A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Imsidolimab (ANB019) in the Treatment of Subjects with Hidradenitis Suppurativa

Protocol Number: ANB019-208

Investigational New Drug (IND) Number: 136145

European Clinical Trials Database (EudraCT) Number: TBD

Sponsor Name: AnaptysBio, Inc.

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Sponsor Medical Expert and Signatory: [redacted]

Amendment 1

24 September 2021

SPONSOR SIGNATURE PAGE

I confirm that I have read and approved this protocol in its entirety and will comply with the obligations as detailed in all applicable regulations and guidelines (eg, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use [ICH] Good Clinical Practice [GCP] guidelines) and the protocol.

DocuSigned by:
[redacted]

24-SEP-2021

Date (DD-MMM-YYYY)

INVESTIGATOR'S AGREEMENT

PROTOCOL TITLE: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Imsidolimab (ANB019) in the Treatment of Subjects with Hidradenitis Suppurativa

PROTOCOL NO: ANB019-208

VERSION: Amendment 1

This protocol is a confidential communication of AnaptysBio, Inc. 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 GCP 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 Acceptance of this document constitutes my agreement that no unpublished information contained herein will be published or disclosed without prior written approval from AnaptysBio.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 (DD-MMM-YYYY) this signature page. PRINT your name, title, and the name of the study site in which the study will be conducted. Return the signed copy to AnaptysBio or designee.

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 Site: _____

_____

_____

_____

DOCUMENT HISTORY

DOCUMENT HISTORY	
Document	**Date**
Amendment 1	24 September 2021
Original Protocol (Version 1.0)	25 February 2021

Amendment 1

Date: 24 September 2021

Overall rationale for amendment:

This amendment was prepared to apply the following changes:

- To implement small editorial changes for correctness.
- To update the Sponsor's address.
- To add the Patient Global Impression of Bother (PGIB) questionnaire.
- To add the collection of the Fitzpatrick skin type at screening.
- To add collection of Smoking history at D1
- To clarify photography is an optional procedure rather than for documentation purposes only.
- To add a few exploratory efficacy endpoints.
- To remove the body mass index (BMI) limits from inclusion criterion 9.
- To clarify Inclusion Criterion 10 for male subjects and for a woman not of childbearing potential and a postmenopausal woman.
- To clarify Exclusion Criterion 4 regarding the use of systemic treatment.
- To clarify Exclusion Criterion 21 related to live and live-attenuated vaccines.
- To clarify that the tuberculosis test is to be done for all subjects at screening.
- To update the introduction with up-to-date information on current clinical studies.
- To clarify that the observation period is 30 minutes after each subcutaneous (SC) dose.
- To revise study treatment description and the needle position for injection.
- To clarify the procedure for subject's discontinuation in case of emergency unblinding.
- To clarify procedures in case of a subject's early withdrawal.
- To correct the blood pressure measurement to once rather than twice.
- To specify that a PK sample will not be collected postdose on Day 1.
- The order of assessments was updated to *recommended* rather than *specific*.
- Changed the response options for the Hidradenitis Suppurativa Physician's Global Assessment (HS-PGA) from "0 (clear) or 1 (minimal)" to "0 (inactive) or 1 (almost inactive)".
- Updated the exploratory endpoint to: "Proportion of subjects with ≥2-point reduction from Baseline on HS PGA at each visit".
- Changed the response options for the Patient Global Impression of Severity (PGIS) from "Clear skin" to "No activity".
- To specify the estimand to be considered in this study.
- To correct the definition of the Safety Analysis Set.
- To clarify that noncompartmental analysis (NCA) will not be performed for the pharmacokinetic (PK) analysis.
- To specify that if data permits, potential correlation may be analyzed between anti-drug antibody (ADA) levels, serum concentration, and safety and efficacy endpoints.
- To include that ADA incidences (overall, treatment-emergent, and treatment-boosted) will be summarized in the statistical section.

- To clarify that tubal ligation is an accepted method of contraception.
- To remove troponin from the biochemistry panel

Section # and Name	Description of Change	Brief Rationale
Global	Small editorial changes and corrections.	To add clarity and implement corrections to text
Title Page	To update the Sponsor's address.	Administrative changes for Amendment 1
Title Page; Document Header; Document History Table	To add Amendment 1 and date.	Administrative changes for Amendment 1
Investigator's Agreement	To add amendment number.	Administrative change for Amendment 1
Section 8.1.2 Patient Global Impression of Severity; Appendix 3 Patient Global Impression of Severity	Changed the response options for the PGIS from "C*lear skin*" to *"No activity".*	To clarify the response option should be "no activity" rather than "clear skin"
Abbreviations; Section 1.1 Synopsis; Section 1.3 Schedule of Activities; Section 3.3 Exploratory Objectives and Endpoints; Section 4.1 Overall Design; Section 8.1.3 Patient Global Impression of Bother; Section 9.4.7 Analysis of the Exploratory Endpoints; Appendix 4 Patient Global Impression of Bother	Added PGIB questionnaire and all corresponding endpoints.	To evaluate if signs and symptoms of hidradenitis suppurativa are bothersome for the subjects.
Section 1.3 Schedule of Activities; Section 8.3.1 Fitzpatrick Skin Type Classification; 10.1.9.1 Data Collection and Management Responsibilities; Appendix 12 Fitzpatrick Skin Type Classification	Added an evaluation of subjects' skin type using the Fitzpatrick skin type classification.	To evaluate subjects' skin pigment type.
Section 1.3 Schedule of Activities; Section 10.1.9.1 Data Collection and Management Responsibilities	Added collection of smoking history at D1	To allow for sub-population efficacy analyses based on smoking status
Section 1.3 Schedule of Activities; Section 8	Clarify that a PK sample will not be collected postdose on Day 1.	A PK sample within hours of the first SC dose is not necessary.
Section 1.3 Schedule of Activities; Section 8.3.3	The order of assessments was updated to *recommended* rather than *specific.*	To allow for some flexibility in order of assessments.
Section 1.1 Synopsis; Section 1.3 Schedule of Activities; Section 4.1 Overall Design; Section 8.3.2 Photography	Modified photography to be an optional procedure rather than for documentation purposes only.	To add photography as optional for all subjects at each visit.
Section 1.1 Synopsis; Section 3.3 Exploratory Objectives and Endpoints; Section 9.4.7 Analysis of the Exploratory Endpoints	• Added a few exploratory efficacy endpoints. • Updated the exploratory endpoint to: "Proportion of	To refine the exploratory efficacy analyses.

Section # and Name	Description of Change	Brief Rationale
	subjects with **≥2**-point reduction from Baseline on HS PGA at each visit". • Changed the response options for the HS-PGA from "0 (clear) or 1 (minimal)" to "0 (inactive) or 1 (almost inactive)".	
Section 1.1 Synopsis; Section 5.1 Inclusion Criteria	The BMI limits were removed from Inclusion Criterion 9.	To include HS population based on weight and not limit inclusion by BMI calculation.
Section 1.1 Synopsis; Section 5.1 Inclusion Criteria	Inclusion Criterion 10a updated to: *A male subject who has not had a vasectomy must agree to use contraception as detailed in Appendix 1….*	To clarify that male subjects who are sterile following a vasectomy do not need to use additional contraception method(s).
Section 1.1 Synopsis; Section 5.1 Inclusion Criteria	Added the following clarification to the Inclusion Criterion 10.b.ii: *A woman not of childbearing potential as defined in Appendix 1 is eligible to participate in the study. A postmenopausal woman must have a follicle stimulating hormone (FSH) test confirming nonchildbearing potential.*	To clarify the inclusion criterion for a woman not of childbearing potential and for a postmenopausal woman.
Section 1.1 Synopsis; Section 5.2 Exclusion Criteria	Exclusion Criterion 4 was modified as follows: *Any evidence of active infection that required treatment with a systemic antibiotic, antiviral, or antifungal agent within 4 weeks of Day 1 (eg, bronchopulmonary, urinary, or gastrointestinal).*	To clarify the systemic treatments that are not allowed within 4 weeks of Day 1 in case of active infection.
Section 1.1 Synopsis; Section 5.2 Exclusion Criteria	Exclusion Criterion 8 was deleted. "Known or suspected autoimmune disorder, including but not limited to rheumatoid arthritis, …."	This exclusion criterion is overly restrictive and unnecessary, as a comprehensive general listing of concurrent medical conditions that adequately represents potential safety risks for subjects is already covered by Exclusion Criterion 2.
Section 1.1 Synopsis; Section 5.2 Exclusion Criteria; Section 6.5 Concomitant Therapy; Section 6.5.1 Permitted Therapies; Section 6.5.2	Exclusion Criterion 21 was clarified to include live in addition to live-attenuated vaccines, and corresponding	To clarify the exclusion criterion related to live and live-attenuated vaccines.

Section # and Name	Description of Change	Brief Rationale
Prohibited Medications or Procedures	sections referring to vaccines were revised too.	
Section 1.1 Synopsis; Section 1.3 Schedule of Activities; Section 5.2 Exclusion Criteria	The following note was removed from the schedule of activities in footnote related to tuberculosis testing: *If a negative QuantiFERON®-TB Gold test result was obtained within 6 months of screening, it can be skipped at screening.* Corresponding exclusion criterion (Exclusion Criterion 24) was also updated.	To clarify that the tuberculosis testing is to be performed for all subjects at screening.
Section 2.2.2 Clinical Studies; Section 2.3.1 Known Potential Risks	Information on current clinical studies and new information on risks, including occurrence of serious adverse events, were added.	To revise the introduction with up-to-date information on current clinical studies.
Section 2.3.1 Known Potential Risks; Section 6.1.2 Dosing and Administration	Observation period after dosing was clarified and harmonized throughout the protocol to 30 minutes after each SC dose.	To clarify the observation period after each SC dose.
Section 6.1.2 Dosing and Administration	The study treatment description was revised to the following: *-for the active product, the total volume in each vial was removed to indicate only the final concentration of active product.* *-for the placebo, the volume in each vial was reduced from 1.2 mL to 1 mL.* The needle position for injection was revised to the following: *The needle is to be injected at a 45- to 90-degree angle to the skin.*	To revise study treatment description of each investigational product for accuracy and to clarify the needle position for injection.
Section 6.3 Measures to Minimize Bias	The following sentences were added: *In case of emergency unblinding of treatment randomization of individual subjects, subjects for whom the blind has been broken will be discontinued from treatment at the time of unblinding. After discontinuation from treatment, subjects should remain in the study for the duration of the safety follow-up period and complete a D281 (W40) EOS/ET visit 12 weeks*	To clarify the procedure in case of subject's discontinuation of study treatment due to emergency unblinding.

Section # and Name	Description of Change	Brief Rationale
	after their last dose of study treatment.	
Section 6.5 Concomitant Therapy	Deleted the sentence: *The concomitant treatments for other indications that are not listed in the prohibited therapies or procedures (Section 6.5.2 must be on a stable dose for at least 4 weeks before study treatment administration (Day 1).*	This is overly restrictive and unnecessary.
Section 7.2 Subject Discontinuation/Withdrawal from the Study	The following sentences were edited: *In case of early withdrawal from the study treatment, the subject will be required to attend an ET visit* ***at the time the decision is made to stop study treatment early*** *(see the SoA in Section 1.3).* ***After completion of the ET visit, the subject should then return for a final follow up EOS/ET visit approximately 12 weeks after receiving their last dose of study treatment.*** Deleted the sentence: *Subjects withdrawing from the study prematurely for reasons other than a study treatment-related AE may be replaced at the discretion of AnaptysBio.*	To clarify procedures in case of a subject's early withdrawal. This sentence was included in error as the study is adequately powered to allow for an anticipated reasonable number of early terminations.
Section 8.2.5 Vital Signs	The measurement of blood pressure was modified to be performed only once and not twice at each specified visit.	To correct the number of blood pressure measurements required at each specified visit.
Section 9.3 Populations for Analyses, Table 7	Safety Analysis Set and Extension Analysis Set were corrected to indicate that <u>at least</u> 1 dose of imsidolimab or placebo is required to be part of this population.	To correct the Safety Analysis Set to subjects who receive at least 1 dose of investigational product.
Section 9.4.5 Analysis of the Primary Efficacy Endpoint	Estimand statement was added.	To specify the estimand to be considered in this study for the primary analysis.
Abbreviations; Section 9.4.9 Pharmacokinetic Analyses; Section 9.4.9.1 Derivation of Pharmacokinetic Parameters; and	Removed analysis of PK parameters and added the following note relative to the PK analyses:	To remove analysis of PK parameters and to specify that NCA is not planned for the PK analyses.

