providing urgent subject care, and knowledge of the subject's treatment assignment (ANB020 or placebo) will alter subsequent care, the treatment code for the specific subject will be obtained. Prior to unblinding, the investigator or appropriate designee should attempt to contact the Sponsor's Medical Monitor to discuss the need to unblind a subject. In the event the Medical Monitor cannot be reached, the investigator should ensure that the unblinding of the treatment code is performed in a discrete manner and the treatment is disclosed only to those persons involved with the direct medical care of the subject. The investigator should contact the Sponsor's Medical Monitor immediately (within 24 hours to include weekends) following emergency unblinding. Once the subject's treatment assignment has been obtained in the event of an emergency, the date, time, and reason for the unblinding must be recorded in the pharmacy log, on the subject's CRF and source notes and signed by the investigator.

5.7.3 Single-Blind Oral Food Challenge

The oral food challenge (BPCFC) procedure will be single-blind. All patients will be administered the placebo challenge first and then proceed with the peanut challenge. The Investigator, Sponsor, and pharmacy staff will be unblinded and only the patients will be blinded to the oral food challenge assignment (i.e., to receive the placebo challenge first or the peanut challenge). The Investigator should ensure that the patient reacted to the peanut challenge and not the placebo challenge prior to IP administration and continuation in the study. The post-dosing BPCFC order should also remain blinded to the patients.

5.8 Prior and Concomitant Treatments

5.8.1 Excluded Medications

The following medications will not be permitted during the study. Use of these excluded medications is a protocol violation and should be recorded in the electronic case report form (eCRF).

- Treatment with systemic corticosteroids, nonsteroidal, immunosuppressants, or immunomodulating drugs within 2 weeks before screening.
- Treatment with beta blockers, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, or calcium channel blockers within 2 weeks before screening.

- Any antibiotic treatment within 1 week before screening.
- Use of biologics such as omalizumab within 6 months before screening or subject is in build-up phase of allergen immunotherapy (excluding peanut) and has not reached maintenance dose.

In addition, the medications included in the Appendix III should be avoided prior to BPCFC.

5.8.2 Allowed Medications

Use of EpiPen and other medications as clinically indicated per the PRACTALL guidelines for BPCFC reactions (See Section 6.1.1).

Females of childbearing potential are to continue using their hormonal contraceptives and postmenopausal women are allowed to use hormone replacement therapy.

The Investigator must record the use of all concomitant medications, both prescribed and over-the-counter, into the eCRF and patient's medical records. This includes medications used on both a regular and an as needed basis. Patients should be discouraged from starting any new medication, both prescribed and over-the-counter, without consulting the Investigator, unless the new medication is required for emergency use or has been prescribed for clinical need.

5.9 Medical Care of Patients after End of Study

All patients will return to the study center for the EOS (Day 45) or ET visit for final safety and EOS assessments. After this visit, patients should be treated according to the Investigator's clinical judgment. Care after EOS/ET will not be provided by AnaptysBio. Any significant AE which in the opinion of the Investigator is related to the IP, SAE, or pregnancy occurring within 30 days of the dose of IP should be reported to the safety team of QuintilesIMS and followed up until outcome.

5.10 Treatment Compliance

The prescribed dosage, timing, and mode of administration may not be changed. Any deviations from the intended regimen must be recorded in the eCRF.

5.11 Investigational Product Accountability

The Investigator, a member of the investigational staff, or a hospital pharmacist must maintain an adequate record of the receipt and distribution of all the IPs using the Drug Accountability Form. These forms must be available for inspection at any time.

All the IP supplies should be accounted for at the termination of the study and a written explanation provided for discrepancies. All unused IP supplies and packaging materials are to be

inventoried and returned to QuintilesIMS/AnaptysBio by the Investigator or may be destroyed on site following institutions standard operating procedures (SOPs) and proper accountability by QuintilesIMS site monitor. The Investigator is not permitted to return or destroy unused IP supplies or packaging materials unless authorized by QuintilesIMS.

6.0 STUDY PROCEDURES

Study procedures will be performed as detailed in the Schedule of Events in Table 4.1. Assessments scheduled on the day of IP administration must be performed prior to the IP infusion unless otherwise noted. All assessments will be performed on the day of the specified visit; however, a window period of +4 days is available for the Day 14/15 visit. Day 14 and Day 15 visits should remain consecutive. A window period of +/-2 days can be implemented for visits occurring after completion of the Day 14/15 visit (i.e. Day 45). In addition, the blood sample collected from Stanford University patients for the ex vivo peanut challenge assay scheduled at Screening (prior to OFC), can be collected on Day 1 (prior to IP administration), if necessary.

6.1 Screening

Each potential patient will provide informed consent prior to participation in the study. The eligibility of patients will be determined during the screening period. Each eligible patient will be administered a graded oral BPCFC according to the PRACTALL consensus report (See Section 6.1.1). Symptoms will be monitored using the OFC Symptom Scoring Assessment Tool (See Section 6.1.2). Blood samples collected from Stanford University patients for PD assessments (ex vivo whole blood peanut antigen challenge) will be collected (See Section 18.0, Appendix 2) to determine the intensity of the response and establish a baseline value of peanut antigen induced activation. Other screening procedures will be carried out in accordance with the Schedule of Events in Table 4.1.

6.1.1 Oral Blind Placebo-Controlled Food Challenge

The oral BPCFC will be administered in accordance with the PRACTALL consensus report with the following parameters.[15]

The patient should refrain from consuming any meals within 3 hours of the oral food challenge. If a light meal is necessary, fatty foods should be avoided. Restricted medications prior to proceeding with the OFC[16] should be assessed and verified as per Appendix III. Clinical evaluations using the OFC Symptom Scoring Assessment Tool[15] and vital signs measurements will be done prior to the start of the oral BPCFC. For patients with a history of asthma, spirometry or peak flow will be obtained with the initial vital signs.

The Investigator must confirm the availability of EpiPen with each patient at screening (prior to BPCFC) and educate the patients to use it when they experience any symptom of allergic reaction. The patients will be asked to bring the EpiPen to their subsequent oral food challenges (BPCFC) at the study center.

The patients will be administered the placebo challenge first and then proceed with the peanut challenge. The patients will not be privy to which challenge (placebo or peanut) is being administered. As per the guidelines, all patients need to undergo the challenges (peanut challenge and placebo challenge). If the patient develops any signs of an allergic reaction, the challenge will be stopped and the patient will be immediately treated accordingly. A standard anaphylaxis treatment plan[17] is presented in Section 16.0 (Appendix IV). The BPCFC will be done at screening, Day 14, and Day 45. The challenge can be completed in 2 days if the Investigator feels that it is the best for patient's safety and convenience, otherwise all patients will undergo the peanut challenge and placebo challenge on the same day. All patients will be blinded to the challenge assignments. The study staff administering the challenge will be unblinded.

Peanut flour will be used as the suggested form of testing for peanut allergen. The peanut flour or placebo will be mixed with non-allergic food vehicle (i.e., applesauce or pudding) for blinded administration.

The initial dose will be 5 mg of peanut protein or placebo. Doses will be increased stepwise to 20 mg, 50 mg, 100 mg, 100 mg, 100 mg, and 125 mg to a total of 500 mg cumulative dose. The total cumulative dose of blinded peanut/placebo tolerated and dosing step/threshold reached prior to the objective reaction will be recorded.

Dosing intervals will be 20 to 30 minutes. Patient's vital signs, physical examination, and clinical assessments using the OFC Symptom Scoring Assessment Tool (provided in Appendix II) will be performed. There will be a 1-2 hour interval between the challenges (peanut challenge and placebo challenge). Patients will be observed for 2 hours after the last dose of BPCFC.

Criteria for Monitoring and Stopping the Oral Food Challenge

The Investigator or Sub-Investigator (clinician) should be in the study center during BPCFC.

Monitoring will include recording the vital signs before starting the initial placebo challenge, after completion of the placebo challenge, before starting the initial peanut challenge, upon completion of the final peanut challenge, and 2 hours after completion of the final peanut challenge. (See Section 7.1.3 for more details). A physical examination will be conducted before starting the initial placebo food challenge and upon completion of the final peanut challenge (prior to discharge). For patients with a history of asthma, peak flow or spirometry will be collected before starting the initial placebo challenge and again before starting the initial peanut challenge. The time of dose administration will be recorded. The OFC Symptom Scoring System will be used before starting the initial placebo challenge, after completion of the placebo challenge, before starting the initial peanut challenge, upon completion of the final peanut challenge, and 2 hours after completion of the final peanut challenge.

At the first sign of an objective allergic reaction, the challenge will be stopped and the patient will be immediately assessed and treated accordingly. The EpiPen (1:1000) should be readily available with the patients at the start of the challenge and the Investigator should confirm the availability of other emergency medications and equipment (IV fluid, Benadryl, oxygen, Ambubags, etc.) at the study center. A standard anaphylaxis treatment plan[17] is presented in Section 16.0 (Appendix IV). Any treatments given will be recorded along with the time given and clinical status of the patient. The patient will continue to be assessed and observed as the PI or Sub-Investigator deems appropriate.

A longer observation period may be warranted prior to proceeding with the next dose or discontinuation depending on the patient's clinical status and will be at the judgement of the Investigator.

All patients should have an emergency treatment plan available upon discharge from the study center regardless of the outcome of the study challenge and an EpiPen readily available.

6.1.2 Oral Food Challenge Symptom Scoring Assessment Tool

The OFC Symptom Scoring Assessment Tool will be used to assess the patient for common symptoms that can be suspected to be an allergic reaction involving the skin, upper respiratory, lower respiratory, gastrointestinal, and cardiovascular systems based on a 0-3 scale of absent to severe. The OFC Symptom Scoring Assessment Tool is presented in Appendix II.

6.1.3 Skin Prick Testing

Skin prick test and ImmunoCAP testing will be performed only if these tests had not been performed within 8 weeks before screening.

Skin prick testing will be performed (only at screening) on the flexor surface of the forearm utilizing standard testing procedures recommended by the American Academy of Allergy, Asthma, and Immunology and the American College of Allergy, Asthma, and Immunology Joint Practice Parameter on Allergy Diagnostic Testing[18]. Peanut will be tested in the form of a commercial extract with appropriate positive and negative controls.

The orthogonal diameter will be measured at the mid-point of the longest axis and the average of the longest and the orthogonal diameter must be calculated. Pseudopodia will not be assessed. During screening, the negative control must be <2 mm for the test to be considered valid. If the negative control is >2 mm the test should be repeated on another day.

A wheal that is >3 mm of the negative control will be considered positive.

6.2 Study Day Procedures

6.2.1 Blood volume

The total blood volume for each Stanford University patient will be approximately 177 mL and 147 mL for non-Stanford patients. The blood volume drawn during each visit is provided in Table 6.1. The blood draw for various assessments throughout the study will be performed according to safety guidelines established by the National Institutes of Health.