Section # and Name	Description of Change	Brief Rationale
Section 9.4.9.3 Pharmacokinetic Parameter Data Analyses	*Due to limited PK sampling, noncompartmental analysis (NCA) will not be conducted in this study.*	
Section 9.4.9.5 Immunogenicity Analyses	Added the specification that if data permits, *potential* correlation *may* be analyzed between ADA levels, serum concentration, and safety and efficacy endpoints and removed the following: *Frequency and percentage of ADA response will be presented and listed and correlated to safety and PK endpoints.* Added the following note relative to the ADA analyses: *In addition, ADA incidences (overall, treatment-emergent, and treatment-boosted) will be listed and summarized.*	To specify that potential correlation may be analyzed between ADA levels, serum concentration, and safety and efficacy endpoints and to clarify how data will be presented for the ADA results.
Section 11 References	Added new references to the list of references.	To add new references relative to the Fitzpatrick skin type classification.
Appendix 1 Contraceptive Guidance and Collection of Pregnancy Information	Added tubal ligation in the list of effective methods of contraception.	To add tubal ligation in addition to tubal occlusion to the list of accepted methods of contraception.
Appendix 11 Clinical Laboratory Tests	Removed troponin from the biochemistry panel	Troponin was included erroneously. It should not be collected routinely for imsidolimab Phase 2 trials and is not necessary for this patient population.

TABLE OF ABBREVIATIONS

ADA	anti-drug antibody
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AN	abscess and inflammatory nodule
AN50	reduction in AN count of ≥50% relative to Baseline
AN75	reduction in AN count of ≥75% relative to Baseline
AST	aspartate aminotransferase
BMI	body mass index
CFR	Code of Federal Regulations
CI	confidence interval
CK	creatine kinase
C_{max}	maximum observed concentration
CONSORT	Consolidated Standards of Reporting Trials
COVID-19	Coronavirus Disease 2019
CRO	contract research organization
CV	coefficient of variation
D	day
DLQI	Dermatology Life Quality Index
EC	Ethics Committee
ECG	electrocardiogram
eCRF	electronic case report form
EDC	electronic data capture
EGFRi/MEKi	epidermal growth factor receptor inhibitors/MEK inhibitors
EOS	end of study
ET	early termination
EudraCT	European Clinical Trials Database
FDA	Food and Drug Administration
FSH	follicle-stimulating hormone
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GPP	generalized pustular psoriasis
H_0	null hypothesis
HHS	Health and Human Services
HIPAA	Health Information Portability and Accountability Act
HiSCR50	Hidradenitis Suppurativa Clinical Response 50
HiSCR75	Hidradenitis Suppurativa Clinical Response 75
HiSQoL	Hidradenitis Suppurativa Quality of Life
Hr	hour
HRT	hormonal replacement therapy
HS	hidradenitis suppurativa
HS-PGA	Hidradenitis Suppurativa Physician's Global Assessment
HS-PtGA	Hidradenitis Suppurativa Patient's Global Assessment
IA	interim analysis
IB	Investigator's Brochure
ICF	Informed Consent Form

ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IgG4	immunoglobulin G4
IHS4	International Hidradenitis Suppurativa Severity Score System
IL	interleukin
IL-36R	interleukin 36 receptor
IL-36Ra	IL-36 receptor antagonist
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	intent-to-treat
IUD	intrauterine device
IUS	intrauterine hormone-releasing system
IV	intravenous
IWRS	Interactive Web Response System
K_D	dissociation constant
LSM	least-squares means
mAb	monoclonal antibody
MAD	multiple ascending dose
MedDRA	Medical Dictionary for Regulatory Activities
min	minute
MMRM	mixed effects model for repeated measures
mRNA	messenger ribonucleic acid
NaCl	sodium chloride
NCA	noncompartmental analysis
NOAEL	no observed adverse effect level
NRS	numeric rating scale
PD	pharmacodynamics
PGIB	Patient Global Impression of Bother
PGIC	Patient Global Impression of Change
PGIS	Patient Global Impression of Severity
PK	pharmacokinetic(s)
PPP	palmoplantar pustulosis
PRN	as needed (*pro re nata)*
PT	preferred term
QC	quality control
SAD	single ascending dose
SAE	serious adverse event
SAP	Statistical Analysis Plan
SC	subcutaneous(ly)
SD	standard deviation
SoA	Schedule of Activities
SOC	system organ class
SOP	standard operating procedure
$t_{1/2}$	terminal half-life
TB	tuberculosis
TEAE	treatment-emergent adverse event
Th-17	T-helper 17
TK	toxicokinetic
TNFα	tumor necrosis factor alpha

ULN	upper limit of normal
URTI	upper respiratory tract infection
W	week
WOCBP	woman of childbearing potential

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STATEMENT OF COMPLIANCE

The study will be conducted in accordance with the protocol, applicable ICH GCP guidelines, and applicable local laws and regulations. The Investigator will assure that no planned deviation from, or changes to the protocol will take place without prior agreement from the IND Sponsor and documented approval from the Institutional Review Board (IRB)/Ethics Committee (EC), except where necessary to eliminate an immediate hazard(s) to the study subjects. All personnel involved in the conduct of this study have completed ICH GCP Training.

The protocol, informed consent form(s) (ICFs), recruitment materials, and all subject materials will be submitted to the IRB/EC for review and approval. Approval of the protocol and the consent forms must be obtained before any subject is enrolled. Any amendment to the protocol will require review and approval by the IRB/EC before the changes are implemented to the study. In addition, all changes to the consent forms will be IRB/EC-approved; a determination will be made regarding whether a new consent needs to be obtained from subjects who provided consent, using previously approved consent forms.

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Imsidolimab (ANB019) in the Treatment of Subjects with Hidradenitis Suppurativa

Short Title: Efficacy and Safety of Imsidolimab in Subjects with Hidradenitis Suppurativa

Study Description: This is a Phase 2, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of imsidolimab in adult subjects with hidradenitis suppurativa (HS). This study also will characterize the pharmacokinetic (PK) profile of imsidolimab and explore the immune response to imsidolimab in subjects with HS.

To be eligible for this study, subjects must have a clinically confirmed diagnosis of HS with a disease duration of at least 6 months before Day 1. In addition, subjects will have the following characteristics at screening and Day 1: 1) HS lesions present in at least 2 distinct anatomical areas, 1 of which must be Hurley Stage II (ie, single or multiple, widely separated, recurrent abscesses with tract formation and cicatrization) or Hurley Stage III (ie, diffuse or near-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area); 2) total abscess and inflammatory nodule (AN) count of ≥ 5; 3) ≤ 20 draining fistulas. Randomization will be stratified based on Hurley Stage at baseline (Stage II or III).

The maximum study duration per subject is approximately 44 weeks, which includes a screening period of up to 30 days, followed by a 16-week placebo-controlled period, a 16-week treatment extension period, and an 8-week follow up period. The placebo-controlled period ends at Day 113 (Week 16) and the treatment extension period starts when study treatment is administered at the Week 16 visit. Of note, during the extension period all subjects will receive imsidolimab but their treatment will remain blinded (see Figure 1).

During the placebo-controlled period, eligible subjects will be randomized (1:1:1) to receive either imsidolimab (at 1 of 2 different regimens) or placebo, subcutaneously (SC) administered on 4 occasions: Day 1, Day 29 (Week 4), Day 57 (Week 8), and Day 85 (Week 12).

The treatment arms during the placebo-controlled period will be as follows:

1. Imsidolimab 400 mg on Day 1, followed by 200 mg on Days 29, 57, and 85
2. Imsidolimab 200 mg on Day 1, followed by 100 mg on Days 29, 57, and 85
3. Placebo on Days 1, 29, 57, and 85

During the extension period, all subjects will receive imsidolimab, SC administered on 4 occasions: Day 113 (Week 16), Day 141 (Week 20), Day 169 (Week 24), and Day 197 (Week 28). Subjects randomized to imsidolimab during the placebo-controlled period will continue to receive the same dose of imsidolimab on Days 113, 141, 169, and 197. Subjects randomized to placebo during the placebo-controlled period will receive either a 400-mg dose of imsidolimab on Day 113, followed by a 200-mg dose of imsidolimab on Days 141, 169, and 197, or 200-mg dose of imsidolimab on Day 113, followed by a 100-mg dose of imsidolimab on Days 141, 169, and 197 based on a 1:1 randomization.

For scheduled on-site study visits, subjects will come to the study site on 12 occasions: screening and Days 1, 29, 57, 85, 113, 141, 169, 197, 225, 253, and 281 (End of Study [EOS]/Early Termination [ET]). All procedures will be conducted in accordance with the Schedule of Activities (SoA) in Section 1.3.

Disease activity will be evaluated for all subjects using AN count, draining fistula count, Hidradenitis Suppurativa Clinical Response 50 (HiSCR50) (a responder HiSCR50 is defined as a subject with at least a 50% decrease in AN count from Baseline with no increase in abscess count and no increase in draining fistula count relative to Baseline), Hidradenitis Suppurativa Clinical Response 75 (HiSCR75) (a responder HiSCR75 is defined as a subject with at least a 75% decrease in AN count from Baseline with no increase in abscess count and no increase in draining fistula count relative to Baseline), Hurley Stage, Hidradenitis Suppurativa Physician's Global Assessment (HS-PGA), International Hidradenitis Suppurativa Severity Score System (IHS4), HS Pain Numeric Rating Scale (NRS), Patient Global Impression of Change (PGIC), Patient Global Impression of Severity (PGIS), Patient Global Impression of Bother (PGIB), Dermatology Life Quality Index (DLQI), Hidradenitis Suppurativa Quality of Life (HiSQoL), and Hidradenitis Suppurativa Patient's Global Assessment (HS-PtGA).

Safety assessments will include adverse event (AE)/serious adverse event (SAE) monitoring, vital signs, physical examination, electrocardiograms (ECGs), and clinical laboratory tests (hematology, biochemistry, and urinalysis).

Blood samples will be collected during the study to determine pharmacokinetics (PK) and immunogenicity (presence of anti-drug antibodies [ADA] to imsidolimab) on Day 1 before the administration of the study treatment and at other time points specified in the SoA (Section 1.3). Any remaining serum/plasma from samples collected for PK/pharmacodynamic (PD) immunogenicity endpoints may be retained for assay method development, troubleshooting, or validation. The samples will not be used for any type of genetic analyses.

Photography is an optional procedure for all subjects at each of the specified visits at selected sites.

Skin tape strips will be collected at Day 1, Week 4, Week 16, and Week 32 to study gene expression.

Interim analyses (IA) may be performed for assessment of all primary and secondary efficacy endpoints and evaluation of all safety data available.

Objectives: Primary Objective:

- To evaluate the efficacy of imsidolimab in subjects with HS

Secondary Objectives:

- To evaluate the safety of imsidolimab in subjects with HS
- To evaluate the effect of imsidolimab on HS signs and symptoms in subjects with HS

Exploratory Objectives:

- To further evaluate the effect of imsidolimab on HS signs and symptoms, and quality of life in subjects with HS
- To explore the effect of imsidolimab on cutaneous biomarkers
- To test for immunogenicity to imsidolimab
- To describe the PK profile of imsidolimab in subjects with HS

Endpoints: Primary Endpoint:

- Change from Baseline in AN count at Week 16

Secondary Efficacy Endpoints:

- Percent change from Baseline in AN count at Week 16
- Proportion of subjects achieving HiSCR50 at Week 16
- Change from Baseline in HS Pain NRS at Week 16

- Percent change from Baseline in HS Pain NRS at Week 16

Safety Endpoint:

- Incidence of AEs, SAEs, and AEs leading to treatment discontinuation, as well as changes in vital signs, clinical laboratory parameters (hematology, biochemistry, and urinalysis), and 12-lead ECGs

Exploratory Endpoints:

- Change from Baseline in AN count at visits other than Week 16
- Percent change from Baseline in AN count at visits other than Week 16
- Proportion of subjects achieving a reduction in AN count of ≥50% and ≥75% relative to Baseline (AN50 and AN75 responses)
- Percentage of subjects experiencing flare, defined as a ≥25% increase in AN count with an absolute increase in AN count of ≥2 relative to Baseline at each visit
- Change from Baseline in abscess count at each visit
- Change from Baseline in inflammatory nodule count at each visit
- Change from Baseline in draining fistula count at each visit
- Proportion of subjects achieving HiSCR50 at visits other than Week 16
- Proportion of subjects achieving HiSCR75 at each visit
- Proportion of subjects achieving 0 (inactive) or 1 (almost inactive) on HS-PGA at each visit
- Proportion of subjects with ≥2-point reduction from Baseline on HS-PGA at each visit
- Change from Baseline in HS-PGA
- Change from Baseline in calculated composite of abscesses, draining fistulas, and inflammatory and non-inflammatory nodules
- Change from Baseline in HS Pain NRS at visits other than Week 16
- Percent change from Baseline in HS Pain NRS at visits other than Week 16
- Proportion of subjects achieving a ≥3-point reduction on the HS Pain NRS for subjects with Baseline HS Pain NRS of at least 3
- Proportion of subjects requiring rescue medication or treatment at each visit
- Change from Baseline in DLQI score at each visit
- Change from Baseline in IHS4 at each visit
- Change from Baseline in HiSQoL at each visit
- Change from Baseline in HS-PtGA at each visit

- Proportion of subjects in each response category for the HS-PtGA at each visit
- Proportion of subjects in each response category for the PGIC at each visit
- Proportion of subjects achieving improvement ("Much better" or "Very much better") according to the PGIC at each visit
- Proportion of subjects achieving improvement ("A little better", "Much better" or "Very much better") according to the PGIC at each visit
- Proportion of subjects in each response category for the PGIB at each visit
- Change from Baseline in PGIB at each visit
- Proportion of subjects achieving "A little bothered" or "Not at all bothered" for the PGIB at each visit
- Proportion of subjects in each response category for the PGIS at each visit
- Proportion of subjects achieving "Mild" or "No activity" according to the PGIS at each visit
- Change from Baseline in PGIS at each visit
- Proportion of subjects in each category of Hurley Stage at each visit
- Change from Baseline in Hurley Stage at Weeks 16, 32, and 40
- Proportion of subjects achieving at least a 1-stage improvement in Hurley Stage
- Skin tape strip and drainage fluid biomarkers analysis including, but not limited to, IL-36 and Th-17
- Presence of ADAs to imsidolimab
- Serum concentration following imsidolimab administration and other parameters as appropriate will be determined to describe the PK profile of imsidolimab

Study Population:	Approximately 120 male and female subjects aged 18 to 75 years with clinically confirmed diagnosis of HS

Inclusion Criteria:

1. Male or female aged 18 to 75 years (inclusive) at the time of signing informed consent.
2. Clinically confirmed diagnosis of active HS with a disease duration of ≥ 6 months before Day 1 as determined by the Investigator through subject interview and/or review of the medical history.
3. HS lesions present in at least 2 distinct anatomical areas, 1 of which must be Hurley Stage II (ie, single or multiple, widely separated, recurrent abscesses with tract formation and cicatrization) or Hurley Stage III (ie, diffuse or near-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area).

4. Total AN count ≥ 5
5. Draining fistulas ≤ 20.
6. Stable HS for at least 6 weeks prior to Day 1 visit as determined by the Investigator through subject interview and review of medical history.
7. Agree to daily use (and throughout the study) of one of the following over-the-counter topical treatments on their body areas affected with HS lesions: chlorhexidine gluconate, triclosan, benzoyl peroxide, dilute bleach in bathwater, or soap and water.
8. Meet the following laboratory criteria at screening:
   a) Hemoglobin ≥ 90 g/L (≥ 9 g/dL)
   b) White blood cell count ≥ 3.0×10^9/L (≥ 3.0×10^3/μL)
   c) Platelets ≥ 100×10^9/L (≥ 100×10^3/μL)
   d) Serum creatinine < 132.6 μmol/L (< 1.5 mg/dL)
   e) Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤ 2 upper limit of normal (ULN)
   f) Total bilirubin ≤ 1.5 × ULN. Subjects with known Gilbert's disease who have serum bilirubin < 3 × ULN may be included
9. Body weight ≥ 40 kg.
10. Contraceptive use by men and women should be consistent with local regulations regarding the methods of contraception for subjects participating in clinical studies.

    Contraception and Pregnancy:

    a) A male subject who has not had a vasectomy must agree to use contraception as detailed in Appendix 1 of this protocol during the treatment period and for at least 220 days (which includes the duration of relevant exposure plus the duration of sperm cycle) after the last study treatment administration and refrain from donating sperm during this period.
    b) Female subjects:
       i) A woman of childbearing potential (WOCBP) is eligible to participate if she has a negative serum pregnancy test (β-human chorionic gonadotropin) at screening and a negative urine pregnancy test at Day 1 (see Appendix 1), is not breastfeeding, and agrees to follow the contraceptive guidance in Appendix 1 during the treatment period and for at least 6 months after receiving the study treatment, and refrains from donating oocytes for assisted reproduction during this period. The female subject's selected form of contraception must be effective by the time the female subject enters into the study at Day 1 (eg, hormonal contraception should be initiated at least 12

Weeks before Day 1. For WOCBP, hormonal contraceptives must be used without schedule changes and in steady doses during the study treatment. Starting hormonal contraceptives during the study is not permitted. Use of any hormonal contraceptives containing drospirenone, chlormadinone acetate, or cyproterone acetate is prohibited unless part of a stable contraceptive regimen as described in Section 6.5.1.

ii) A woman not of childbearing potential as defined in Appendix 1 is eligible to participate in the study. A postmenopausal woman must have a follicle -stimulating hormone (FSH) test confirming nonchildbearing potential.

11. Willing to participate and capable of giving written informed consent, which must be personally signed and dated by the subject and obtained prior to any trial-related activities.
12. Willing to comply with all study procedures and available for the duration of the study.

Exclusion Criteria:

1. Concomitant dermatological or medical conditions that may interfere with the Investigators' ability to evaluate the subject's response to therapy.
2. History of clinically significant (as determined by the Investigator) cardiac, pulmonary, neurologic, gastrointestinal, endocrine, hematological, renal, hepatic, cerebral or psychiatric disease, or other major uncontrolled disease.
3. Chronic or recurrent infectious disease, including but not limited to upper and lower respiratory infection (eg, bronchiectasis), urinary tract infection (eg, recurrent pyelonephritis), within 6 months prior to screening. Note: A subject with a history of localized oral or genital herpes simplex that, in the opinion of the Investigator, is well controlled will be eligible for study participation.
4. Any evidence of active infection that required treatment with a systemic antibiotic, antiviral, or antifungal agent within 4 weeks of Day 1 (eg, bronchopulmonary, urinary, or gastrointestinal), excluding localized oral or genital herpes simplex that, in the opinion of the Investigator, is well-controlled.
5. Any factors that would predispose the subject to develop an infection in the Investigator's opinion.
6. Opportunistic infection (eg, Pneumocystis carinii, aspergillosis, or mycobacteria other than tuberculosis [TB]) or parasitic infections (eg, helminths, protozoa, Trypanosoma cruzi) within 6 months prior to screening.
7. Herpes zoster infection within 2 months prior to screening.
8. *[intentionally blank]*

9. Known or suspected congenital or acquired immunodeficiency state, or condition that would compromise the subject's immune status (eg, history of splenectomy).
10. Major surgery within 4 weeks of Day 1.
11. History of cancer or lymphoproliferative disease within 5 years of Day 1. Subjects with successfully treated nonmetastatic cutaneous squamous cell or basal cell carcinoma and/or localized carcinoma in situ of the cervix are not to be excluded.
12. History of any significant drug allergy or reaction to polysorbate-20, a component of imsidolimab formulation, or the inactive ingredients (excipients).
13. Any systemic antibiotic treatment for HS within 4 weeks of Day 1.
14. Prescription topical therapies for the treatment of HS within 2 weeks of Day 1.
15. Over-the-counter topical antiseptic washes, creams, soaps, ointments, gels, and liquids containing antibacterial agents to treat HS within 2 weeks prior to Day 1 (unless specified as permitted in Section 6.5.1)
16. Systemic non-biologic therapies with potential therapeutic impact for HS within 4 weeks of Day 1, including methotrexate (MTX), cyclosporine, retinoids, and fumaric acid esters, and oral or injectable corticosteroids (unless clearly specified as permitted; see Section.6.5.1).
17. Oral analgesics (including opioids) within 2 weeks of Day 1, unless a subject is on a stable dose (as needed [PRN] is not considered a stable dose) of non-opioid analgesics for a non-HS medical condition (eg, osteoarthritis), and is stable for 2 weeks prior to Baseline and is anticipated to remain stable throughout study participation.
18. Subject requires or is expected to require opioid analgesics during the study for any reason (excluding tramadol as described in Section 6.5.1).
19. Nonbiologic investigational drug within 4 weeks or 5 half-lives of Day 1, whichever is longer.
20. Biologics for at least 12 weeks or 5 half-lives prior to Day 1 (eg, adalimumab).
21. Live or live-attenuated vaccines within 12 weeks prior to Day 1. Live and live-attenuated vaccines may be utilized 12 weeks after the last study treatment administration. Note: Currently authorized nonlive and nonlive-attenuated vaccines for Coronavirus Disease 2019 (COVID-19) (eg, RNA-based vaccines, protein-based vaccines, and nonreplicating viral vector-based vaccines) are allowed during the study.

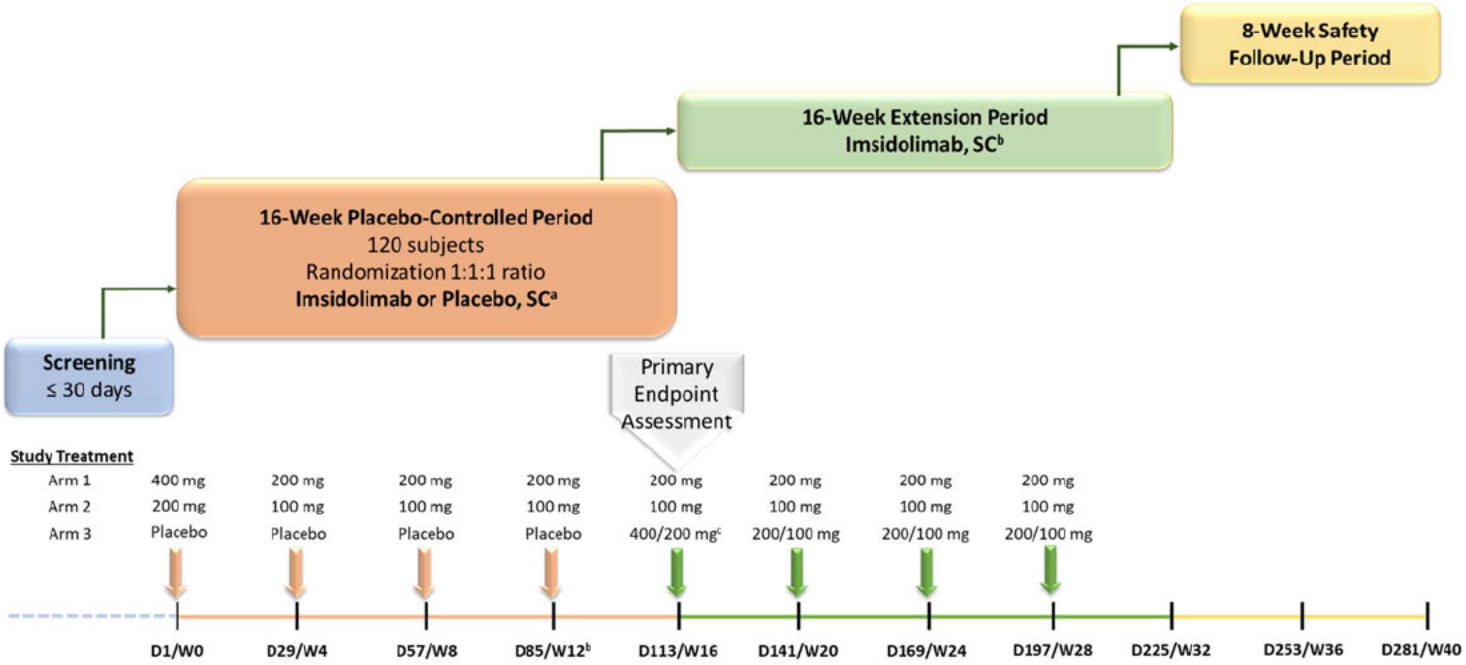
22. Surgical, laser, or intense pulsed light (IPL) intervention in area with HS lesion within 4 weeks prior to Day 1.
23. Phototherapy (psoralen and ultraviolet A [PUVA] and/or UVB) within 4 weeks prior to Day 1
24. Active TB or latent TB infection as indicated by a positive QuantiFERON®-TB Gold test at screening (if the test is indeterminate, it can be repeated only once), chest X-ray, and/or clinical examination, or has had active TB disease at any time in the past.
25. Clinically significant drug or alcohol abuse in the last year prior to Day 1, or other factors limiting the ability to cooperate and to comply with the study protocol, as determined by the Investigator.
26. Subject is a pregnant or lactating woman, or a woman who intends to become pregnant during the study period.
27. Any other physical, mental, or medical conditions, which, in the opinion of the Investigator, make study participation inadvisable or could confound study assessments.
28. Clinically significant abnormality on chest X-ray at screening or within 6 months prior to screening.
29. Positive blood screen for hepatitis C antibody and hepatitis C RNA, antibodies to hepatitis B core antigen, hepatitis B surface antigen, or human immunodeficiency virus 1 and 2 antibodies.
30. Subject is not able to tolerate SC drug administration.