Table 6.1 Blood Volume Sampling During Each Visit

Visits	Screening	Day 1 Predose	Day 1 Predose (PK)	Day 1 (0.5H) (PK)	Day 1 (EOI) (PK)	Day 1 (EOI 3H) (PK)	Day 2	Day 5	Day 14	Day 15/16	Day 45
Stanford Univ. Only Total blood volume sampled during each visit (mLs)	up to 41 (31-41)[a]	up to 22 (12-22)[a]	5	5	5	5	34	25.5	12	15.5	17
Total blood volume sampled during each visit (mLs)	31	12	5	5	5	5	24	15.5	12	15.5	17

Abbreviation: EOI = actual time of end of infusion; PK = pharmacokinetics
a. The blood sample for ex vivo peanut challenge assay (approximately 10 mL) can be collected either at screening or on Day 1. Based on this sample collection, blood volume required at screening and Day 1 will vary.

6.2.2 Day 1 (Randomization)

On Day 1, the patients will be randomized to receive either ANB020 or placebo in a 3:1 ratio (15 patients will receive ANB020 and 5 patients will receive placebo). If the blood sample collected from Stanford University patients for ex vivo peanut challenge assay was not collected at screening visit it must be collected on Day 1 (prior to IP administration). Additional Day 1 procedures will be carried out in accordance with the Schedule of Events in Table 4.1. Patients with any ongoing AEs or SAEs at the time of scheduled discharge from the study center should remain at the study center until the Investigator has determined that these events have been resolved or deemed as not clinically significant by the Investigator.

6.2.3 Day 2 to Day 15

Patients will return to the study center on Days 2, 5, 14, and 15. Various assessments will be performed and blood samples will be collected. On Day 14, oral BPCFC will be administered and the symptoms will be monitored (See Section 6.1.1 and Section 6.1.2). The oral BPCFC will be continued on Day 15 if the patient has received only the placebo challenge on Day 14 and the

blood samples scheduled on Day 15 will be collected on Day 16 (only applicable if the Investigator decides to complete the challenge in 2 days). Additional procedures will be carried out in accordance with the Schedule of Events in Table 4.1.

6.2.4 Follow-up Period

After completing the oral food challenge and related procedures (post administration of IP), the patients will be followed up for another 30 days. During the 30 days follow-up period, the patients will be contacted weekly via telephone by study staff to assess the patient's well-being. Concomitant medications and AE/SAEs will be recorded in the patient's medical source documents and eCRFs.

6.2.5 End of Study

After the follow-up period, all patients will return to the study center for the EOS visit on Day 45. If any objective reaction occurred at Day 14/15, the BPCFC will not be required but may be performed at the discretion of the Investigator on Day 45 and the symptoms will be monitored (See Section 6.1.1 and Section 6.1.2). If the Investigator decides to perform the BPCFC, it can be completed in 2 days (one challenge on Day 45 and the second challenge on Day 46) if the Investigator feels that it is the best for patient's safety and convenience. Otherwise all patients will undergo the challenges (peanut challenge and placebo challenge) on Day 45 (EOS visit) itself. All blood samples scheduled for the EOS visit will be collected on Day 45 (EOS visit) regardless of splitting the BPCFC assessments. Additional procedures will be carried out in accordance with the Schedule of Events in Table 4.1.

6.2.6 Early Termination

Patients who discontinue the study early will be asked to return to the study center for the ET procedures as shown in the Schedule of Events (Table 4.1). Patients will only complete the final BPCFC if they discontinue between Day 35 to 45 for non-medical related reasons.

6.2.7 Timing of Procedures

There are times where the protocol requires more than one procedure to be completed at the same time point. In these instances, the following will apply to post-dose time points:

- The PK samples will take precedence over other procedures and will therefore be collected at the nominal time.

All safety assessments will be timed and performed relative to the start of dosing.

6.2.8 Discharge from the Study Center

A patient will be allowed to leave the study center 6-8 hours after the ANB020/placebo administration at the study center and completion of study-specific procedures providing that:

- No AEs have been reported during the study visit.
- The patient responds in the affirmative when asked if they are feeling well.

If any of these conditions are not met, then the patient will only be allowed to leave the study center with the authorization of the Investigator or appropriately qualified delegate.

7.0 SAFETY, PHARMACODYNAMIC, AND PHARMACOKINETIC ASSESSMENTS

7.1 Safety

Safety assessments will be based on medical review of AE reports, the results of physical examinations, and clinical laboratory tests. The incidence of observed AEs will be reviewed for potential significance and clinical importance. Patients with any ongoing AEs or SAEs at the time of scheduled discharge from the study center, should remain at the study center until the Investigator has determined that these events have been resolved or deemed as not clinically significant by the Investigator.

7.1.1 Adverse Events

The Investigator is responsible for recording all AEs observed during the study (screening, treatment, and follow-up) period.

Definition of AE: An AE is any untoward medical occurrence in a patient or clinical investigation patient administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.

Definition of SAE: An SAE, experience or reaction, is any untoward medical occurrence (whether considered to be related to the IP or not) that at any dose:

- Results in death.
- Is life-threatening (the patient is at a risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe).
- Requires inpatient hospitalization or prolongation of existing hospitalization: Hospital admissions and/or surgical operations planned before or during a study are not considered AEs if the illness or disease existed before the patient was enrolled in the study, provided that it did not deteriorate in an unexpected way during the study.
- Results in persistent or significant disability/incapacity.
- Is a congenital abnormality/birth defect.
- Other: Medically significant events, which do not meet any of the criteria above, but may jeopardize the patient and may require medical or surgical intervention to prevent one of the other serious outcomes listed in the definition above. Examples of such events are blood dyscrasias (e.g., neutropenia or anemia requiring blood transfusion, etc.) or convulsions that do not result in hospitalization.

An adverse drug reaction (ADR) is defined as all noxious and unintended responses to a medicinal product related to any dose.

An unexpected ADR is defined as any adverse reaction, the nature of which is not consistent with the applicable product information.

Each AE is to be evaluated for duration, severity, seriousness, and causal relationship to the IP. The action taken and the outcome must also be recorded.

Severity

The severity of the AE will be characterized as "mild, moderate, or severe" according to the following definitions:

- Mild events are usually transient and do not interfere with the patient's daily activities.
- Moderate events introduce a low level of inconvenience or concern to the patient and may interfere with daily activities.
- Severe events interrupt the patient's usual daily activity.

Relationship

The causal relationship between the IP and the AE has to be characterized as unrelated, unlikely, possible, probable, or unknown (unable to judge).

Events can be classified as "unrelated" if there is not a reasonable possibility that the IP caused the AE.

An "unlikely" relationship suggests that only a remote connection exists between the IP and the reported AE. Other conditions, including chronic illness, progression or expression of the disease state or reaction to concomitant medication, appear to explain the reported AE.

A "possible" relationship suggests that the association of the AE with the IP is unknown; however, the AE is not reasonably supported by other conditions.

A "probable" relationship suggests that a reasonable temporal sequence of the AE with drug administration exists and, in the Investigator's clinical judgment, it is likely that a causal relationship exists between the drug administration and the AE, and other conditions (concurrent illness, progression or expression of disease state, or concomitant medication reactions) do not appear to explain the AE.

All efforts should be made to classify the AE according to the above categories. The category "unknown" (unable to judge) may be used only if the causality is not assessable, e.g., because of insufficient evidence, conflicting evidence, conflicting data, or poor documentation.

7.1.1.1 Reporting of Adverse Events

All AEs, regardless of severity occurred during the study (screening, treatment, or follow-up period) are to be recorded on the appropriate AE pages (either 'serious' or 'non-serious') in the eCRF. All AEs reported prior to IP administration will also be recorded on the medical history CRF page. The Investigator should complete all the details requested including dates of onset, severity, action taken, outcome, and relationship to the IP. Each event should be recorded separately.

The ANB020 or placebo infusion may be slowed or interrupted for patients experiencing infusion-related AEs. Following the infusion, all patients will be observed for fever, chills, rigors, hypotension, nausea, or other infusion-related AEs.

All SAEs (as described in Section 7.1.1) that occur after the patient has signed informed consent (including the protocol defined follow-up period), regardless of judged relationship to the IP, or after the study period, if considered serious and related to IP or to the patient's participation in the study, must be reported to QuintilesIMS within 24 hours of the Investigator's knowledge of the event. The SAE reporting will originate in the electronic data capture (EDC) system and an email will be sent to the designated responsible parties defined in the Safety Plan. The paper SAE form is in place as a back-up in the rare event that EDC is not accessible to the reporter of the SAE and the paper SAE form should be sent to ***QLS_Anaptys@quintiles.com.***

The following documents should be submitted to QuintilesIMS Safety:

- Serious Adverse Event Report Form.
- The following eCRFs or de-identified source documents:
    - Demographics page(s).
    - Medical history page(s).
    - Adverse event page(s).
    - Concomitant medication page(s).
    - Hospital discharge summary: If the patient is hospitalized because of or during the course of an SAE, then a copy of the hospital discharge.

Following are Investigator responsibilities:

- Record diagnosis instead of signs and symptoms when available using accepted medical terminology.

- The events recorded on the safety event report form must be consistent with the information entered on the respective CRFs.
- Include any relevant medical history, concurrent illnesses, and concomitant medicines.
- Include treatment(s) provided.
- The Investigator must assess causality at the time of the first SAE notification.
- The Investigator is responsible for obtaining and forwarding or recording the details of the outcome of the SAE on the appropriate eCRF, as well as any other details which may be requested by AnaptysBio and/or QuintilesIMS in a timely manner**:**
    - Hospital records.
    - Medical records.
    - Data clarification.
    - Death certificate/autopsy results.
    - Events should be followed until they are resolved or stabilized, "Resolved with sequelae" will require specification of the sequelae.
    - For a fatal or life-threatening SAE, please call QuintilesIMS Safety Group (contact information is located on the SAE form), in addition to entering the SAE details in the eCRF.
    - The SAEs should continue to be reported for at least 5.5 half-lives of IP following last dose.
    - Queries on SAE reports will be generated when there is missing/discrepant information, or when there is a need for additional information to completely evaluate the report. All supplemental SAE information and or documentation is to be recorded on the appropriate eCRF and must be submitted upon request.

7.1.1.2 Reporting of Serious Adverse Events to Regulatory Authorities and Investigators

All SAEs that are considered unexpected and related to the IP will be reported by QuintilesIMS as a 15-Day report to the regulatory authorities as applicable and to all participating Investigators. The SAEs that are considered unexpected, related to the study and are life-threatening or result in death will be reported by QuintilesIMS to the regulatory authorities as applicable, and to all participating Investigators as a 7-Day report. QuintilesIMS will ensure that all SAEs are reported to the appropriate regulatory authorities.

Investigators will be notified by QuintilesIMS of all SAEs that require prompt submission to their Institutional Review Board (IRB). Each Investigator must notify the IRB responsible for reviewing the study at their site of all 15-Day or 7-Day safety reports required by local regulations or IRB requirements and should provide written documentation of IEC notification for each report to QuintilesIMS. This study will comply with all local regulatory requirements and adhere to the full requirements of ICH Guideline for Clinical Safety Data Management, Definitions and Standards for Expedited Reporting, Topic E2.

7.1.1.3 Follow-Up of Adverse Events

Any AEs observed from the time of informed consent signed up to the end of the study will be followed up to resolution. Resolution means that the patient has returned to a baseline state of health or the Investigator does not expect any further improvement or worsening of the AE or the patient is deemed lost to follow-up. All AEs that occur after the patient completed a clinical study should also be reported to AnaptysBio and/or QuintilesIMS within 30 days of the patient's last visit.