Phase:	2
Study Centers Enrolling Subjects:	Approximately 40 study sites are expected to participate in this study.
Description of Study Treatments:	Imsidolimab (ANB019) will be provided in a glass vial as a sterile, colorless to yellow, and clear to slightly opalescent solution for injection. The placebo contains no active ingredient and will be provided as a sterile, colorless to slightly yellowish, and clear to very slightly opalescent solution for injection. Imsidolimab will be administered as SC injection. Placebo will also be administered as SC injection in the same volumes as imsidolimab.

Rescue Treatments:	Criteria for use of rescue treatments and permitted rescue treatments are further described in Section 6.6 of the protocol.
Subject Duration:	The maximum study duration per subject included in this study is approximately 44 weeks from first visit to last visit.

1.2 SCHEMA

Figure 1: ANB019-208 Study Schema



Abbreviations: D, day; SC, subcutaneous; W, week.

[a] During the placebo-controlled period, subjects will be randomized (1:1:1) to receive either imsidolimab (at 1 of 2 different regimens) or placebo, SC administered on 4 occasions: 1) 400-mg dose of imsidolimab on Day 1, 200-mg dose of imsidolimab on Days 29, 57, and 85; 2) 200-mg dose of imsidolimab on Day 1, 100-mg dose of imsidolimab on Days 29, 57, and 85, 3) placebo on Days 1, 29, 57, and 85.

[b] The placebo-controlled period ends on Day 113 (Week 16) visit, before study treatment administration. Predose assessments performed on Day 113 (Week 16) will be used to evaluate the primary and secondary efficacy endpoints, as well as the safety, tolerability, and immune response of imsidolimab compared with placebo. The extension period starts when the study treatment is administered on Day 113 (Week 16) visit. All subjects will receive imsidolimab SC administered on 4 occasions during the extension period.

[c] Subjects in Arm 3 randomized to placebo during the placebo-controlled period will be randomized 1:1 to receive either a 400-mg dose of imsidolimab on Day 113, followed by a 200-mg dose on Days 141, 169, and 197; or a 200-mg dose of imsidolimab on Day 113, followed by a 100-mg dose of imsidolimab on Days 141, 169, and 197. Subjects randomized to imsidolimab in Arms 1 and 2 during the placebo-controlled period will continue to receive the same maintenance dose of imsidolimab (200 mg or 100 mg) on Days 113, 141, 169, and 197.

1.3 SCHEDULE OF ACTIVITIES

The screening evaluation will only be performed after the subject has agreed to participate and has signed and dated the ICF. No treatment or study-related procedures will be initiated before the informed consent is signed. The Day 1 visit must be performed, at the latest, 30 days after the screening visit.

The screening evaluation will be performed according to the inclusion and exclusion criteria. If the subject fulfills all inclusion criteria and no exclusion criteria, he or she may be included in the study.

Table 1 provides a description of the procedures to be performed at each visit during the study.

Of note, the placebo-controlled period ends at Day 113 (Week 16). Predose assessments performed at Day 113 (Week 16) will be used to evaluate the primary and secondary efficacy endpoints, and safety, tolerability, and immune response of imsidolimab compared with placebo. The treatment extension period starts when study treatment is administered at the Week 16 visit. All subjects will receive imsidolimab during the treatment extension period.

Unless specified otherwise, the study assessments scheduled on Day 1 must be performed before study treatment administration. The recommended order for performing the study assessments is as follows (applicable to all visits):

- Subject-reported questionnaires (worst HS Pain NRS should be performed before average HS Pain NRS)
- Efficacy assessments (global assessments [eg, HS-PGA] should be performed before more quantitative assessments [eg, abscess and inflammatory nodule (AN) count])
- Physical examination
- ECG
- Vital signs
- Blood samples collection (for safety, PK, ADA)
- Photography (may be performed anytime predose provided it is before skin sample collection)
- Tape stripping

The COVID-19 pandemic may impact the ability to adhere to the study procedures described in Table 1 due to challenges that include, but are not limited to, subject preferences, site closures, travel restrictions, and quarantines. Please refer to Section 4.5 for more details on allowable, as necessary, modifications to the protocol due to COVID-19 restrictions, including conducting optional home visits when on-site study visits are considered not feasible. Such modifications in study conduct always must be in accordance with local regulations/mandates.

Table 1: Schedule of Activities

	Screening Period			Placebo-Controlled Period			Extension Period			Follow-Up Period		
Study visit **Window (days)**	**(-30 to -1)**	**D1**	**D29 (W4) (±4)**	**D57 (W8) (±4)**	**D85 (W12) (±4)**	**D113 (W16)[a] (±4)**	**D141 (W20) (±4)**	**D169 (W24) (±4)**	**D197 (W28) (±4)**	**D225 (W32) (±4)**	**D253 (W36) (±4)**	**D281 (W40) EOS/ ET[b] (±5)**
Informed consent	X											
Demographics	X											
Fitzpatrick skin type classification[c]	X											
Inclusion and exclusion criteria	X	X										
Medical and surgical history	X	X										
Smoking History[c]		X										
Height and weight[d]	X	X				X				X		X
Complete physical examination[e]	X	X	X	X	X	X				X		X
Vital signs[f]	X	X	X	X	X	X	X	X	X	X	X	X
12-Lead ECG[g]	X	X	X			X	X			X		X
Chest X-ray[h]	X											
Hematology and biochemistry	X	X	X	X	X	X	X	X	X	X	X	X
Urinalysis	X	X	X		X	X	X		X	X		X

	Screening Period			Placebo-Controlled Period			Extension Period			Follow-Up Period		
Study visit **Window (days)**	**(-30 to -1)**	**D1**	**D29 (W4) (±4)**	**D57 (W8) (±4)**	**D85 (W12) (±4)**	**D113 (W16)[a] (±4)**	**D141 (W20) (±4)**	**D169 (W24) (±4)**	**D197 (W28) (±4)**	**D225 (W32) (±4)**	**D253 (W36) (±4)**	**D281 (W40) EOS/ ET[b] (±5)**
TB screening (QuantiFERON®-TB Gold test)	X											
Viral serology	X											
FSH[i]	X											
Serum pregnancy test (WOCBP only)[i]	X											X
Urine pregnancy test (WOCBP only)[i]		X	X	X	X	X	X	X	X	X	X	
HS Pain NRS, PGIB, PGIS, HS-PtGA, DLQI, HiSQoL[j]		X	X	X	X	X	X	X	X	X	X	X
PGIC[j]			X	X	X	X	X	X	X	X	X	X
HS-PGA[j]	X	X	X	X	X	X	X	X	X	X	X	X
Hurley Stage[j]	X	X				X				X		X
AN count, draining fistula count, HiSCR[j]	X	X	X	X	X	X	X	X	X	X	X	X
IHS4[j]		X	X	X	X	X	X	X	X	X	X	X
Blood samples for PK[k]		X	X	X	X	X	X	X	X	X	X	X
Blood samples for ADA[k]		X	X	X	X	X	X			X		X
Tape strips collection[l]		X	X			X				X		
Drainage fluid collection[l]		X	X	X	X	X	X	X	X	X	X	X

	Screening Period			Placebo-Controlled Period			Extension Period			Follow-Up Period		
Study visit Window (days)	**(-30 to -1)**	**D1**	**D29 (W4) (±4)**	**D57 (W8) (±4)**	**D85 (W12) (±4)**	**D113 (W16)[a] (±4)**	**D141 (W20) (±4)**	**D169 (W24) (±4)**	**D197 (W28) (±4)**	**D225 (W32) (±4)**	**D253 (W36) (±4)**	**D281 (W40) EOS/ ET[b] (±5)**
Photography[m]	X	X	X			X				X		X
Randomization[n]		X				X						
Study treatment administration[o]		X	X	X	X	X	X	X	X			
AE/SAE review	X						Continuously					
Concomitant medication review[p]	X						Continuously					

Abbreviations: ADA, anti-drug antibody; AE, adverse event; AN, abscess and inflammatory nodule; D, day; DLQI, Dermatology Life Quality Index; ECG, electrocardiogram; EOS, end of study; ET, early termination; FSH, follicle-stimulating hormone; HiSCR, Hidradenitis Suppurativa Clinical Response; HiSQoL, Hidradenitis Suppurativa Quality of Life; HS, hidradenitis suppurativa; HS-PGA, Hidradenitis Suppurativa Physician Global Assessment; HS-PtGA, Hidradenitis Suppurativa Patient Global Assessment; IHS4, International Hidradenitis Suppurativa Severity Score System; NRS, Numeric Rating Scale; PGIB, Patient Global Impression of Bother; PGIC, Patient Global Impression of Change; PGIS, Patient Global Impression of Severity; PK, pharmacokinetics; SAE, serious adverse event; SC, subcutaneously; SoA, Schedule of Activities; TB, tuberculosis; W, week; WOCBP, woman of childbearing potential.

[a] All subjects will receive imsidolimab during the extension period starting on Day 113 (Week 16) visit until Day 197 (Week 28) visit. The placebo-controlled period ends on Day 113 (Week 16) visit, before study treatment administration. The extension period starts when the study treatment is administered on Day 113 (Week 16) visit.

[b] The ET visit will include all procedures to be done at the EOS visit (Day 281/Week 40 visit).

[c] If the Fitzpatrick skin type and/or Smoking history are not collected at screening and D1 respectively, they may be collected at any subsequent visit.

[d] Height to be measured at screening only for subjects.

[e] Refer to Section 8.2.4 for details regarding the complete physical examination.

[f] Refer to Section 8.2.5 for details and instructions regarding vital signs.

[g] Refer to Section 8.2.6 for details and instructions regarding the ECG. In addition to the time points specified in the SoA, ECGs may be performed at any time during the study if in the opinion of the Investigator it is clinically warranted.

[h] Bidirectional posterior-anterior view and lateral view chest X-ray will be performed at screening. If a chest X-ray was performed within 6 months of screening and no clinically significant abnormality was observed, it can be skipped at screening.

[i] The FSH testing is performed for women not of childbearing potential who are postmenopausal (at least 12 months of amenorrhea without an alternative medical cause). Additional pregnancy testing may be performed whenever a menstrual cycle is missed or when pregnancy is otherwise suspected. Refer to Appendix 11 for details and instructions regarding clinical laboratory parameters.

[j] Refer to Section 8.1 for details and instructions on AN count, draining fistula count, HiSCR, Hurley Stage, HS-PGA, IHS4, HS Pain NRS, PGIC, PGIB, PGIS, DLQI, HS-PtGA, and HiSQoL. From screening through Week 32, subjects will not be permitted to use any analgesics related to HS pain within 24 hours of a scheduled study visit. Subjects may use analgesics after the questionnaires are completed at the study visit.

[k] Sample for PK will be collected predose. See Table 5 for PK and ADA sample collection time points.

[l] Tape stripping will be performed for all randomized subjects as part of this study (not optional). Tape strips will be collected from non-lesional and lesional skin at Day 1 and Week 16 and from lesional skin at Week 4 and Week 32. Drainage fluid may be collected (optional) at any visit after screening in which HS lesional drainage is present, and stored for future biomarker analysis.

[m] Photography (of representative lesion[s], fistulas, and scarring) is an optional procedure for all subjects at each of the specified visits at selected site. Two images from two distinct regions of highest density inflammatory nodules/abscesses/fistulas should be taken at baseline if possible. The anatomic regions should be identifiable from the images. These regions should be recorded and consistently photographed throughout the duration of the study if possible.

[n] Starting at Day 113 (Week 16), subjects who received placebo during the placebo-controlled period will be randomized 1:1 to receive imsidolimab at 1 of 2 different regimens. Subjects who received imsidolimab during the placebo-controlled period will not be randomized at the Week 16 visit.