7.1.2 Clinical Laboratory Evaluations

Blood samples for hematology, clinical chemistry evaluations including serum pregnancy test, FSH, and serological assays, will be collected at the visits specified in Table 4.1. A list of specific clinical laboratory evaluations is provided in Table 7.1 below:

Table 7.1 Clinical Laboratory Parameters

Hematology	Clinical Chemistry	Virology	Urinalysis	Drugs of Abuse (*Only at Screening*)
Hematocrit Packed Cell Volume Hemoglobin Mean Cell Haemoglobin Mean Cell Hemoglobin Concentration Mean Cell Volume Platelet Count Red Blood Cell Count White Blood Cell Count Basophils Eosinophils Monocytes Neutrophils Lymphocytes Immunoglobulins (IgA, IgG, IgM, IgE, and IgD)	ALT Albumin ALP AST Bicarbonate Bilirubin (Total) Bilirubin (Direct) (only if Total is elevated) Calcium Chloride C-Reactive Protein Creatinine GGT Glucose Potassium Phosphate (Inorganic) Protein (Total) Sodium Troponin Urea **WOCBP Only** - hCG levels **Postmenopausal woman aged over 45 years with at least 1 year of amenorrhea only** - FSH levels (*only at Screening visit*)	Hepatitis B Surface Antigen Hepatitis C Antibody HIV Antibody **TB Screening** Quantiferon Gold® test *(only at Screening visit)*	Bilirubin Blood Glucose Ketones Leukocytes Nitrates pH Protein Specific gravity Urobilinogen **At discretion of Investigator based on urinalysis results** Microbiology Urine Microscopy	Amphetamines Barbiturates Benzodiazepines Cocaine Marijuana/Cannabis Methadone Methamphetamine/ Ecstasy Morphine/Opiates Phencyclidine Tricyclic Antidepressants

Abbreviations: ALP = alkaline phosphatase; ALT = alanine transaminase; AST = aspartate aminotransferase; FSH = follicle stimulating hormone; GGT = gamma glutamyl transferase; hCG = human chorionic gonadotropin hormone; HIV = human immunodeficiency virus; TB = tuberculosis; WOCBP = women of childbearing potential.

The clinical laboratory tests will be reviewed for results of potential clinical significance, based on Investigator's discretion, at all time points throughout the study. The Investigator will evaluate any change in laboratory values. If the Investigator determines a laboratory abnormality to be clinically significant, it is considered a laboratory AE; however, if the abnormal laboratory value is consistent with a current diagnosis, it may be documented accordingly.

7.1.3 Vital Signs, Physical Findings, and Other Safety Assessments

Vital signs will be measured, and physical examinations and ECGs will be performed at the time points indicated in the Schedule of Events (Table 4.1).

Vital signs include pulse rate, respiratory rate, body temperature, systolic BP, and diastolic BP. The physical examination includes evaluation of general appearance, head, eyes, ears, nose, and throat, and pulmonary, cardiovascular, gastrointestinal, renal/genitourological, endocrine (including thyroid), musculoskeletal/spinal, lymphatic, and dermatologic systems.

During the BPCFC, clinical evaluations using the OFC Symptom Scoring Assessment Tool and vital signs will be done before starting the initial placebo challenge, after completion of the final placebo challenge, before starting the initial peanut challenge, upon completion of the final peanut challenge, and 2 hours after completion of the final peanut challenge. Full physical examinations will be performed before starting the initial placebo food challenge and upon completion of the final peanut challenge (prior to discharge), and more frequent if deemed appropriate by the Investigator on the challenge day.

A standard 12-lead ECG will be performed by a qualified physician or nurse. The following parameters will be documented: HR, PR interval, QRS interval, QT interval, and QTc interval. The ECG will be reviewed by the Investigator or an authorized representative who is experienced in the evaluation of ECGs and assessed for clinical significance.

7.1.4 Safety Monitoring

There is no data monitoring committee for this study.

Timely and complete reporting of safety information assists the Sponsor in identifying any untoward medical occurrence, thereby allowing: (1) protection of safety of study patients; (2) a greater understanding of the overall safety profile of the IP; (3) recognition of dose-related IP toxicity; (4) appropriate modification of study protocols; (5) improvements in study design or procedures; and (6) adherence to worldwide regulatory requirements.

7.2 Pharmacodynamics

For circulating leukocytes, whole blood (2 mL) samples will be taken in ethylenediaminetetraacetic acid (EDTA) Vacutainer (2 mL). Differential WBC counts in whole blood will be measured to monitor the circulating leukocyte populations. The sample for leukocytes will be obtained as part of the hematology safety laboratory panel at screening, Day 2, and Day 45/ET. On Day 5 and Day 15, sample for leukocytes will be collected separately as there is no safety laboratory assessments on Day 5 and Day 15.

For circulating cytokines, whole blood samples (total 7.5 mL) will be taken in serum separator tube (SST). Circulating cytokines measured will include, but may not be limited to, IL-4, IL-5, IL-9, IL-13, IL-33, and sST2 (see lab manual for detailed collection and processing instructions).

For the ex vivo peanut antigen challenge, whole blood (10 mL) samples collected from Stanford University patients will be taken in 10 mL SST vacutainer. The whole blood peanut response assay (ex vivo) will measure cytokine levels released from pathogenic T cells, and should include, but may not be limited to, IL-4, IL-5, IL-9, IL-13, and IL-33.

The serum and whole blood biomarker time points are presented in Section 18.0 (Appendix 2). The actual date and time of the sample collection will be recorded in the patient's eCRF. The details of blood sample collection, sample tube labelling, sample preparation, storage, and shipping procedures will be described in a separate laboratory manual.

The measurement of circulating leukocytes and circulating cytokines will be performed using validated assay methods. The measurement of cytokine levels released from pathogenic T cells (ex vivo peanut response assay) will be performed using an exploratory assay method developed by [redacted]. The analytical methods used to measure these PD endpoints will be described in a separate bioanalytical report.

7.3 Pharmacokinetics

Samples (5 mL) of whole blood will be obtained in a 5 mL Vacutainer® SST for the determination of ANB020 in human serum. Samples will be collected according to the schedule presented in Section 18.0 (Appendix 2). Approximately 40.0 mL of whole blood will be obtained from each patient for PK assessments during the study.

If a patient refuses blood collection for PK analysis, this will not be considered a protocol violation as the PK analysis is a secondary objective.

The actual date and time of dosing and of the blood sample collection will be recorded in the patient's eCRF. The details of blood sample collection, sample tube labelling, sample preparation, storage, and shipping procedures will be described in a separate laboratory manual.

Bioanalysis

The measurement of the concentrations of ANB020 will be performed using a validated assay method. The analytical methods used to measure concentrations of ANB020 will be described in a separate bioanalytical report.

7.4 Efficacy

Primary and secondary efficacy endpoints included difference in total cumulative tolerated peanut dose during BPCFC between baseline and post-treatment with ANB020 or placebo on Day 14 and OFC symptom scores on Day 14.

Exploratory efficacy endpoints included difference in total cumulative tolerated peanut dose during BPCFC between baseline and post-treatment with ANB020 or placebo on Day 45 and OFC symptom scores on Day 45.

The oral BPCFC will be performed according to the PRACTALL guidelines and Symptoms will be monitored using the OFC Symptom Scoring Assessment Tool. Refer section 6.1.1 and Appendix II for more details.

7.5 Health Outcomes

Not applicable.

7.6 Pharmacogenetics

Not applicable.

7.7 Appropriateness of Measurements

All safety assessments used in this study are standard, i.e., widely used and generally recognized as reliable, accurate, and relevant.

8.0 QUALITY CONTROL AND QUALITY ASSURANCE

According to the Guidelines of Good Clinical Practice (GCP) (CPMP/ICH/135/95), QuintilesIMS is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs.

Quality control will be applied to each stage of data handling.

The following steps will be taken to ensure the accuracy, consistency, completeness, and reliability of the data:

- Central laboratories for clinical laboratory parameters.
- Center Qualification visit.
- Center Initiation visit.
- Early center visits post-enrollment.
- Routine center monitoring.
- Ongoing center communication and training.
- Data management quality control checks.
- Continuous data acquisition and cleaning.
- Internal review of data.
- Quality control check of the final clinical study report.

In addition, AnaptysBio and/or QuintilesIMS Clinical Quality Assurance Department may conduct periodic audits of the study processes, including, but not limited to study center, center visits, central laboratories, vendors, clinical database, and final clinical study report. When audits are conducted, access must be authorized for all study related documents including medical history and concomitant medication documentation to authorized AnaptysBio's representatives and regulatory authorities.

8.1 Monitoring

AnaptysBio has engaged the services of a contract research organization, QuintilesIMS, to perform all monitoring functions within this clinical study. QuintilesIMS monitors will work in accordance with QuintilesIMS SOPs. The monitor will establish and maintain regular contact between the Investigator and AnaptysBio.

The monitor will evaluate the competence of the study center, informing AnaptysBio about any problems relating to facilities, technical equipment, or medical staff. During the study, the monitor will check that written informed consent has been obtained from all patients correctly and that data are recorded correctly and completely. The monitor is also entitled to compare entries in eCRFs with corresponding source data and to inform the Investigator of any errors or omissions. The monitor will also assess and control adherence to the protocol and ICH/GCP guidelines at the study center. The monitor will arrange for the supply of IP, ensure proper IP dispensing/accountability, and appropriate storage conditions are maintained.

Monitoring visits will be conducted according to all applicable regulatory requirements and standards. Regular monitoring visits will be made to each center while patients are enrolled in the study.

During monitoring visits, all entries in the eCRFs will be compared with the original source documents (source data verification). For the following and all other items, this check will be 100%:

- Patient identification number.
- Patient consent obtained.
- Patient eligibility criteria (inclusion and exclusion criteria).
- Efficacy variables.
- Safety variables.
- Medical record of AE.

8.2 Data Management/Coding

Data generated within this clinical study will be handled according to the relevant SOPs of the Data Management and Biostatistics departments of QuintilesIMS.

Electronic data capture will be used for this study, meaning that all eCRF data will be entered in electronic forms at the study center. Data collection will be completed by authorized study center staff designated by the Investigator. Appropriate training and security measures will be completed with the Investigator and all authorized study center staff prior to the study being initiated and any data being entered into the system for any study patients.

All data must be entered in English. The eCRFs should always reflect the latest observations on the patients participating in the study. Therefore, the eCRFs are to be completed as soon as possible during or after the patient's visit. To avoid inter-observer variability, every effort should be made to ensure that the same individual who made the initial baseline determinations

completes all efficacy and safety evaluations. The Investigator must verify that all data entries in the eCRFs are accurate and correct. If some assessments are not done, or if certain information is not available or not applicable or unknown, the Investigator should indicate this in the eCRF. The Investigator will be required to electronically sign off on the clinical data.