[o] During the placebo-controlled period, subjects will receive either imsidolimab or placebo SC administered as follow according to randomization arm:1) 400-mg dose of imsidolimab on Day 1; followed by 200-mg dose of imsidolimab on Days 29, 57, and 85; 2) 200-mg dose of imsidolimab on Day 1; followed by a 100-mg dose of imsidolimab on Days 29, 57, and 85; 3) placebo. The placebo-controlled period ends at the Day 113 (Week 16) visit, before study treatment administration. During the extension period, subjects assigned to imsidolimab during the placebo-controlled period will continue to receive the same maintenance dose of imsidolimab, 200 mg or 100 mg. Subjects assigned to placebo during the placebo-controlled period will receive either a 400-mg dose of imsidolimab on Day 113, followed by 200-mg doses of imsidolimab on Days 141, 169, and 197; or a 200 mg dose of imsidolimab on Day 113, followed by 100-mg doses of imsidolimab on Days 141, 169, and 197.

[p] At screening, prior medications should be reviewed and documented. Refer to Section 6.5.

2 INTRODUCTION

2.1 STUDY RATIONALE

Hidradenitis suppurativa (HS) is a chronic inflammatory dermatological condition that can be progressive, painful, and dramatically reduce quality of life. Hidradenitis suppurativa frequently presents in the second decade of life and is observed more in women than men (Von der Werth 2000). Typically, HS begins with follicular occlusions that progress to inflammatory nodules/lesions. Multiple inflammatory nodules may form deep dermal abscesses that become infected with bacteria and result in chronically draining sinus tracts with extensive scarring. These nodules and abscesses most frequently occur in the axillae, groin, buttocks and mammary areas. Common courses of treatment include systemic and topical antibiotics, intralesional corticosteroids, and surgical drainage of nodules (Micheletti 2014).

While the pathogenesis of HS has not been fully elucidated, HS has previously been shown to be associated with dysregulation of various inflammatory pathways. As a result, multiple investigations of anti-inflammatory therapies have been conducted including biologic therapies targeting the tumor necrosis factor alpha (TNFα) pathway (infliximab/adalimumab) (Delage 2011, Kimball 2016) and the interleukin (IL)-12/IL- pathways (ustekinumab). Other proinflammatory pathways that may precipitate HS have also been identified (Blok 2016). Hessam et al. (2018) investigated expression of inflammatory markers from punch biopsies taken from 30 subjects including 15 subjects with HS with Hurley Stage II/III disease and 15 healthy controls and found that lesional skin in subjects with HS had elevated expression of IL-36α, β, and γ compared to healthy controls. While IL-36 receptor antagonist (IL-36Ra) was also elevated in subjects with HS, it was hypothesized that the activity of IL-36Ra was outcompeted by the cytokine expression levels. IL-36Ra is known to inhibit the effects of Interleukin-36 cytokines (IL-36α, IL-36β and IL-36γ) via competing with their receptor IL-36R and thereby inhibiting their proinflammatory effects. In an analysis of lesional biopsy samples from 25 subjects with HS, Thomi et al. (2017) found that protein levels of IL-36β and γ, but not IL-36α, were significantly elevated compared to healthy controls. However, it was observed that messenger ribonucleic acid (mRNA) expression of IL-36α was significantly elevated in lesional skin in HS subjects compared to healthy controls. In sum, the IL-36 pathway may be a viable treatment target for HS.

Imsidolimab is a high affinity, humanized immunoglobulin G4 (IgG4) monoclonal antibody (mAb) that specifically binds IL-36R and antagonizes IL-36 signaling. The IL-36 cytokines (IL-36α, IL-36β, and IL-36γ) engage with IL-36R to initiate signaling events leading to proinflammatory responses. IL-36 signaling is counterbalanced by IL-36Ra. Because the IL-36 pathway has been implicated in amplifying inflammatory skin diseases, inhibition of IL-36 signaling, by targeting IL-36R with a specific mAb, may represent a novel strategy to control the pathological inflammatory cascade driven by IL-36 pathway activation. Imsidolimab is currently being studied as a potential first-in-class therapy for several cutaneous indications, including palmoplantar pustulosis (PPP), generalized pustular psoriasis (GPP), ichthyosis, and other inflammatory diseases in which the IL-36 pathway may play a significant role in augmenting the

disease. Imsidolimab may be beneficial in suppressing the inflammation and decreasing pain in patients with HS.

2.2 BACKGROUND

2.2.1 NONCLINICAL STUDIES

Imsidolimab exhibits strong inhibitory activity for human as well as cynomolgus monkey IL36R (cyIL-36R) cell populations. Nonclinical data obtained from studies with imsidolimab in primary human and cynomolgus monkey cells and from in vivo nonhuman primate studies demonstrated that imsidolimab shows reactivity with human and cynomolgus monkey IL36R (dissociation constant [K_D] of 67.9 ± 31.4 pM and 80.0 ± 49.6 pM, respectively), but not with mouse or rat IL-36R.

In primary human and cynomolgus monkey cell populations, keratinocytes, peripheral blood mononuclear cells, and human whole blood, imsidolimab inhibited IL-36R mediated release of IL-8.

The terminal half-life ($t_{1/2}$) of imsidolimab in cynomolgus monkeys was 304 h after single intravenous (IV) dose administration, and 310 h after a single SC dose administration at 10 mg/kg, with bioavailability approximately 76% consistent with the anticipated PK characteristics for a human IgG4 scaffold mAb in the cynomolgus monkey.

Repeat-dose, Good Laboratory Practice (GLP) toxicity and toxicokinetic (TK) studies of 4, 13, and 26 weeks in duration have been conducted with imsidolimab administered by weekly SC and IV injection in cynomolgus monkeys. There were only minor treatment-related injection site findings in the 4-week repeat-dose study. Treatment-related effects in the 13-week toxicity study included increased observations of nonformed feces and prolapsed rectum, and protozoa in the stomachs of cynomolgus monkeys; the latter was consistent with the mechanism of action of an immune-modulator in cynomolgus monkeys (Dubey 2002). Weekly administrations of vehicle control article, 30 mg/kg/dose imsidolimab via SC injection, or 60 mg/kg/dose imsidolimab via SC or IV bolus injection, to male and female sexually mature cynomolgus monkeys during the 26-week toxicity and TK study was well tolerated. Imsidolimab-related effects were limited to a low incidence of liquid feces not considered AEs for animals administered 60 mg/kg/dose IV. Thus, the no observed adverse effect level (NOAEL) is 60 mg/kg/dose administered by SC or IV injection. These data provide a strong scientific rationale for advancing imsidolimab through clinical development.

A detailed description of the physical, chemical, and pharmaceutical properties of imsidolimab and nonclinical studies is provided in the Investigator's Brochure (IB).

2.2.2 CLINICAL STUDIES

Currently, three clinical studies (ANB019-001, ANB019-002, and ANB019-005) have been completed. Study ANB019-001 was a Phase 1, first-in-human, single ascending dose (SAD) and multiple ascending dose (MAD) study in healthy volunteers and in subjects with psoriasis. Study ANB019-002 was a single-arm, multiple-dose study conducted in subjects with active GPP.

Study ANB019-005 was a Phase 1, ethno-bridging study, a single-dose safety, tolerability, PK, and immunogenicity study of imsidolimab in healthy Japanese and Caucasian subjects. A detailed description of the safety and tolerability, and PK/PD results of these studies is provided in the IB.

In addition, four Phase 2 studies (ANB019-003, ANB019-206, ANB019-207 and ANB019-209) to evaluate clinical activity and safety of imsidolimab in PPP, ichthyosis, epidermal growth factor receptor inhibitors/MEK inhibitors (EGFRi/MEKi) related acneiform rash, and acne vulgaris, respectively, are ongoing. Study ANB019-003 is a randomized, placebo-controlled, multiple dose study to be conducted in subjects with PPP. Study ANB019-206 is a randomized, placebo-controlled, multiple dose study to be conducted in adolescent and adult subjects with ichthyosis. Study ANB019-207 is a randomized, placebo-controlled, multiple dose study to be conducted in subjects with acneiform rash resulting from treatment with EGFRi/MEKi therapy. Study ANB019-209 is a randomized, placebo-controlled, multiple-dose study conducted in subjects with acne vulgaris.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

No major toxicities were observed in the 4-week repeat-dose toxicity study in cynomolgus monkeys. The main finding consisted of minor, injection site reactions associated with the SC route of administration and not considered AEs.

In cynomolgus monkeys, treatment-related effects observed in the 13-week repeat-dose toxicity study included protozoa in the stomach, an increase in nonformed feces and prolapsed rectum observations; the latter observation was not considered dose related. The increase in protozoa in the stomach has been observed in monkeys treated with immune-modulating drugs (Dubey 2002) and is consistent with the putative mechanism of action of imsidolimab. During the 26-week repeat-dose toxicity study, imsidolimab-related effects were limited to a low incidence of liquid feces. In the monkeys, the increased incidence of protozoa, nonformed feces, and prolapsed rectum were not considered AEs as they responded to veterinarian intervention. In humans, gastrointestinal infections can be clinically monitored and, in the case of most protozoa, are readily treatable even in the context of immunocompromised individuals (Farthing 2006).

One female monkey receiving 60 mg/kg imsidolimab IV was found moribund on Study Day 34. The cause of death was not determined and had an uncertain relationship to imsidolimab but could be due to treatment-related immune modulation. However, data published on IL-36R-deficient humans shows no deleterious effect on general health, and normal immune function is broadly preserved, indicating that inhibition of IL-36R does not generally compromise host defenses. Similar to other immune-modulating treatment paradigms, subjects should be closely monitored for any clinical gastrointestinal manifestations including infections and evaluated on an ongoing basis. If a gastrointestinal infection is suspected, the subject should be treated as clinically indicated.

In the ANB019-001 study in healthy adults, single doses of imsidolimab up to 750 mg administered by IV infusion or SC injection to 32 healthy adults in the SAD part of the Phase 1

study were generally well tolerated with a similar number of treatment-emergent adverse events (TEAEs) reported in subjects receiving imsidolimab or placebo, 29 subjects (81%) and 11 subjects (92%), respectively. The most frequently reported AEs were upper respiratory tract infection (URTI; 10 [28%] imsidolimab; 6 [50%] placebo), headache (10 [28%] imsidolimab; 3 [25%] placebo), and viral URTI (4 [11%] imsidolimab; 1 [8%] placebo). Additionally, multiple doses of imsidolimab up to 300 mg administered by IV infusion once weekly for 4 weeks to 18 healthy adults were also well tolerated. Overall, TEAEs occurred in 16 subjects (89%) receiving imsidolimab and in 3 subjects (50%) receiving the placebo. The most common AEs were headache (7 [39%] imsidolimab; 1 [17%] placebo) and URTI (3 [17%] imsidolimab; 1 [17%] placebo).

In ANB019-005, single doses of imsidolimab up to 750 mg administered by IV infusion or SC injection to 32 healthy Japanese and Caucasian adults were generally well tolerated. The most common TEAEs were alanine aminotransferase (ALT) increased (3 subjects [9.4%]) and aspartate aminotransferase (AST) increased (2 subjects [6.3%]).

One serious adverse event (SAE) of sepsis was reported in the recently completed ANB019-002 study in subjects with GPP; the SAE was considered possibly related to the study drug. The subject had a medical history of sepsis and experienced the SAE after the 750 mg IV dose administration. Antibiotic treatment rapidly resolved the sepsis episode with complete subject recovery. A second SAE of COVID-19 infection which was unrelated to imsidolimab was also reported. Further details of imsidolimab clinical studies are in the IB.

As allergic or anaphylactic reactions may occur in any subjects treated with mAbs, subjects should be observed during study drug administration and for a period of 30 minutes after each SC drug administration. Subjects with true allergic/anaphylactic reactions should not receive further doses of the monoclonal antibody. Symptoms of an apparent allergic reaction to the drug, also known as ‘cytokine release syndrome’, 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 (eg, blood and mucus in the lung)

Such reactions should be managed as clinically indicated and according to standard clinical practice.

2.3.2 KNOWN POTENTIAL BENEFITS

Subjects with HS may or may not receive direct benefit from participating in this study. An improvement in the condition as a result of participating in the study may be observed since all subjects will receive the active treatment at some point during the study.

Participation in this study also may help generate future benefit for larger groups of patients with HS if imsidolimab proves to be successful in treating this disease.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

All quality, pharmacology and toxicology data, and satisfactory safety and tolerability data demonstrated in nonclinical and clinical studies are considered sufficient to expect a positive benefit/risk ratio for the treatment of HS with imsidolimab, and therefore to initiate this study.

The risk to subjects in this trial will be minimized by compliance with the eligibility criteria, proper study design, and close monitoring.

3 OBJECTIVES AND ENDPOINTS

3.1 PRIMARY OBJECTIVE AND ENDPOINT

Primary Objective	Primary Endpoint
To evaluate the efficacy of imsidolimab in subjects with HS	Change from Baseline in AN count at Week 16

3.2 SECONDARY OBJECTIVES AND ENDPOINTS

Secondary Objectives	Secondary Endpoints
To evaluate the safety of imsidolimab in subjects with HS	Incidence of AEs, SAEs, and AEs leading to treatment discontinuation, as well as changes in vital signs, clinical laboratory parameters (hematology, biochemistry, and urinalysis), and 12-lead electrocardiograms (ECGs)
To evaluate the effect of imsidolimab on HS signs and symptoms in subjects with HS	• Percent change from Baseline in AN count at Week 16 • Proportion of subjects achieving Hidradenitis Suppurativa Clinical Response 50 (HiSCR50) at Week 16 • Change from Baseline in HS Pain Numeric Rating Scale (NRS) at Week 16 • Percent change from Baseline in HS Pain NRS at Week 16

3.3 EXPLORATORY OBJECTIVES AND ENDPOINTS

Exploratory Objectives	Exploratory Endpoints
To further evaluate the effect of imsidolimab on HS signs and symptoms, and quality of life in subjects with HS	• Change from Baseline in AN count at visits other than Week 16 • Percent change from Baseline in AN count at visits other than Week 16 • Proportion of subjects achieving a reduction in AN count of ≥50% and ≥75% relative to Baseline (AN50 and AN75 responses) • Percentage of subjects experiencing flare, defined as a ≥25% increase in AN count with an absolute increase in AN count of ≥2 relative to Baseline at each visit • Change from Baseline in abscess count at each visit • Change from Baseline in inflammatory nodule count at each visit • Change from Baseline in draining fistula count at each visit • Proportion of subjects achieving HiSCR50 at visits other than Week 16

Exploratory Objectives	Exploratory Endpoints
	• Proportion of subjects achieving Hidradenitis Suppurativa Clinical Response 75 (HiSCR75) at each visit • Proportion of subjects achieving 0 (inactive) or 1 (almost inactive) on Hidradenitis Suppurativa Physician's Global Assessment (HS-PGA) at each visit • Proportion of subjects with ≥2-point reduction from Baseline on HS-PGA at each visit • Change from Baseline in HS-PGA • Change from Baseline in calculated composite of abscesses, draining fistulas, and inflammatory and non-inflammatory nodules • Change from Baseline in HS Pain NRS at visits other than Week 16 • Percent change from Baseline in HS Pain NRS at visits other than Week 16 • Proportion of subjects achieving a ≥3-point reduction on the HS Pain NRS for subjects with Baseline HS Pain NRS of at least 3 • Proportion of subjects requiring rescue medication or treatment at each visit • Change from Baseline in Dermatology Life Quality Index (DLQI) score at each visit • Change from Baseline in International Hidradenitis Suppurativa Severity Score System (IHS4) at each visit • Change from Baseline in Hidradenitis Suppurativa Quality of Life (HiSQoL) at each visit • Change from Baseline in Hidradenitis Suppurativa Patient's Global Assessment (HS-PtGA) at each visit • Proportion of subjects in each response category for the HS-PtGA at each visit • Proportion of subjects in each response category for the Patient Global Impression of Change (PGIC) at each visit • Proportion of subjects achieving improvement ("Much better" or "Very much better") according to the PGIC at each visit • Proportion of subjects achieving improvement ("A little better", "Much better" or "Very much better") according to the PGIC at each visit • Proportion of subjects in each response category for the Patient Global Impression of Bother (PGIB) at each visit • Change from Baseline in PGIB at each visit • Proportion of subjects achieving "A little bothered" or "Not at all bothered" for the PGIB at each visit • Proportion of subjects in each response category for the Patient Global Impression of Severity (PGIS) at each visit

Exploratory Objectives	Exploratory Endpoints
	• Proportion of subjects achieving "Mild" or "No activity" according to the PGIS at each visit • Change from Baseline in PGIS at each visit • Proportion of subjects in each category of Hurley Stage at each visit • Change from Baseline in Hurley Stage at Weeks 16, 32, and 40 • Proportion of subjects achieving at least a 1-stage improvement in Hurley Stage
To explore the effect of imsidolimab on cutaneous biomarkers	Skin tape strip and drainage fluid biomarkers analysis including, but not limited to, IL-36 and Th-17
To test for immunogenicity to imsidolimab	Presence of ADAs to imsidolimab
To describe the PK profile of imsidolimab in subjects with HS	Serum concentration following imsidolimab administration and other parameters as appropriate will be determined to describe the PK profile of imsidolimab

4 STUDY DESIGN

4.1 OVERALL DESIGN

This is a Phase 2, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of imsidolimab in adult subjects with HS. This study also will characterize the PK profile of imsidolimab and explore the immune response to imsidolimab in subjects with HS.

To be eligible for this study, subjects must have a clinically confirmed diagnosis of HS with a disease duration of at least 6 months before Day 1. In addition, subjects will have the following characteristics at screening and Day 1: 1) HS lesions present in at least 2 distinct anatomical areas, 1 of which must be Hurley Stage II (ie, single or multiple, widely separated, recurrent abscesses with tract formation and cicatrization) or Hurley Stage III (ie, diffuse or near-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area); 2) total AN count of ≥ 5; 3) ≤ 20 draining fistulas.

The maximum study duration per subject is approximately 44 weeks, which includes a screening period of up to 30 days, followed by a 16-week placebo-controlled period, a 16-week treatment extension period, and an 8-week follow up period. The placebo-controlled period ends at Day 113 (Week 16) and the treatment extension period starts when study treatment is administered at the Week 16 visit. Of note, during the extension period all subjects will receive imsidolimab but their treatment will remain blinded (see Figure 1).

During the placebo-controlled period, eligible subjects will be randomized (1:1:1) to receive either imsidolimab (at 1 of 2 different regimens) or placebo, SC administered on 4 occasions: Day 1, Day 29 (Week 4), Day 57 (Week 8), and Day 85 (Week 12). Randomization will be stratified based on Hurley Stage at baseline (Stage II or III).

The treatment arms during the placebo-controlled period will be as follows:

1. Imsidolimab 400 mg on Day 1, followed by 200 mg on Days 29, 57, and 85
2. Imsidolimab 200 mg on Day 1, followed by 100 mg on Days 29, 57, and 85
3. Placebo on Days 1, 29, 57, and 85

During the extension period, all subjects will receive imsidolimab, SC administered on 4 occasions: Day 113 (Week 16), Day 141 (Week 20), Day 169 (Week 24), and Day 197 (Week 28). Subjects randomized to imsidolimab during the placebo-controlled period will continue to receive the same dose of imsidolimab on Days 113, 141, 169, and 197. Subjects randomized to placebo during the placebo-controlled period will receive either a 400-mg dose of imsidolimab on Day 113, followed by a 200-mg dose of imsidolimab on Days 141, 169, and 197, or 200-mg dose of imsidolimab on Day 113, followed by a 100-mg dose of imsidolimab on Days 141, 169, and 197 based on a 1:1 randomization.

For scheduled on-site study visits, subjects will come to the study site on 12 occasions: screening and Days 1, 29, 57, 85, 113, 141, 169, 197, 225, 253, and 281 (EOS)/ET. All procedures will be conducted in accordance with the Schedule of Activities (SoA) in Section 1.3.

Disease activity will be evaluated for all subjects using AN count, draining fistula count, HiSCR50, HiSCR75, Hurley Stage, HS-PGA, IHS4, HS Pain NRS, PGIC, PGIB, PGIS, DLQI, HiSQoL, and HS-PtGA.

Safety assessments will include AE/SAE monitoring, vital signs, physical examination, ECGs, and clinical laboratory tests (hematology, biochemistry, and urinalysis).

Blood samples will be collected during the study to determine PK and immunogenicity (presence of ADA to imsidolimab) on Day 1 before the administration of the study treatment and at the other time points specified in the SoA (Section 1.3). Any remaining serum/plasma from samples collected for PK/PD immunogenicity endpoints may be retained for assay method development, troubleshooting, or validation. The samples will not be used for any type of genetic analyses.

Photography is an optional procedure for all subjects at each of the specified visits at each site.

Skin tape strips will be collected at Day 1, Week 4, Week 16, and Week 32 to study gene expression.

Interim analyses may be performed for assessment of all primary and secondary efficacy endpoints and evaluation of all safety data available.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

To date, only the anti-TNFα monoclonal antibody, adalimumab has received Food and Drug Administration (FDA) approval for treatment of HS. However, based on the results of the Phase 3 studies PIONEER I and PIONEER II, ~40-60% of treated subjects failed to achieve treatment response (Kimball 2016). Given the high prevalence of HS (Jemec 2012) and the substantial fraction of subjects failing to achieve treatment response, a significant unmet medical need persists. In this context, the development of agents with new mechanisms of action is considered important for future clinical practice. As imsidolimab offers the potential for inhibition of IL-36 signaling by blocking IL-36R, it may provide a novel strategy for treatment of patients with HS.

The proposed design is considered appropriate for assessing the safety and tolerability of imsidolimab in subjects with HS and the efficacy of imsidolimab compared with placebo in subjects with HS.

In the placebo-controlled period, randomization will ensure random allocation of subjects to treatment arms to reduce bias. Because efficacy assessments of HS have a high degree of subjectivity, the study will be double-blinded. The highest degree of subject and assessor (Investigator or designee) blinding should be sought to achieve credible inference. It is also important to have a placebo-control period in this Phase 2 study to control for confounding factors, such as potential Investigator bias, and to ensure that the statistical procedures can be appropriately applied.

4.3 JUSTIFICATION FOR DOSE

During the placebo-controlled period, imsidolimab will be administered by SC injection as a 400-mg dose on Day 1, followed by 200-mg doses on Days 29, 57, and 85; or as 200 mg dose on Day 1, followed by 100-mg doses on Days 29, 57, and 85.

The doses selected for the study demonstrated a favorable safety and tolerability profile in a Phase 1 study conducted in healthy volunteers. In addition, imsidolimab demonstrated linear PK with an estimated $t_{1/2}$ of approximately 28 days at all doses tested with persistent pharmacodynamic activity. The loading dose of 400 mg SC administered on Day 1 was chosen to achieve maximum observed concentration (C_{max}) soon after dosing in order to provide optimal potential benefit to HS subjects and to reach steady state concentrations rapidly following 200 mg SC dosing. The loading dose of 200 mg SC administered on Day 1 followed by 100 mg doses every four weeks is expected to be lower than the exposure-response curve, allowing for the assessment of dose-dependent effects and to inform dosing in future studies. The 16-week placebo-controlled period is expected to provide better clinical outcome, thus potentially benefiting subjects with HS and further assessing the long-term safety and efficacy of imsidolimab.

The extension period was added to provide potential benefits to subjects with HS randomized to placebo during the placebo-controlled period and to further assess the long-term efficacy of imsidolimab.

4.4 END OF STUDY DEFINITION

A subject is considered to have completed the study if he/she has completed all periods of the study including the last specified visit (Day 281 [Week 40]/ET) shown in the SoA (Section 1.3).

The end of the study is defined as completion of the last visit or procedure shown in the SoA by the last subject included the study.

4.5 MODIFICATIONS TO STUDY CONDUCT DUE TO THE CORONAVIRUS DISEASE 2019 (COVID-19) PANDEMIC

As a consequence of the COVID-19 pandemic that had a worldwide impact, including cases in North America and Europe, control measures in place in different regions may impact the ability to adhere to some of the study procedures described in this protocol. Due to challenges that include, but are not limited to, subject preferences, study site closures, travel restrictions, and quarantines, some modifications to study conduct during the COVID-19 pandemic may be necessary to ensure study continuity, including conducting optional home visits when on-site study visits are considered not feasible. Such modifications in study conduct always must be in accord with local regulations/mandates. The following are allowable, as necessary, modifications to study conduct during the COVID-19 pandemic:

- Prior to a visit at the study site, the subject may be contacted and screened for potential exposure to or infection with COVID-19 per site, local or federal requirements. If the

subject is suspected of having been or is currently infected with COVID-19, the on-site visit should either be re-scheduled or a virtual visit may be performed, as applicable.