The monitor will review the eCRFs and evaluate them for completeness and consistency. The eCRF will be compared with the source documents to ensure that there are no discrepancies between critical data. All entries, corrections and alterations are to be made by the responsible Investigator or his/her designee. The monitor cannot enter data in the eCRFs. Once clinical data of the eCRF have been submitted to the central server, corrections to the data fields will be audit trailed, meaning that the reason for change, the name of the person who performed the change, together with time and date will be logged. Roles and rights of the center staff responsible for entering the clinical data into the eCRF will be determined in advance. If additional corrections are needed, the responsible monitor or Data Manager will raise a query in the EDC application. The appropriate study center staff will answer queries sent to the Investigator. This will be audit trailed by the EDC application meaning that the name of investigational staff, time and date stamp are captured.

The eCRF is essentially considered a data entry form and should not constitute the original (or source) medical records unless otherwise specified. Source documents are all documents used by the Investigator or hospital that relate to the patient's medical history, that verify the existence of the patient, the inclusion and exclusion criteria and all records covering the patient's participation in the study. They include but are not limited to laboratory notes, ECG results, memoranda, pharmacy dispensing records, patient files, etc.

The Investigator is responsible for maintaining source documents. These will be made available for inspection by the study monitor at each monitoring visit. The Investigator must submit a completed eCRF for each patient who receives IP, regardless of duration. All supportive documentation submitted with the eCRF, such as laboratory or hospital records, should be clearly identified with the study and patient number. Any personal information, including patient name, should be removed or rendered illegible to preserve individual confidentiality.

Electronic case report form records will be automatically appended with the identification of the creator, by means of their unique User ID. Specified records will be electronically signed by the Investigator to document his/her review of the data and acknowledgement that the data are accurate. This will be facilitated by means of the Investigator's unique User ID and password; date and time stamps will be added automatically at time of electronic signature. If an entry on an eCRF requires change, the correction should be made in accordance with the relevant software procedures. All changes will be fully recorded in a protected audit trail, and a reason for the change will be required.

Adverse events will be coded using current Medical Dictionary for Regulatory Activities (MedDRA). Concomitant medications will be coded using World Health Organization Drug Dictionary. Concomitant diseases/medical history will be coded using MedDRA.

8.3 Quality Assurance Audit

Study centers, the study database, and study documentation may be subjected to Quality Assurance audit during the course of the study by AnaptysBio or QuintilesIMS on behalf of AnaptysBio. In addition, inspections may be conducted by regulatory bodies at their discretion.

9.0 STATISTICS

Statistical analyses will be performed by QuintilesIMS using statistical analysis system (SAS®), (SAS Institute, Cary, NC, U.S.) Version 9.2 or higher. QuintilesIMS SOPs and work instructions will be used as the default methodology if not otherwise specified.

Details of statistical analysis methods will be provided in the statistical analysis plan (SAP) that will be prepared and signed off prior to database lock. Any change to the data analysis methods will be documented in the SAP. Any additional analyses, and the justification for making the change, will be described in the clinical study report. Additional exploratory analyses of the data will be conducted as deemed appropriate.

9.1 Determination of Sample Size

As this is the third study with an anti-IL-33 inhibitor, the number of patients to be enrolled is not based on statistical power considerations.

A total of approximately 20 patients will be randomized in a 3:1 ratio to receive ANB020 or placebo.

9.1.1 Analysis populations

Randomized Analysis Set

All patients who have been allocated to a randomized treatment arm, regardless of whether they received the planned treatment or not.

Full Analysis Set

All patients who have received ANB020 or placebo and present in study till Day 14. The full analysis set will be used for all efficacy analyses.

Safety Analysis Set

All patients who have received ANB020 or placebo. The safety analysis set will be used for all safety analyses.

Pharmacokinetics Analysis Set

All patients who have received ANB020 and have at least one post-dose serum concentration data value available for ANB020 without any events or protocol deviation deemed to affect PK assessments. The PK analysis set will be used for all PK analyses.

Pharmacodynamics Analysis Set

All patients who have received at least one dose of ANB020 or placebo and provide at least one evaluable post-dose PD measurement without any events or protocol deviation deemed to affect PD assessment. The PD analysis set will be used for all PD analyses.

9.2 Patient Disposition

A tabular presentation of the patient disposition will be provided. It will include the number of patients screened, enrolled, assigned treatment ANB020, completed till Day14, completed as well as the number of dropouts, with reasons for discontinuation, and major protocol deviations or violations. A listing will be presented to describe dates of screening, assigned treatment, screen failed with reason, completion or early withdrawal, and the reason for early discontinuation, if applicable, for each patient. A list of protocol violations will be identified and discussed with the Investigator/AnaptysBio in dry-run to categorize as major or minor and the same will be reported.

9.3 Patient Characteristics and Concomitant Medications

Patient characteristics obtained at screening will be summarized for all patients taking ANB020 and placebo. Summaries will include descriptive statistics for continuous variables (sample size, mean, standard deviation [SD], median, minimum, and maximum) and for categorical variables (sample size, frequency, and percent). Patient characteristics may include, but are not limited to age, gender, race/ethnicity, height, weight, and BMI.

Categorical use of concomitant medication will be summarized by treatment period and overall. All concomitant medications used will be listed.

9.4 Safety analyses

Following are the primary safety endpoints:

- Assessment of AEs/SAEs (potentially significant and clinically important AEs, SAEs, and AEs leading to withdrawal).
- Physical examinations.
- Vital signs.
- Clinical safety laboratory tests (hematology, biochemistry, and urinalysis).
- Electrocardiograms.

9.4.1 Adverse Events

Adverse events will be coded using the current MedDRA. For each treatment, numbers of events and percentage will be tabulated by preferred term and system organ class. An event that

occurred one or more times on treatment will contribute one observation to the numerator and denominator comprise all safety patients exposed to ANB020 or placebo for respective treatment. If the intensity or seriousness of the AE changes, the overall intensity or seriousness will be the maximum intensity or seriousness of the multiple occurrences. The AEs, SAEs, AEs leading to treatment discontinuation, and AEs leading to withdrawal of patient will be tabulated for each treatment period.

Summaries over system organ class, preferred term and listings of AEs, AEs leading to death, SAEs, potentially significant AEs, clinically important AEs, and AEs that led to discontinuation from the study or of the IP will be presented by treatment. Summaries will also be presented by relatedness to IP and the severity of the AE.

9.4.2 Vital Signs Measurements, Physical Findings, and Clinical Laboratory Evaluations

Summaries and listings of data for vital signs, hematology, clinical chemistry, and urinalysis laboratory tests, ECGs and physical examination findings will be presented. Appropriate descriptive statistics will be summarized for the observed value at each scheduled assessment and for the corresponding change from baseline.

For hematology and clinical chemistry tests, listings of patient data will also flag up any abnormal or out-of-range values. Clinically significant changes in the laboratory test parameters will be summarized and listed. Hematology and clinical laboratory data will be reported in System International units.

For ECG variables, the QT correction factor will be based on both the Bazett and Fridericia formulae (QTcB and QTcF). Categorical summaries of absolute QT, QTcB and QTcF values and change from (baseline) values in QT, QTcB and QTcF values will be presented by treatment and visit.

Descriptive statistics will be used to present the safety outcomes including, physical examination results, weight, BMI, vital signs measurements, clinical laboratory test results, and ECG results. Change from baseline will also summarized for vital signs measurements, clinical laboratory test results.

9.4.3 Missing Data

No imputation will be performed for the missing data.

9.5 Efficacy analysis

The following are efficacy endpoints.

- Difference in total cumulative tolerated peanut dose during BPCFC between baseline and post-treatment with ANB020 or placebo on Day 14.
- Difference in total cumulative tolerated peanut dose during BPCFC between baseline and post-treatment with ANB020 or placebo BPCFC on Day 45.
- The OFC score change from baseline on Day 14 and Day 45.

For the quantitative efficacy variables, descriptive statistics (including n, mean, minimum, maximum, and 95% confidence interval [CI]) will be presented.

Total cumulative peanut dose tolerated at screening and post ANB020 or placebo administration on Day 14 (Day 14 and Day 15, if the BPCFC was completed in 2 days) and Day 45 (Day 45 and Day 46, if the BPCFC was completed in 2 days) will be summarized with descriptive statistics.

Change from baseline on Day 14 for tolerated dose and OFC scores will be compared between ANB020 and placebo using analysis of covariance (ANCOVA) with treatment as fixed effect and baseline results as covariate. Treatment differences will be presented with corresponding p-values for the test of no difference and 95% CI.

Change from baseline on Day 45 for tolerated dose and OFC scores will be compared between ANB020 and placebo using mixed model for repeated measures. The 95% CI for the difference between ANB020 and placebo on Day 45 will be estimated. This model will include treatment, visit, and treatment by visit interaction as fixed effect and baseline results as covariate. The data collected at baseline, Day 14, and Day 45 will be used in this model.

9.6 Pharmacokinetic Analyses

9.6.1 Evaluation of Pharmacokinetic Data

The PK parameters will be derived using non-compartmental methods. The actual sampling times will be used in the PK parameter calculations. The PK analyses will follow QuintilesIMS SOPs. Further details of PK analysis will be specified in the SAP.

Where possible, the following PK parameters will be determined for ANB020 after a single IV infusion:

- Maximum observed concentration (C_{max})
- Time to maximum observed concentration (t_{max})

Additional PK parameters may be determined if deemed appropriate.

9.6.2 Pharmacokinetic Concentration Data Analyses

A by-patient listing of all concentration-time data for each treatment will be presented.

Concentration data of ANB020 will be summarized by treatment and nominal time point using the number of observations (n) and number of observations ≥lower limit of quantification (LLOQ), arithmetic mean, SD, coefficient of variation (CV), minimum, median, and maximum.

Graphs of concentration-time data may be added at the discretion of the PK scientist, as appropriate, and will be described in detail in the SAP.

9.6.3 Pharmacokinetic Parameter Data Analyses

All PK parameters will be summarized by treatment using n, arithmetic mean, SD, CV, minimum, median, maximum, geometric mean (Gmean), and geometric CV (gCV) defined as

$$100 \cdot \sqrt{\left(\exp\left(s^2\right)-1\right)}$$

where 's' is the SD of the data on a log scale, except that t_{max} will be reported with n, minimum, median, and maximum only.

Graphs of parameters may be added at the discretion of the PK scientist, as appropriate, and will be described in detail in the SAP.

9.7 Pharmacodynamic Analyses

Observed and relative change from baseline for circulating cytokines, differential WBC counts (circulating leukocytes), and cytokine levels released from pathogenic T-cells (ex vivo whole blood peanut response assay) will be summarized with descriptive statistics including 95% CIs for the mean by nominal time point and treatment. Graphical summaries will be generated, as appropriate.

Graphs of PD data may be added, as appropriate, and will be described in detail in the SAP.

For secondary and exploratory continuous PD endpoints, change from baseline will be evaluated where possible. Actual and change in data from baseline will be summarized descriptively for each treatment. Comparison between ANB020 and placebo will be performed using a mixed-effect model with treatment, time point of measurement, and treatment by time point interaction as fixed effects, and baseline results as a covariate. Appropriate correlation matrix will be used. Treatment differences will be presented with corresponding p-values for the test of no difference and 95% CI. Graphical summaries will be generated, as appropriate. Log transformations may be applied as appropriate.

9.8 Interim Analyses

No interim analysis is planned for this study.