- In the event that a subject cannot attend their regularly scheduled study visits in person due to COVID-19 necessitating a limit on in-person contact, the Investigator may perform safety and efficacy assessments by phone or video, with home nursing visit support for procedures that cannot be done virtually. The Investigator may use the technology platform that is currently available to them. Suggested platforms include Apple FaceTime, Zoom for Healthcare, Facebook Messenger video chat, Microsoft Team, Google Hangouts video, and Skype. Home nursing visit support may be used in addition to phone or video at visits that require procedures that cannot be done via phone or video alone, such as but not limited to, ECG, PK draws, clinical laboratory draws, study drug administration. The home nurse will collect the lab samples and perform all applicable study assessments that are possible during a home visit, including collection of adverse events and concomitant medications. During the COVID period, if any data is collected at a home visit, it will be recorded by the home nurse in the source documents and the originals will be sent back to the site for data entry into the electronic data capture system for storage/archiving.
- Clinical laboratory tests (chemistry and hematology) and pregnancy tests may be performed by local laboratory if home nursing visits are not possible and sample collection cannot be performed at the study site due to COVID 19-related limitations, including but not limited to site closure. Abnormal laboratory results should be promptly communicated to the Medical Monitor. Subjects' anonymity must be maintained when communicating results to the Medical Monitor.
- At home study drug administration by home health nurses may be done.
- Source documentation should note that the visit was performed virtually (not face-to-face), and note the name of the local laboratory where laboratory tests were done.
- If certain study procedures or assessments cannot be completed per the schedule of events, the reason for the missed assessment (ie, laboratory, vital signs, physical exams, etc.) must be noted in the source documentation (eg, COVID-19), captured in the protocol deviations documentation, and reported to the IRB/Ethics Committee, as applicable.

A detailed assessment of COVID-19 related risk and mitigation measures will be documented in the appropriate study plans.

5 STUDY POPULATION

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.

It is imperative that subjects fully meet all the inclusion criteria and none of the exclusion criteria.

5.1 INCLUSION CRITERIA

To be eligible to participate in this study, a subject must meet all of the following criteria, either at the screening and Day 1 visits or only at one of the specified visits (screening or Day 1) as noted in the criterion:

1. Male or female aged 18 to 75 years (inclusive) at the time of signing informed consent.
2. Clinically confirmed diagnosis of active HS with a disease duration of ≥ 6 months before Day 1 (information obtained from medical chart or subject's physician, or directly from the subject).
3. HS lesions present in at least 2 distinct anatomical areas, 1 of which must be Hurley Stage II (ie, single or multiple, widely separated, recurrent abscesses with tract formation and cicatrization) or Hurley Stage III (ie, diffuse or near-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area).
4. Total AN count ≥ 5.
5. Subject has ≤ 20 draining fistulas
6. Stable HS for at least 6 weeks prior to Day 1 visit as determined by the Investigator through subject interview and review of medical history.
7. Agree to daily use (and throughout the study) of one of the following over-the-counter treatments on their body areas affected with HS lesions: chlorhexidine gluconate, triclosan, benzoyl peroxide, dilute bleach in bathwater, or soap and water.
8. Meet the following laboratory criteria at screening:
    a) Hemoglobin ≥ 90 g/L (≥ 9 g/dL)
    b) White blood cell count ≥ 3.0×10^9/L (≥ 3.0×10^3/µL)
    c) Platelets ≥ 100×10^9/L (≥ 100×10^3/µL)
    d) Serum creatinine <132.6 µmol/L (< 1.5 mg/dL)
    e) Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤ 2 upper limit of normal (ULN)
    f) Total bilirubin ≤ 1.5 × ULN. Subjects with known Gilbert's disease who have serum bilirubin < 3 × ULN may be included
9. Body weight ≥ 40 kg.
10. Contraceptive use by men and women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.

Contraception and pregnancy:

a) A male subject who has not had a vasectomy must agree to use contraception as detailed in Appendix 1 of this protocol during the treatment period and for at least 220 days (which includes the duration of relevant exposure plus the duration of sperm cycle) after the last study treatment administration and refrain from donating sperm during this period.
b) Female subjects:
   i) A woman of childbearing potential (WOCBP) is eligible to participate if she has a negative serum pregnancy test (β-human chorionic gonadotropin) at screening and a negative urine pregnancy test at Day 1 (see Appendix 1), is not breastfeeding, and agrees to follow the contraceptive guidance in Appendix 1 during the treatment period and for at least 6 months after receiving the study treatment, and refrains from donating oocytes for assisted reproduction during this period. The female subject's selected form of contraception must be effective by the time the female subject enters into the study at Day 1 (eg, hormonal contraception should be initiated at least 12 Weeks before Day 1. For WOCBP, hormonal contraceptives must be used without schedule changes and in steady doses during the study treatment. Starting hormonal contraceptives during the study is not permitted. Use of any hormonal contraceptives containing drospirenone, chlormadinone acetate, or cyproterone acetate is prohibited unless part of a stable contraceptive regimen as described in Section 6.5.1.
   ii) A woman not of childbearing potential as defined in Appendix 1 is eligible to participate in the study. A postmenopausal woman must have a follicles -timulating hormone (FSH) test confirming nonchildbearing potential.

11. Willing to participate and capable of giving written informed consent, which must be personally signed and dated by the subject and obtained prior to any trial-related activities.
12. Willing to comply with all study procedures and must be available for the duration of the study.

5.2 EXCLUSION CRITERIA

A subject who meets any of the following criteria at the screening and/or Day 1 visits, as applicable, will be excluded from participation in this study:

1. Concomitant dermatological or medical conditions that may interfere with the Investigators' ability to evaluate the subject's response to therapy.
2. History of clinically significant (as determined by the Investigator) cardiac, pulmonary, neurologic, gastrointestinal, endocrine, hematological, renal, hepatic, cerebral or psychiatric disease, or other major uncontrolled disease.

3. Chronic or recurrent infectious disease, including but not limited to upper and lower respiratory infection (eg, bronchiectasis), urinary tract infection (eg, recurrent pyelonephritis), within 6 months prior to screening. Note: A subject with a history of localized oral or genital herpes simplex that, in the opinion of the Investigator, is well controlled will be eligible for study participation.
4. Any evidence of active infection that required treatment with a systemic antibiotic, antiviral, or antifungal agent within 4 weeks of Day 1 (eg, bronchopulmonary, urinary, or gastrointestinal), excluding localized oral or genital herpes simplex that, in the opinion of the Investigator, is well-controlled.
5. Any factors that would predispose the subject to develop an infection in the Investigator's opinion.
6. Opportunistic infection (eg, *Pneumocystis carinii*, aspergillosis, or mycobacteria other than tuberculosis [TB]) or parasitic infections (eg, helminths, protozoa, *Trypanosoma cruzi*) within 6 months prior to screening.
7. Herpes zoster infection within 2 months prior to screening.
8. *[intentionally blank]*
9. Known or suspected congenital or acquired immunodeficiency state, or condition that would compromise the subject's immune status (eg, history of splenectomy).
10. Major surgery within 4 weeks of Day 1.
11. History of cancer or lymphoproliferative disease within 5 years of Day 1. Subjects with successfully treated nonmetastatic cutaneous squamous cell or basal cell carcinoma and/or localized carcinoma in situ of the cervix are not to be excluded.
12. History of any significant drug allergy or reaction to polysorbate-20, a component of imsidolimab formulation, or the inactive ingredients (excipients).
13. Any oral antibiotic treatment for HS within 4 weeks of Day 1.
14. Prescription topical therapies for the treatment of HS within 2 weeks of Day 1.
15. Over-the-counter topical antiseptic washes, creams, soaps, ointments, gels, and liquids containing antibacterial agents to treat HS within 2 weeks prior to Day 1 (unless specified as permitted in Section 6.5.1)
16. Systemic non-biologic therapies with potential therapeutic impact for HS within 4 weeks of Day 1, including methotrexate (MTX), cyclosporine, retinoids, and fumaric acid esters, and oral or injectable corticosteroids (unless clearly specified as permitted; see Section.6.5.1).
17. Oral analgesics (including opioids) within 2 weeks of Day 1, unless a subject is on a stable dose (PRN is not considered a stable dose) of non-opioid analgesics for a non-HS medical condition (eg, osteoarthritis), and the is stable for 2 weeks prior to Baseline and is anticipated to remain stable throughout study participation.
18. Subject requires or is expected to require opioid analgesics during the study for any reason (excluding tramadol as described in Section 6.5.1).
19. Nonbiologic investigational drug within 4 weeks or 5 half-lives of Day 1, whichever is longer.

20. Biologics for at least 12 weeks or 5 half-lives prior to Day 1 (eg, adalimumab).
21. Live or live-attenuated vaccines within 12 weeks prior to Day 1. Live and live-attenuated vaccines may be utilized 12 weeks after the last study treatment administration Note: Currently authorized non-live and non-live-attenuated vaccines for COVID-19 (eg, RNA-based vaccines, protein-based vaccines, and nonreplicating viral vector-based vaccines) are allowed during the study.
22. Surgical, laser, or intense pulsed light (IPL) intervention in area with HS lesion within 4 weeks prior to Day 1.
23. Phototherapy (psoralen and ultraviolet A [PUVA] and/or UVB) within 4 weeks prior to Day 1
24. Active TB or latent TB infection as indicated by a positive QuantiFERON®-TB Gold test at screening (if the test is indeterminate, it can be repeated only once), chest X-ray, and/or clinical examination, or has had active TB disease at any time in the past.
25. Clinically significant drug or alcohol abuse in the last year prior to Day 1, or other factors limiting the ability to cooperate and to comply with the study protocol, as determined by the Investigator.
26. Subject is a pregnant or lactating woman, or a woman who intends to become pregnant during the study period.
27. Any other physical, mental, or medical conditions, which, in the opinion of the Investigator, make study participation inadvisable or could confound study assessments.
28. Clinically significant abnormality on chest X-ray at screening or within 6 months prior to screening.
29. Positive blood screen for hepatitis C antibody and hepatitis C RNA, antibodies to hepatitis B core antigen, hepatitis B surface antigen, or human immunodeficiency virus 1 and 2 antibodies.
30. Subject is not able to tolerate SC drug administration.

5.3 LIFESTYLE CONSIDERATIONS

Subjects are allowed to take a bath/shower as desired throughout the study, but not allowed 3 hours prior to a study visit. Over-the-counter topical antiseptic washes, creams, soaps, ointments, gels, and liquids containing antibacterial agents to treat HS are not allowed unless clearly specified as permitted (see Section 6.5.1).

5.4 SCREEN FAILURES

Screen failures are defined as subjects who consent to participate in the clinical study but are not subsequently randomized in the study. A minimal set of screen failure information is required to ensure transparent reporting of screen failure subjects to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory

authorities. Minimal information includes demography, screen failure reasons, eligibility criteria not met, and any SAE that occurred.

Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened once after discussion with the Medical Monitor. Rescreened subjects should not be assigned the same subject number as for the initial screening. All procedures planned at the screening visit, including signature of a new consent form, will be performed.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

The recruitment and retention strategies for the study will be covered in other study plans.

6 STUDY TREATMENT

Study treatment is defined as any investigational treatment or placebo intended to be administered to a clinical study subject according to the study protocol.

6.1 STUDY TREATMENT ADMINISTRATION

6.1.1 STUDY TREATMENT DESCRIPTION

Imsidolimab is a humanized IgG4 (S228P)/kappa mAb that belongs in the class of anti-IL-36R mAb. Details regarding imsidolimab and placebo study treatment are described in Table 2 and further information will be provided in the Pharmacy Manual.

6.1.2 DOSING AND ADMINISTRATION

Study treatment dosing and administration details are provided in Table 2. Further information will be provided in the Pharmacy Manual.