10.0 ETHICS

10.1 Institutional Review Board

An IRB should approve the final protocol, including the final version of the Informed Consent Form (ICF) and any other written information and/or materials to be provided to the patients. The Investigator will provide AnaptysBio or QuintilesIMS with documentation of IRB approval of the protocol and informed consent before the study may begin at the study center. The Investigator should submit the written approval to AnaptysBio or representative before enrolment of any patient into the study.

AnaptysBio or representative should approve any modifications to the ICF that are needed to meet local requirements.

The Investigator will supply documentation to AnaptysBio or QuintilesIMS of required IRB's annual renewal of the protocol, and any approvals of revisions to the informed consent document or amendments to the protocol.

The Investigator will report promptly to the IRB, any new information that may adversely affect the safety of patients or the conduct of the study. Similarly, the Investigator will submit written summaries of the study status to the IRB as per IRB's requirements. Upon completion of the study, the Investigator will provide the IRB with a brief report of the outcome of the study, if required.

AnaptysBio or representative will handle the distribution of any of these documents to the national regulatory authorities.

QuintilesIMS or a representative will provide Regulatory Authorities, IRB, and Investigators with safety updates/reports according to local requirements, including Suspected Unexpected Serious Adverse Reactions, where relevant.

Each Investigator is responsible for providing the IRB with reports of any serious and unexpected adverse drug reactions from any other study conducted with the IP. QuintilesIMS or a representative will provide this information to the Investigator so that he/she can meet these reporting requirements.

10.2 Ethical Conduct of the Study

This study will be conducted and the informed consent will be obtained according to the ethical principles stated in the Declaration of Helsinki (2008), the applicable guidelines for GCP, or the applicable drug and data protection laws and regulations of the countries where the study will be conducted.

10.3 Patient Information and Informed Consent

The ICF will be used to explain the risks and benefits of study participation to the patient in simple terms before the patient will be entered into the study. The informed consent form contains a statement that the consent is freely given, that the patient is aware of the risks and benefits of entering the study, and that the patient is free to withdraw from the study at any time. Written consent must be given by the patient and/or legal representative, after the receipt of detailed information on the study.

The Investigator is responsible for ensuring that informed consent is obtained from each patient or legal representative and for obtaining the appropriate signatures and dates on the informed consent document prior to the performance of any protocol procedures and prior to the administration of IP. The Investigator will provide each patient with a copy of the signed and dated ICF.

10.4 Patient Data Protection

Patient data generated through the study is the property of Sponsor and disclosure to third parties is not permitted other than as per Health Insurance Portability and Accountability Act (HIPAA) provisions.

At the patient's request, medical information may be given to his/her personal physician or other appropriate medical personnel responsible for his/her welfare.

Data generated by this study must be available for inspection on request by the representatives of Health Authorities, Sponsor, and IRB, if appropriate. The Investigator must ensure that each subject's anonymity is maintained.

10.5 Procedures for Premature Termination or Suspension of the Study or the Participation of Investigational Site(s)

In the event that the Sponsor, an IRB, or regulatory authority elects to terminate or suspend the study (due to such events as, but not limited to new information becomes available that may negatively impact patient safety, IP integrity, withdrawal of IND), a study-specific procedure for early termination or suspension will be provided by the Sponsor; the procedure will be followed by applicable investigational sites during the course of termination or study suspension.

11.0 STUDY ADMINISTRATION

11.1 ADMINISTRATIVE STRUCTURE

Table 11.1 Administrative Structure

Sponsor AnaptysBio Inc. 10421 Pacific Center Ct Suite 200 San Diego, CA 92121 United States	**Drug Safety Monitoring** QuintilesIMS Customer Safety Services Global Data & Safety Monitoring 5927 S. Miami Blvd. Morrisville, NC 27560 United States
Clinical Study Supply Management Investigational Product AnaptysBio Inc. 10421 Pacific Center Ct Suite 200 San Diego, CA 92121 United States	**Clinical Study Supply Management Other than Investigational product** QuintilesIMS 10188 Telesis Court, Suite 400 San Diego, CA 92121 United States
Data Management QuintilesIMS Data Management Etamin Block (Building B3) Prestige Technology Park II Sarjapur-Marathalli Outer Ring Road Bangalore - 560103 India	**Biostatistics** QuintilesIMS 12th Floor, G-Corp Tech Park Ghodbunder Road, Kasarwadawli, Thane (West) Thane - 400 607 India
Study Monitoring QuintilesIMS 10188 Telesis Court, Suite 400 San Diego, CA 92121 United States	**Medical Writing** QuintilesIMS Global Medical Writing and Document Publishing 12th Floor, G-Corp Tech Park Ghodbunder Road, Kasarwadawli, Thane (West) Thane - 400 607 India
Medical Monitoring AnaptysBio Inc. 10421 Pacific Center Ct Suite 200 San Diego, CA 92121 United States	

11.2 Data Handling and Record Keeping

The Investigator must maintain essential study documents (protocol and protocol amendments, completed eCRFs, signed ICFs, relevant correspondence, and all other supporting documentation). The study center should plan on retaining such documents for approximately 15 years after study completion. The study center should retain such documents until at least 2 years after the last approval of a marketing application in an ICH region and until there are no

pending or contemplated marketing applications in an ICH region or at least 2 years after the formal discontinuation of clinical development of the IP. These documents should be retained for a longer period if required by the applicable regulatory requirements or the hospital, institution, or private practice in which the study is being conducted. Patient identification codes (patient names and corresponding study numbers) will be retained for this same period of time. These documents may be transferred to another responsible party, acceptable to AnaptysBio, who agrees to abide by the retention policies. Written notification of transfer must be submitted to AnaptysBio. The Investigator must contact AnaptysBio prior to disposing of any study records.

11.3 Direct Access to Source Data/Documents

The Investigator will prepare and maintain adequate and accurate source documents to record all observations and other pertinent data for each patient randomized into the study.

The Investigator will allow AnaptysBio, QuintilesIMS, and authorized regulatory authorities to have direct access to all documents pertaining to the study, including individual patient medical records, as appropriate. Such information must be kept confidential and must have locked facilities that allow for this. Patient identification number and not the patient's name will be recorded on all documents related to the study.

11.4 Investigator Information

11.4.1 Investigator Obligations

This study will be conducted in accordance with the ICH Harmonized Tripartite Guideline for GCP (GCP, 1997), European Legislation; and the ethical principles that have their origin in the Declaration of Helsinki.

The Investigator is responsible for ensuring that all study center personnel, including Sub-Investigators, adhere to all applicable regulations and guidelines, including local laws and regulations, regarding the study, both during and after study completion. The Investigator is responsible for informing the IRB of the progress of the study and for obtaining annual IRB renewal. The Investigator is responsible for informing the IRB of completion of the study and will provide the IRB with a summary of the results of the study.

11.4.2 Protocol Signatures

After reading the protocol, each Investigator will sign the protocol signature page and send a copy of the signed page to AnaptysBio or representative (Section 17.0). By signing the protocol, the Investigator confirms in writing that he/she has read, understands and will strictly adhere to the study protocol and will conduct the study in accordance with ICH Guidelines for GCP and

applicable regulatory requirements. The study will not be able to start at any center where the Investigator has not signed the protocol.

11.4.3 Publication Policy

The data generated by this study are confidential information of AnaptysBio. AnaptysBio will make the results of the study publicly available. The publication policy with respect to the Investigator and study center will be set forth in the Clinical Trial Agreement.

11.5 Financing and Insurance

AnaptysBio will provide insurance in accordance with local guidelines and requirements as a minimum for the patients participating in this study. The terms of the insurance will be kept in the study files.

12.0 REFERENCES

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13.0 APPENDIX I

Global Initiative for Asthma Assessment of symptom control

A. Symptom Control	Level of Asthma Symptom Control		
In the past 4 weeks, has the patient had:	Well-controlled	Partially controlled	Uncontrolled
.Daytime asthma symptoms more than twice a week? Yes☐ No ☐	None of these	1-2 of these	3-4 of these
.Any night waking due to asthma? Yes ☐ No ☐			
.Reliever needed for symptoms more than twice a week? Yes☐ No ☐			
.Any activity limitation due to asthma? Yes☐ No ☐			

14.0 APPENDIX II

Oral Food Challenge Symptom Scoring Assessment Tool

Category	Grade	Symptoms
Skin		
Rash	Grade 0:	Sign or symptom not observed
	Grade 1:	Few areas of faint erythema
	Grade 2:	Areas of erythema, macular and raised rash
	Grade 3:	Generalized marked erythema (>50%); extensive raised lesion (>25%); vesiculation and/or piloerections
Pruritus	Grade 0:	Sign or symptom not observed
	Grade 1:	Occasional scratching
	Grade 2:	Scratching continuously for >2 minutes at a time
	Grade 3:	Hard continuous scratching leading to excoriations
Urticaria	Grade 0:	Sign or symptom not observed
	Grade 1:	<3 Hives
	Grade 2:	3 to <10 Hives
	Grade 3:	Generalized involvement
Angioedema	Grade 0:	Sign or symptom not observed
	Grade 1:	One site of angioedema
	Grade 2:	Two or more sites of angioedema
	Grade 3:	Generalized involvement, including airway involvement
Nasal		
Sneezing	Grade 0:	Sign or symptom not observed
	Grade 1:	Rare bursts of sneezing
	Grade 2:	<10 bursts of sneezing

Category	Grade	Symptoms
	Grade 3:	Continuous rubbing of nose and/or eyes; periocular swelling and/or long bursts of sneezing
Nasal itching	Grade 0:	Sign or symptom not observed
	Grade 1:	Mild itching
	Grade 2:	Intermittent rubbing of nose or eyes
	Grade 3:	Continuous rubbing of nose and/or eyes; periocular swelling and/or long bursts of sneezing
Nasal congestion	Grade 0:	Sign or symptom not observed
	Grade 1:	Some hindrance to breathing
	Grade 2:	Nostrils feel blocked, breathes through mouth most of the time
	Grade 3:	Nostrils occluded
Rhinorrhea	Grade 0:	Sign or symptom not observed
	Grade 1:	Occasional sniffing
	Grade 2:	Frequent sniffing, requires tissues
	Grade 3:	Nose runs freely despite sniffing and tissues
Airway obstruction	Grade 0:	Sign or symptom not observed
	Grade 1:	Voice change mild
	Grade 2:	Voice change moderate
	Grade 3:	Voice change severe or hoarseness or stridor
Chest		
Wheezing	Grade 0:	Sign or symptom not observed
	Grade 1:	Expiratory wheezing to auscultation or 15% decrease from highest FEV1 value observed on study or FEV1 ≤65%
	Grade 2:	Dyspnea, inspiratory, and expiratory wheezing

Category	Grade	Symptoms
	Grade 3:	Dyspnea, use of accessory muscles, audible wheezing
Abdomen		
Nausea	Grade 0:	Sign or symptom not observed
	Grade 1:	Mild complaint of nausea
	Grade 2:	Frequent complaint of nausea
	Grade 3:	Nausea causing notable distress
Abdominal pain	Grade 0:	Sign or symptom not observed
	Grade 1:	Complaint of abdominal pain
	Grade 2:	Frequent complaints of abdominal pain, decreased activity
	Grade 3:	In bed, crying, or notably distressed
Emesis	Grade 0:	Sign or symptom not observed
	Grade 1:	1 Episode of emesis
	Grade 2:	2-3 Episodes of emesis or 1 of emesis and 1 of diarrhea
	Grade 3:	>3 Episodes of emesis or ≥2 of emesis and ≥2 of diarrhea
Diarrhea	Grade 0:	Sign or symptom not observed
	Grade 1:	1 Episode of diarrhea
	Grade 2:	2–3 Episodes of diarrhea or 1 of emesis and 1 of diarrhea
	Grade 3:	>3 Episodes of diarrhea or ≥2 of emesis and ≥2 of diarrhea

Grade 1 = mild; Grade 2 = moderate, Grade 3 = severe

15.0 APPENDIX III

Guidelines for Discontinuation of Medications that might interfere with the Interpretation of Oral Food Challenge

Medication	**Last Dose before Oral Food Challenge**
Oral antihistamines	3-10 days
Cetirizine	5-7 days
Diphenhydramine	3 days
Fexofenadine	3 days
Hydroxyzine	7-10 days
Loratadine	7 days
Antihistamine nose spray	12 hours
Oral H2 receptor antagonist	12 hours
Antidepressants	3 days-3 weeks, drug-dependent and dose-dependent
Oral/intramuscular/intravenous steroids	3 days-2 weeks
Leukotriene antagonist	24 hours
Short-acting bronchodilator (albuterol, metaproterenol)	8 hours
Short-acting bronchodilator (terbutaline, isoproterenol)	24 hours
Long-acting bronchodilator (salmeterol, formoterol)	8 hours
Inhaled cromolyn sodium	48 hours
Nedocromil sodium	12 hours
Theophylline (liquid)	24 hours
Theophylline long-acting	48 hours
Ipratropium bromide (inhaled/intranasal)	4-12 hours depending on formulation and dosing
Oral/intranasal α-adrenergic agents	Interval
Oral β-agonist	12 hours
Oral long-acting β_2-agonist	24 hours
Drugs that may be continued	
Antihistamine eye drops	
Inhaled/intranasal corticosteroids	
Topical steroids	
Topical immunosuppressive preparations: pimecrolimus, tacrolimus	

16.0 APPENDIX IV

Standard Anaphylaxis Treatment Plan

Treatment of Anaphylaxis in the Physician's office		
Immediate Measures		
1	Allergen	Remove the inciting allergen, if possible
2	Airway	Assess airway, breathing, circulation, and orientation; if needed, support the airway using the least invasive but effective method (e.g., bag-valve-mask)
3	Cardiopulmonary resuscitation	Start chest compressions (100/min) if cardiovascular arrest occurs at any time
4	Epinephrine intramuscular	Inject epinephrine 0.3-0.5 mg (0.01 mg/kg for children) intramuscularly in the vastus lateralis (lateral thigh)
5	Get help	Summon appropriate assistance in office
6	Position	Place adults and adolescents in recumbent position; place young children in position of comfort; place pregnant patient on left side
7	Oxygen	Give 8-10 L/min through facemask or up to 100% oxygen as needed; monitor by pulse oximetry if available
7	Epinephrine intramuscular	Repeat intramuscular epinephrine every 5-15 min for up to 3 injections if the patient is not responding
6	EMS	Activate Emergency Medical Service (call 911 or local rescue squad) if no immediate response to first dose of intramuscular epinephrine or if anaphylaxis is moderate to severe (Grade ≥2 on World Allergy Organization grading scale)
7	Intravenous fluids	Establish intravenous line for venous access and fluid replacement; keep open with 0.9 normal saline, push fluids for hypotension or failure to respond to epinephrine using 5-10 mg/kg as quickly as possible and up to 30 mL/kg in first hour for children and 1-2 L for adults
Additional Measures		
8	Albuterol	Consider administration of 2.5-5 mg of nebulized albuterol in 3 mL of saline for lower airway obstruction; repeat as necessary every 15 min
9	Glucagon	Patients on β-blockers who are not responding to epinephrine should be given 1-5 mg of glucagon intravenously slowly over 5 min because rapid administration of glucagon can induce vomiting

10	Epinephrine infusion	For patients with inadequate response to intramuscular epinephrine and intravenous saline, give epinephrine by continuous infusion by micro-drip in office setting (infusion pump in hospital setting); add 1 mg (1 mL of 1:1,000) of epinephrine to 1,000 mL of 0.9 normal saline; start infusion at 2 µg/min (2 mL/min=120 mL/h) and increase up to 10 µg/min (10 mL/min=600 mL/h); titrate dose continuously according to blood pressure, cardiac rate and function, and oxygenation
11	Intraosseous access	If intravenous access is not readily available in patients experiencing refractory anaphylaxis, obtain intraosseous access for administration of intravenous fluids and epinephrine infusion
Refractory anaphylaxis		
12	Advanced airway management	Use supraglottic airway, endotracheal intubation, or cricothyroidotomy for marked stridor, severe laryngeal edema, or when ventilation using the bag-valve-mask is inadequate and Emergency Medical Service has not arrived
13	Vasopressors	Consider administration of dopamine (in addition to epinephrine infusion) if patient is unresponsive to above treatment; this will likely be in the hospital setting where cardiac monitoring is available
Optional treatment (efficacy has not been established)		
14	H_1 antihistamine	Consider giving 25-50 mg of diphenhydramine intravenously for adults and 1 mg/kg (maximum 50 mg) for children; use 10 mg of cetirizine if an oral antihistamine is administered; once there is full recovery, there is no evidence that this medication needs to be continued
15	Corticosteroids	Administer 1-2 mg/kg up to 125 mg per dose, intravenously or orally, of methylprednisolone or an equivalent formulation; once there is full recovery, there is no evidence that this medication needs to be continued
Observation and monitoring		
16	Observation in hospital	Transport to emergency department by EMS for further treatment and observation for 8 hours
17	Observation in office	Observe in office until full recovery +additional 30-60 min for all patients who are not candidates for Emergency Medical Service transport to emergency department
Discharge management		
18	Education	Educate patient and family on how to recognize and how to treat anaphylaxis

19	Auto-injectable epinephrine	Prescribe 2 doses of auto-injectable epinephrine for patients who have experienced an anaphylactic reaction and for those at risk for severe anaphylaxis; train patient, patient provider, and family on how to use the auto-injector
20	Anaphylaxis action plan	Provide patients with an action plan instructing them on how and when to administer epinephrine

EMS = Emergency Medical Service

17.0 APPENDIX 1: SIGNATURE OF INVESTIGATOR

PROTOCOL TITLE: Placebo-Controlled Proof of Concept Study to Investigate ANB020 Activity in Adult Patients with Peanut Allergy

PROTOCOL NO: ANB020-003

This protocol is a confidential communication of AnaptysBio. I confirm that I have read this protocol, I understand it, and I will work according to this protocol. I will also work consistently with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practices and the applicable laws and regulations. Acceptance of this document constitutes my agreement that no unpublished information contained herein will be published or disclosed without prior written approval from AnaptysBio.

Instructions to the Investigator: Please SIGN and DATE this signature page. PRINT your name, title, and the name of the center in which the study will be conducted. Return the signed copy to QuintilesIMS.

I have read this protocol in its entirety and agree to conduct the study accordingly:

Signature of Investigator: _____ Date: _____

Printed Name: _____

Investigator Title: _____

Name/Address of Center: _____

_____

_____

18.0 APPENDIX 2: PHARMACOKINETIC/WHOLE BLOOD (SERUM) BIOMARKER TIME POINTS

Study Visit	Pharmacokinetic Sample Time Point (Serum)	Sample Time Point for Biomarker Whole Blood collection for Ex vivo Peanut Challenge (Stanford Univ Only)	Sample Time Point for Leukocytes (Whole blood)	Sample Time point for Biomarker serum collection for Cytokines
Screening (Day-7 to -14)		Screening Peanut ex vivo whole blood sample to be obtained (Baseline) prior to administration of BPCFC[d]	Collect Prior to administration of BPCFC[a]	Collect Prior to administration of BPCFC
Day 1 ANB020 Dosing	Pre-Dose (-≤30 minutes)			
	0.50 hours (±5 minutes) post-start of infusion			
	EOI (+≤3 minutes)			
	EOI+3 hours (±10 minutes)			
Day 2	24 hours (±2 hours) post-start of infusion	24 hours (±2 hours) post-start of infusion	24 hours (±2 hours) post-start of infusion	24 hours (±2 hours) post-start of infusion
Day 5	96 hours (±2 hours) post-start of infusion	96 hours (±2 hours) post-start of infusion	96 hours (±2 hours) post-start of infusion	96 hours (±2 hours) post-start of infusion
Day 15[b]	336 hours (+112 hours) post-start of infusion		336 hours (+112 hours) post-start of infusion	336 hours (+112 hours) post-start of infusion
Day 45[c]	1,056 hours (±48 hours) post-start of infusion. Sample to be obtained prior to administration of BPCFC.		1,056 hours (±48 hours) post-start of infusion. Sample to be obtained prior to administration of BPCFC.	

Abbreviation: EOI = actual time of end of infusion, BPCFC = blind placebo-controlled food challenge.

a Leukocytes will be obtained as part of hematology safety laboratory panel at screening, Day 2, and Day 45/ET. On Day 5 and Day 15, whole blood samples for leukocytes will be collected separately as there is no safety laboratory assessment on Day 5 and Day 15.

b If the Investigator decides to complete the BPCFC in 2 days, the blood samples scheduled on Day 15 will be collected on Day 16. If the Investigator decides to utilize the +4 day visit window for Day 14 and separate the two challenges to occur over two consecutive days, the blood samples will be collected the day after the last BPCFC challenge.

c If the patient discontinues from study before Day 45 and returns to site for early termination (ET) visit, the PK sample will be collected at ET visit.

d If necessary, the sample for ex vivo peanut challenge assay can be collected on Day 1 (prior to IP administration) instead of the screening visit.

19.0 APPENDIX 3: SUMMARY OF CHANGES

Protocol ANB020-003: Amendment 5, 01 DEC 2017

Replaces: Amendment 4, 06 OCT 2017

1. Study Synopsis- Pages 3, 4, 5:
    a. Description of Change: Changing study duration to 66 days and screening period to 21 days
    Purpose of Change: Allow time and flexibility for screening procedures

    Description of Change: Add "Informed consent must be obtained prior to participation in the study."

    Purpose of Change: To clarify the Informed consent can be obtained prior to the screening visit.

    b. Description of Change: Remove the requirement of the Day 45 BPCFC if an objective reaction occurred at Day 14/15.
    Purpose of Change: For patient safety, not requiring the Day 45 BPCFC if a reaction was observed at the Day 14/15 BPCFC. The Investigator may decide to conduct the BPCFC per his/her discretion.

    c. Description of Change: Changed "either peanut or placebo" to placebo.
    Purpose of Change: To clarify that subjects would receive placebo challenge first.

2. Summary of Study Design - Pages 21, 22:
    a. Description of Change: Add "Informed consent must be obtained prior to participation in the study."
    Purpose of Change: To clarify the Informed consent can be obtained prior to the screening visit.

    b. Description of Change: Remove the requirement of the Day 45 BPCFC if an objective reaction occurred at Day 14/15.
    Purpose of Change: For patient safety, not requiring the Day 45 BPCFC if a reaction was observed at the Day 14/15 BPCFC. The investigator may decide to conduct the BPCFC per his/her discretion.

    c. Description of Change: Changed "either peanut or placebo" to placebo.
    Purpose of Change: To clarify that subjects would receive placebo challenge first.

3. Figure 4.1: Schematic of Study Design for protocol ANB020-003 –Page 24:
    a. Description of Change: Changing screening period to 21 days
    Purpose of Change: Allow time and flexibility for screening procedures

b. Description of Change: Remove the requirement of the Day 45 BPCFC if an objective reaction occurred at Day 14/15.

Purpose of Change: For patient safety, not requiring the Day 45 BPCFC if a reaction was observed at the Day 14/15 BPCFC. The investigator may decide to conduct the BPCFC per his/her discretion.

c. Description of Change: Changed "either peanut or placebo" to placebo.
Purpose of Change: To clarify that subjects would receive placebo challenge first.

4. Table 4.1: Schedule of Events – Page 25, 26:
   a. Description of Change: Changing screening period to 21 days
   Purpose of Change: Allow time and flexibility for screening procedures

   b. Description of Change: Add "Informed consent must be obtained prior to participation in the study."
   Purpose of Change: To clarify the Informed consent can be obtained prior to the screening visit.

   c. Description of Change: Remove the requirement of the Day 45 BPCFC if an objective reaction occurred at Day 14/15.

   Purpose of Change: For patient safety, not requiring the Day 45 BPCFC if a reaction was observed at the Day 14/15 BPCFC. The investigator may decide to conduct the BPCFC per his/her discretion.

5. Section 6.0: Study Procedures – Page 37:
   a. Description of Change: Change the visit window to + 4 days for Day 14/15.
   Purpose of Change: To provide flexibility to accommodate subject schedules.

6. Section 6.1: Screening – Page 37:
   a. Description of Change: Add "Informed consent must be obtained prior to participation in the study."
   Purpose of Change: To clarify the Informed consent can be obtained prior to the screening visit.

7. Section 6.2.3: Day 2 to Day 15 – Page 40:
   a. Description of Change: Changed "either peanut or placebo" to placebo.
   Purpose of Change: To clarify that subjects would receive placebo challenge first.

8. Section 6.2.5: End of Study – Page 41:
   a. Description of Change: Remove the requirement of the Day 45 BPCFC if an objective reaction occurred at Day 14/15.

Purpose of Change: For patient safety, not requiring the Day 45 BPCFC if a reaction was observed at the Day 14/15 BPCFC. The investigator may decide to conduct the BPCFC per his/her discretion.

9. Appendix 2: Pharmacokinetic/Whole Blood Serum) Biomarker Time Points– Page 77, 78:
    a. Description of Change: Change window from ±16 hours to +112 hours
    Purpose of Change: To provide flexibility to accommodate subject schedules and to be consistent with the visit window. This timing accommodates the +4 day window and +16 hours if the food challenges are separated into two days.
    b. Description of Change: Add "If the Investigator decides to utilize the +4 day visit window for Day 14 and separate the two challenges to occur over two consecutive days, the blood samples will be collected the day after the last BPCFC challenge."
    Purpose of Change: To clarify the expected timing of the blood sample collection if the food challenges are separated into two consecutive days and the +4 day visit window is implemented for the Day 14 visit.

Protocol ANB020-003: Amendment 4, 06 OCT 2017

Replaces: Amendment 3, 30 JUN 2017

10. Study Synopsis- Pages 3, 4, 5:
    a. Description of Change: Remove investigator name.
    Purpose of Change: Allow for the addition of new sites.

    b. Description of Change: Remove Study Center Details: Remove Stanford's Address and indicate conducted at up to 3 study centers in US.
    Purpose of Change: Allow for the addition of new sites.

    c. Description of Change: Exploratory Endpoints, Methodology, Summary, and Exploratory Pharmacodynamic Endpoints: Specify ex-vivo peanut challenge is only to be collected and assessed for those patients treated at Stanford University.
    Purpose of Change: AnaptysBio determined that additional, non-Stanford study sites (i.e., "new sites"), will not collect blood samples for the ex-vivo peanut challenge assay as it was developed specific to the local laboratory as an exploratory endpoint.
11. Section 3.3: Exploratory Objectives – Page 20:
    a. Description of Change: Add "Stanford University Only".

Purpose of Change: To clarify the ex vivo peanut antigen challenge is for Stanford University only. New Sites will not conduct ex vivo peanut antigen challenge.

12. Section 4.1: Summary of Study Design – Page 2, 21:
    a. Description of Change: Add "Stanford University patients".
    Purpose of Change: To clarify the ex vivo peanut antigen challenge is for Stanford University only. New Sites will not collect/evaluate immune response to peanut upon ex vivo peanut antigen.

    b. Description of Change: Add "Stanford University patients" at screening.
    Purpose of Change: To clarify the ex vivo peanut antigen challenge is for Stanford University only. New Sites will not collect/evaluate immune response to peanut upon ex vivo peanut antigen.

    c. Description of Change: Add "Stanford University patients" on Day 2 and 5.
    Purpose of Change: To clarify the ex vivo peanut antigen challenge is for Stanford University only. New Sites will not collect/evaluate immune response to peanut upon ex vivo peanut antigen.

13. Figure 4.1: Schematic of Study Design for protocol ANB020-003 –Page 24:
    a. Description of Change: Add "Stanford University patients" at screening and on Day 2 and 5.
    Purpose of Change: To clarify the ex vivo peanut antigen challenge is for Stanford University only. New Sites will not collect/evaluate immune response to peanut upon ex vivo peanut antigen.

14. Table 4.1: Schedule of Events – Page 25, 26:
    a. Description of Change: Ex vivo Peanut challenge Assay will specify "Stanford University Only" and footnote will be updated accordingly.
    Purpose of Change: To clarify the ex vivo peanut antigen challenge is for Stanford University only. New Sites will not collect/evaluate immune response to peanut upon ex vivo peanut antigen.

15. Section 6.0: Study Procedures – Page 37:
    a. Description of Change: Add "collected from Stanford University patients"
    Purpose of Change: To specify that screening ex vivo blood draw window only applies to Stanford University. New Sites will not collect/evaluate immune response to peanut upon ex vivo peanut antigen.

16. Section 6.1: Screening – Page 37:

a. Description of Change: Specify screening ex-vivo blood draw does not apply to New Sites.
Purpose of Change: New Sites will not collect/evaluate immune response to peanut upon ex vivo peanut antigen.

17. Section 6.2.1: Blood Volume – Page 39:
a. Description of Change: Update total blood draw volume for Stanford patients (177 mL) and non-Stanford patients (147 mL).
Purpose of Change: To indicate decreased total blood draw volume for patients at non-Stanford sites.

18. Table 6.1: Blood Volume Sampling During Each Visit – Page 40:
a. Description of Change: Separate Stanford and new sites total blood volume. New Sites will have decreased volume of blood drawn (-10mL) at Screening, Day 2, and Day 5.
Purpose of Change: To indicate decreased total blood draw volume for patients at non-Stanford sites.

Visits	**Screening**	**Day 1 Predose**	**Day 1 Predose (PK)**	**Day 1 (0.5H) (PK)**	**Day 1 (EOI) (PK)**	**Day 1 (EOI 3H) (PK)**	**Day 2**	**Day 5**	**Day 14**	**Day 15/16**	**Day 45**
Stanford Univ. Only Total blood volume sampled during each visit (mLs)	up to 41 (31-41)[a]	up to 22 (12-22)[a]	5	5	5	5	34	25.5	12	15.5	17
Total blood volume sampled during each visit (mLs)	31	12	5	5	5	5	24	15.5	12	15.5	17

19. Section 6.2.2: Day 1 (Randomization) – Page 40:
a. Description of Change: Add “collected from Stanford University patients”.
Purpose of Change: To specify that screening ex vivo blood draw window only applies to Stanford University. New Sites will not collect/evaluate immune response to peanut upon ex vivo peanut antigen.

20. Section 7.2: Pharmacodynamics – Page 49:
a. Description of Change: Addition of “collected from Stanford University patients”.
Purpose of Change: All reference to the ex vivo peanut antigen challenge, whole blood samples and cytokine levels will only apply to samples collected from patients treated at Stanford University.

21. Appendix 2: Pharmacokinetic/Whole Blood Serum) Biomarker Time Points– Page 77:
    a. Description of Change: Add "Stanford University Only" to the Sample Time Point for biomarker whole blood collection for Ex vivo Peanut Challenge
    Purpose of Change: To clarify the ex vivo peanut antigen challenge is for Stanford University only. New Sites will not conduct ex vivo peanut antigen challenge.

Protocol ANB020-003: Amendment 3, 30 JUN 2017

Replaces: Amendment 2, 18 MAY 2017

1. Inclusion Criteria
    a. Description of change: Increased maximum BMI from 32 to 36 kg/m2
    Purpose of change: Updated BMI to reflect acceptable weight range of patient population.
2. Exclusion Criteria
    a. Description of change: Specified immunotherapy to allergens (excluding peanut) is only excluded during build-up phase of treatment (before reaching maintenance dosing).
    Purpose of change: To allow treatment of typical allergens that will not affect study data or patient safety.
3. Section 5.8.1 (Excluded Medications)
    a. Description of change: Updated timelines for excluded medication use to reflect the changes in the exclusion criteria.
    Purpose of change: To accurately reflect exclusion criteria allowing treatment of typical allergens that will not affect study data or patient safety

Protocol ANB020-003: Amendment 2, 18 MAY 2017

Replaces: Amendment 1, 01 DEC 2016

1. Synopsis
    a. Description of Change: Added oral blind placebo-controlled food challenge (BPCFC) on Day 45 (End of Study [EOS] visit).
    Purpose for Change: The Day 45 oral BPCFC was added to ascertain duration of ANB020 response in peanut allergy.
    b. Description of Change: Updated primary and secondary objectives to specify Day 14.
    Purpose for Change: To differentiate primary and secondary objectives from the new exploratory objectives.
    c. Description of Change: Added new exploratory objectives.

Purpose for Change: To reflect the changes in the study design (to reflect addition of BPCFC on Day 45).

d. Description of Change: Updated methodology to include details about BPCFC on Day 45 (EOS visit) and corresponding procedures.
Purpose for Change: To reflect the changes in the study design.

e. Description of Change: Added text regarding other EOS visit procedures to perform on Day 45.
Purpose for Change: To provide clarity for performing other EOS visit procedures on Day 45.

f. Updated primary and secondary efficacy endpoints to specify Day 14.
Purpose for Change: To differentiate primary and secondary efficacy endpoints from the new exploratory efficacy endpoints.

g. Description of Change: Added exploratory efficacy endpoints to assess on Day 45.
Purpose for Change: To reflect the changes in the study design (to reflect addition of BPCFC on Day 45).

h. Description of Change: Updated statistical analysis methods for primary and secondary endpoints and added statistical analysis methods for new exploratory endpoints.
Purpose for Change: To reflect the appropriate statistical analysis methods for endpoints based on the changes in the study design.

2. Section 3.0 (Study Objectives)
   a. Description of Change: Updated primary and secondary objectives to specify Day 14.
   Purpose for Change: To differentiate primary and secondary objectives from the new exploratory objectives.
   b. Description of Change: Added new exploratory objectives.
   Purpose for Change: To reflect the changes in the study design (to reflect addition of BPCFC on Day 45).

3. Section 4.1 (Summary of Study Design)
   a. Description of Change: Updated study design to include details about BPCFC on Day 45 (EOS visit) and corresponding procedures.
   Purpose for Change: To reflect the changes in the study design (to reflect addition of BPCFC on Day 45).
   b. Description of Change: Added text regarding other EOS visit procedures to perform on Day 45.

Purpose for Change: To provide clarity for performing other EOS visit procedures on Day 45.

4. Figure 4.1
    a. Description of Change: Added BPCFC and other assessments on Day 45 (EOS visit) and added additional Day 46 visit to complete the BPCFC if the Investigator decides to split the food challenges into 2 days.
    Purpose for Change: To reflect the changes in study design (to reflect addition of BPCFC on Day 45).
    b. Description of Change: Added footnotes regarding details and assessments related to BPCFC as well as other assessments on Day 45 and Day 46.
    Purpose for Change: To provide clarity for assessments related to BPCFC as well as other assessments on Day 45 and Day 46.

5. Table 4.1 (Schedule of Events)
    a. Description of Change: Added BPCFC on Day 45 and corresponding procedures with appropriate footnotes.
    Purpose for Change: To reflect the changes in study design.
    b. Description of Change: Added Day 46 visit to complete the BPCFC and corresponding procedures if the Investigator decides to split the food challenges into 2 days.
    Purpose for Change: To reflect the changes in study design.
    c. Description of Change: Updated footnote ‘e’ to increase the window period for collecting the blood sample for ex vivo peanut challenge assay.
    Purpose for Change: Increased collection window allows flexibility for laboratories to process the blood samples.
    d. Description of Change: Modified footnote ‘i’ to clarify spirometry or peak flow collection language.
    Purpose for Change: To provide clarity for spirometry or peak flow collection time points for patients with a history of asthma.
    e. Description of Change: Added footnotes ‘m’ and ‘n’ to provide instructions for BPCFC procedures as well as other procedures on Day 45 and Day 46 visit.
    Purpose for Change: To provide guidance regarding study procedures on Day 45 and 46 if the BPCFC is split into 2 days.
    f. Description of Change: Added footnote ‘o’ to provide instruction for early termination BPCFC and updated early termination (ET) visit header to include reference to footnote ‘o’.

Purpose for Change: To provide guidance on when to conduct the BPCFC if a patient terminates from the study before completing all study visits.

6. Section 4.2 (Discussion of Study Design)
    a. Description of Change: Added Day 45 BPCFC in the study design.
    Purpose for Change: To reflect the changes in the study design.

7. Section 4.3.2 (Exclusion Criteria)
    Description of Change:
    a. Updated exclusion criteria: Decreased restriction for use of systemic corticosteroids, nonsteroidal, immunosuppressant, or immunomodulating drugs treatments from 8 weeks before screening to 2 weeks before screening.
    b. Updated exclusion criteria: Decreased restriction for use of beta blockers, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, or calcium channel blockers from 4 weeks before screening to 2 weeks before screening.
    c. Updated exclusion criteria: Decreased restriction for use of biologics such as omalizumab or any other unconventional allergen immunotherapy from 12 months before screening to 6 months before screening.

    Purpose for Change: The timelines for prior use of treatments were determined to be excessive and review of half-lives allow for decreased timeframe.

8. Section 4.3.2 (Exclusion Criteria)
    Description of Change: Modified exclusion criteria to allow inclusion of asthma patients requiring Global Initiative for Asthma Assessment (GINA) treatment Step 3.
    Purpose for Change: Asthma is commonly found in patients with peanut allergy and affects much of the study population.

9. Section 5.7 (Blinding)
    Description of Change: Updated headings in section 5.7 to include unblinding information and provide details for unblinding procedures.
    Purpose for Change: To provide unblinding information and instruction should unblinding be necessary during the study.

10. Section 5.8.1 (Excluded Medications)
    Description of Change: Updated timelines for excluded medication use to reflect the changes in the exclusion criteria.

a. Decreased restriction for use of systemic corticosteroids, nonsteroidal, immunosuppressant, or immunomodulating drugs treatments from 8 weeks before screening to 2 weeks before screening.
b. Decreased restriction for use of beta blockers, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, or calcium channel blockers from 4 weeks before screening to 2 weeks before screening.
c. Decreased restriction for use of biologics such as omalizumab or any other unconventional allergen immunotherapy from 12 months before screening to 6-months before screening.

Purpose for Change: To reflect the changes regarding prior medication use in the exclusion criteria.

11. Section 6.0 (Study Procedures)
    a. Description of Change: Added a +1 day visit window for Day 14 visit and clarified the existing study window periods.
       Purpose for Change: To provide scheduling flexibility and to provide clarity for existing study windows.
    b. Description of Change: Added text regarding increased window period for collecting the blood sample for ex vivo peanut challenge assay.
       Purpose for Change: Increased collection window allows flexibility for laboratories to process blood samples.

12. Section 6.1.1 (Study Procedures: Oral Blind Placebo-Controlled Food Challenge)
    a. Description of Change: Added text regarding BPCFC to perform on Day 45.
       Purpose for Change: To reflect the changes in the study design.
    b. Description of Change: Modified text regarding administration of BPCFC.
       Purpose for Change: To allow trained study staff to administer OFC.
    c. Description of Change: Added “objective” to assessment of reaction related to the OCF Symptom Scoring Assessment.
       Purpose for Change: To ensure accurate dose is recorded on the OFC Symptom Scoring Assessment Tool.
    d. Description of Change: Deleted text regarding vital signs, physical examination, peak flow or spirometry, and clinical assessment during BPCFC.
       Purpose for Change: Updated text regarding vital signs, physical examination, peak flow or spirometry, and clinical assessment during BPCFC provided under next sub heading (in the following paragraph).

13. Section 6.1.1 (Oral Blind Placebo-Controlled Food Challenge -Criteria for Monitoring and Stopping the Oral Food Challenge)
    Description of Change: Clarified language explaining timing of study procedures (vital signs, physical examination, peak flow or spirometry, and clinical assessment using oral food challenge Symptom Scoring Assessment Tool) during BPCFC.
    Purpose for Change: To provide clarity regarding timing for assessments (vital signs, physical examination, peak flow or spirometry, and clinical assessment) during BPCFC.

14. Section 6.2.1 (Blood Volume)
    Description of Change: Updated blood volume to be collected at Screening and Day 1 (Pre-dose) and added corresponding footnote.
    Purpose for Change: To reflect the extended collection window for ex vivo peanut challenge assay either at screening or on Day 1 and footnote provides additional detail on potential blood volumes.

15. Section 6.2.2 (Day 1 Randomization)
    Description of Change: Added language to collect the blood sample for ex vivo peanut challenge assay on Day 1 if it was not collected during screening.
    Purpose for Change: To provide additional guidance regarding the blood sample collection window for ex vivo peanut challenge assay.

16. Section 6.2.5 (End of Study)
    a. Description of Change: Added Day 45/46 BPCFC and corresponding procedures.
       Purpose for Change: To reflect addition of BPCFC at Day 45.
    b. Description of Change: Added text to specify EOS visit blood samples to be collected on Day 45.
       Purpose for Change: To provide clarity for collecting EOS visit blood samples if visit requires two days.

17. Section 6.2.6 (Early Termination)
    Description of Change: Added instructions to perform BPCFC at the ET visit.
    Purpose for Change: To provide guidance on when to conduct the BPCFC if a patient terminates from the study before completing all study visits.

18. Section 7.1.1.1 (Reporting of Adverse Events)
    Description of Change: Removed repetitive language.
    Purpose for Change: To provide clarity on AE reporting procedures.

19. Section 7.1.3 (Vital Signs, Physical Findings, and Other Safety Assessments)

Description of Change: Clarified language explaining timing of study procedures (vital signs, physical examination, peak flow or spirometry, and clinical assessment using oral food challenge Symptom Scoring Assessment Tool) during BPCFC.
Purpose for Change: To provide clarity regarding timing for assessments (vital signs, physical examination, peak flow or spirometry, and clinical assessment) during BPCFC.

20. Section 7.4 (Efficacy)
    a. Description of Change: Added exploratory efficacy endpoints to assess on Day 45.
       Purpose for Change: To reflect the changes in the study design (to reflect addition of BPCFC on Day 45).
    b. Description of Change: Updated text regarding primary and secondary efficacy endpoints.
       Purpose for Change: To differentiate primary and secondary efficacy endpoints from the new exploratory efficacy endpoints.

21. Section 9.5 (Efficacy analysis)
    a. Description of Change: Updated statistical analysis methods for primary and secondary endpoints analysis and added statistical analysis methods for new exploratory endpoints.
       Purpose for Change: To reflect the appropriate statistical analysis methods for endpoints based on the changes in the study design.
    b. Description of Change: Added exploratory efficacy endpoints and clarified primary and secondary endpoints.
       Purpose for Change: To reflect the changes in the study design.

22. Section 18 (Appendix 2)
    a. Description of change: Added sample collection time points for Day 45 blood tests.
       Purpose for Change: To provide instruction for collecting the Day 45 blood samples prior to the BPCFC.
    b. Description of Change: Added footnote ‘d’ to reflect the window period for blood sample collection for ex vivo peanut challenge assay.
       Purpose for Change: Added to reflect the extended window period for blood sample collection for ex vivo peanut challenge assay either at screening or on Day 1.

23. Administrative Change

Description of Change: Updated Contract Research Organization (CRO) name from Quintiles to QuintilesIMS.
Purpose for Change: To reflect the updated CRO name.

Protocol ANB020-003: Amendment 1, 01 DEC 2016

Replaces: Original: 27 SEP 2016

1. Protocol Cover Page
   Description of Change: Removal of "EnduraCT No.: 2016 002539 14"
   Purpose of change: Information not necessary for U.S. only protocol.

2. Section 4.1; Table 4.1 (Schedule of Events)
   Description of Change: Added FSH at screening visit and additional footnote to indicate the criteria for testing FSH and collection visit.
   Purpose for Change: To include FSH in the screening safety laboratory assessment which was missing in the original protocol.

3. Section 6.2.1
   Description of change:
   a. Updated the total blood volume and modified the text to be "The total blood volume for each patient will be approximately 177 mL."
   b. Revised Table 6.1 (Blood Volume Sampling During Each Visit) to include the updated blood volume required on each study assessment day/visit.

   Purpose of change: To reflect the changes in the safety laboratory assessment and to reflect the changes in the amount of blood volume required for laboratory tests.

4. Section 7.1.2; Table 7.1 (Clinical Laboratory Parameters)
   Description of change: Added Immunoglobulins (IgA, IgG, IgM, IgE, and IgD) under hematology panel.

   Purpose for Change: To include immunoglobulins in the safety laboratory assessments which were missing in the original protocol.

5. Section 7.2
   Description of change: Updated the amount of blood volume required for pharmacodynamic test.
   Purpose for Change: To reflect the changes in the in the amount of blood required for pharmacodynamic laboratory test.