Table 2: Study Treatment Details

Study Treatment Name:	**Imsidolimab (ANB019)** **Anti-interleukin 36 receptor monoclonal antibody**	**Placebo**
Dosage Form:	Solution for injection	
Source of procurement:	AnaptysBio, Inc.	
Study Treatment Description	Imsidolimab will be provided as a sterile, colorless to yellow, and clear to slightly opalescent solution supplied in a single use, 2R, Type I glass vial. Each vial contains 100 mg/1 mL of imsidolimab (ANB019).	The placebo contains no active ingredient and will be provided as a sterile, colorless to slightly yellowish, and clear to very slightly opalescent solution supplied in a single use, 2R, Type I glass vial. Each vial contains 1 mL of placebo.
Dosage Formulation:	100 mg/mL imsidolimab in 25 mM *L*-histidine, 60 mM NaCl, 145 mM sorbitol, and 0.02% (w/v) polysorbate 20 at pH 6.0.	Placebo 25 mM *L*-histidine, 60 mM-NaCl, 145 mM sorbitol, and 0.02% (w/v) polysorbate 20 at pH 6.0.
Unit Dose Strength(s)/ Dosage Level(s):	Study treatment will be administered as 400/200/100 mg of imsidolimab or placebo. Vials containing 1 mL of active and placebo doses will be provided to sites and prepared by an unblinded pharmacist according to Table 3.	
Route of Administration:	SC injection (4 doses during the placebo-controlled period and 4 doses during the extension period)	
Dosing Instructions:	Imsidolimab and placebo should be administered by blinded clinic staff trained in best practices for SC administration of study treatments. For SC injections, imsidolimab and placebo should be prepared by drawing up the required dosing volume into suitable sized syringe and attaching a dosing needle. No further	

Study Treatment Name:	Imsidolimab (ANB019) Anti-interleukin 36 receptor monoclonal antibody	Placebo
	dilution is required. Syringes should be covered in tape by an unblinded pharmacist to obscure color and volume. The preferred anatomical site of SC administration is the abdomen; however, the injection may be made in the upper arm, if needed. A 30-minute observation period should be included after each SC dose administered. The same anatomical site should be used throughout the entire study for a given subject (ie, do not administer one dose into the upper arm and at a subsequent visit or dose, administer the next dose into the abdomen). Subsequent doses should be rotated within an anatomical site (ie, if the upper left abdominal quadrant is used as the initial site of administration, then the next administration at a subsequent visit should be rotated to the upper right quadrant). Subcutaneous injections should not be given into moles, scars, tattoos, or areas where the skin is tender, bruised, red, hard, or not intact. Prior to SC needle insertion, the skin will be pinched between the thumb and index finger to separate the subcutaneous layer from the muscle. The needle is to be injected at a 45- to 90-degree angle to the skin. The plunger will be pressed gently until the entire dose is delivered to the SC space and the needle will be held in place (fully depressed) for 10 seconds after the injection is administered. The needle will be removed and then the skin pinch released; any leakage or backflow of fluid from the administration site onto the surface of the skin will be noted and documented in the eCRF. The site of administration is NOT to be massaged by either the clinic staff or by the subject for at least 60 minutes after drug administration.	

Abbreviations: eCRF, electronic case report form; NaCl, sodium chloride; SC, subcutaneous.

The contents of the label will be in accordance with all applicable regulatory requirements.

Table 3: Treatment Administration Schedule

Arm	Dose regimen	Kit Types Used[a]			
		Day 1 2 x 2 mL	**Days 29, 57, 85** 1 x 2 mL	**Day 113** 2 x 2 mL	**Days 141, 169, 197** 1 x 2 mL
1	400/200 mg	1	4	4, 6	4
2	200/100 mg	2	5	5, 6	5
3A	Placebo w 400/200 mg Extension	3	6	4, 4	4
3B	Placebo w 200/100 mg Extension	3	6	4, 6	5

[a] The following kit types will be provided to study sites and used by an unblinded pharmacist to prepare study treatment according to the schedule above. All treatment will consist of 2 mL volume, drawn from two 1-mL vials of either 100 mg/mL imsidolimab or placebo. On Days 1 and 113, 2 x 2 mL injections will be administered to all subjects to account for the 400 mg loading dose. On all other study visits, 1 x 2 mL injection will be administered. Additional details will be provided in the Pharmacy Manual.

Kit type	1	2	3	4	5	6
Kit name	4xActive	2:2 Mix	4xPlacebo	2xActive	1:1 Mix	2xPlacebo
Contents	4 imsidolimab 1-mL vials	2 imsidolimab + 2 placebo 1-ml vials	4 placebo 1-mL vials	2 imsidolimab 1-mL vials	1 imsidolimab + 1 placebo 1-mL vial	2 placebo 1-ml vials

6.2 PREPARATION/HANDLING/STORAGE/ACCOUNTABILITY

The Investigator or designee must confirm appropriate temperature conditions have been maintained during transit for all study treatments received, and any discrepancies are to be reported and resolved before use of the study treatment.

Only subjects randomized in the study may receive study treatment and only authorized study site staff may supply or administer study treatment. Further guidance and information for the administration of the study treatment are provided in the Pharmacy Manual.

All study treatments must be stored in a secure, environmentally controlled, and monitored (manual or automated) area in accordance with the labeled storage conditions with access limited to the Investigator and authorized study site staff.

Imsidolimab vials must be refrigerated at 2°C to 8°C (36°F to 46°F) until the day of use. Imsidolimab must not be used beyond the expiration date provided by the manufacturer. Vial contents should not be frozen or shaken. Imsidolimab vials undiluted may be stored at room temperature (8°C to 25°C [46°F to 77°F]) for up to 8 hours. Vials are intended for single use only; therefore, any remaining solution should not be used and should be discarded after study treatment accountability and reconciliation.

The Investigator is responsible for study treatment accountability, reconciliation, and record maintenance (ie, receipt, reconciliation, and final disposition records).

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

Further guidance and information for the final disposition of unused study treatment are provided in the Pharmacy Manual.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

This study includes a randomized, double-blind, placebo-controlled period followed by an extension period. The blind will be maintained throughout the study with limited and controlled access to the randomization code.

All subjects will be assigned a unique 'subject identification number' at the time of screening. On Day 1, after verification that all inclusion and no exclusion criteria have been met, the subjects will be randomized in a 1:1:1 ratio to receive imsidolimab at one of two doses or placebo. As subjects become eligible, they will be assigned unique randomization numbers, which will be used to assign the allocated treatment based on a randomization schedule.

After subjects complete the double-blind phase of the study, subjects randomized onto imsidolimab will continue on their maintenance dosage. Subjects who had been randomized to placebo will be re-randomized 1:1 to either 400 mg SC imsidolimab or 200 mg SC imsidolimab at Day 113 (Week 16).

The 400 mg loading dose of imsidolimab will be delivered as two 2-mL injections. To maintain the blind, on Day 1 subjects receiving the 200 mg loading dose will receive one 2-mL injection of imsidolimab and one 2-mL injection of placebo, and subjects receiving placebo will receive two 2-mL injections of placebo. At Day 113 (Week 16), following re-randomization of subjects from the placebo arm into active treatment groups, all subjects will receive two 2-mL injections of either imsidolimab alone or imsidolimab and placebo. On all other study visits, subjects will receive one 2-mL injection (see Table 3).

AnaptysBio, Investigator, and subjects will be blinded to treatment assignment of imsidolimab or placebo. An unblinded Pharmacist will be responsible for study treatment dispensing.

Once the subject has provided an informed consent and meets all inclusion and no exclusion criteria, the study site will request the treatment assignment on Day 1 and Day 113 using a central Interactive Web Response System (IWRS). The process for breaking the blind will be handled through the IWRS. Unblinding is undertaken by a predetermined process to ensure that participating subject and study team are not unblinded unnecessarily and the study results are not compromised. Unblinding of treatment assignment during the study should occur only if it is necessary to know what treatment the subject received during the placebo-controlled period. Unblinding should occur if the Investigator deems identification of the study treatment is necessary for the purpose of providing urgent subject care, and knowledge of the subject's

treatment assignment (imsidolimab or placebo) will alter subsequent care (emergency unblinding).

In the event that emergency unblinding is necessary, the Investigator must 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 must provide the reason for unblinding to the Medical Monitor according to ANB instructions following emergency unblinding. Subjects for whom the blind has been broken will be discontinued from treatment at the time of unblinding. After discontinuation from treatment, subjects should remain in the study for the duration of the safety follow-up period and complete the Day 281 (Week 40) EOS/ET visit 12 weeks after their last dose of study treatment.

AnaptysBio and the contract research organization (CRO) must be notified when a subject and/or Investigator is unblinded during the study. The IWRS will create the blinded and/or unblinded notification when the blind is broken, which can be sent via email as per the user role of IWRS. The unblinding will be captured in the IWRS audit trail. Pertinent information regarding the circumstances of unblinding of a subject's treatment code must be documented in the subject's source documents.

6.4 STUDY TREATMENT COMPLIANCE

Study treatment compliance in this study will be under the direct control of the Investigator; the study treatments will be administered on site.

The prescribed dosage, timing, and mode of administration may not be changed. Any departures from the intended regimen must be recorded in the electronic case report forms (eCRFs).

For the study treatment administrations, date/time of administration, site of administration, and dose administered (entire dose/incomplete dose) will be documented in the eCRF.

6.5 CONCOMITANT THERAPY

Any medication or vaccine (including over the counter or prescription medicines, vitamins, and/or herbal supplements) that the subject is receiving at the time of enrollment and receives during the study must be recorded on the eCRF along with:

- Reason for use
- Dates of administration including start and end dates
- Dosage information including dose, route, and frequency

All medications used to treat HS disease conditions within 6 months prior to enrollment, and any prior use of adalimumab (Humira), must be recorded in the eCRF. Any other medications taken within 4 weeks prior to enrollment must also be recorded in the eCRF. Dose adjustments of these treatments should be avoided during the study. Live and live-attenuated vaccines may be utilized after the subjects complete the safety follow-up period of the study. During the follow-up period, no study drug will be administered and 12 weeks (at least three half-lives of study drug) is

estimated to be a sufficient period after the last dose administration when a live or live-attenuated vaccine can be safety administered.

The Medical Monitor should be contacted if there are any questions regarding concomitant or prior therapy.

6.5.1 PERMITTED THERAPIES

Use of daily washes are required for all subjects participating in the study. Permitted washes are limited to chlorhexidine gluconate, triclosan, benzoyl peroxide, dilute bleach in bathwater, or soap and water.

Starting on Day 1 and if a subject's pain worsens, subjects that require analgesia will be allowed to use ibuprofen (at a dose of up to 800 mg po every 6 hours, not to exceed 3.2 grams/24 hours) and/or acetaminophen as per local labeling. Pain uncontrolled with ibuprofen/acetaminophen may be controlled with tramadol (at a dose of up to 100 mg po every 4 hours, not to exceed 400 mg/24 hours) after Investigator discussion with the Medical Monitor). Of note, dose adjustments of ibuprofen, acetaminophen, or tramadol, and use of these analgesics PRN up to the maximum permitted dose and frequency, are allowed during the study. From screening through Week 32, subjects will not be permitted to use any analgesics related to HS pain within 24 hours of a scheduled study visit.

Oral contraceptives should be continued if stable for the last 12 weeks before Day 1 and if stable in dose and dosing regimen and type (brand) and if the subject plans to continue throughout the study period.

Currently authorized nonlive and nonlive-attenuated vaccines, including those for COVID-19 (eg, RNA-based vaccines, protein-based vaccines, and nonreplicating viral vector-based vaccines), are allowed during the study. If it is unclear if a vaccine is permitted, the Medical Monitor should be consulted prior to subjects' receiving a vaccine. Of note, vaccines, including those for COVID-19, should be captured as a concomitant medication and any related symptoms documented as AEs.

All permitted medications should be recorded as concomitant medications.

The Medical Monitor should be notified if a subject receives antibiotics for more than 10 days for adverse events.

6.5.2 PROHIBITED MEDICATIONS OR PROCEDURES

Prohibited medications/therapy are listed below in Table 4. The use of a prohibited medication/therapy (unless conditions for use of rescue medications have been met, see Section 6.6) is a protocol violation and must be recorded in the eCRF. Subjects who receive prohibited rescue treatment will be discontinued from the study and should return for a final ET visit 12 weeks after their last dose. Study procedures at the ET visit should be completed according to the SoA in Section 1.3. In the case of ongoing AEs/SAEs, the subject should be followed up until it has resolved to a stable outcome or subject is lost to follow-up. The date and time of rescue medication administration, as well as the name and dosage regimen of the rescue medication, must be recorded into the eCRF/study database by study site personnel.

All treatments likely to have efficacy in HS need to be discontinued prior to treatment initiation (prior to Day 1) according to Table 4. All medications listed below are also restricted during the study period. If treatment with any of these prohibited treatments is essential, then the subject must notify the study team.

Rescue therapy should be captured in the source documentation and on the appropriate eCRF.

Table 4: List of Prohibited Medications and Procedures

Prohibited Medication/Procedure	Washout Period
Prescription topical therapies for the treatment of HS, and over-the-counter topical antiseptic washes, creams, soaps, ointments, gels, and liquids containing antibacterial agents to treat HS (unless clearly specified as permitted in Section 6.5.1)	2 weeks of Day 1
Oral analgesics (including opioids) for HS-related pain, unless specified as permitted in Section 6.5.1	2 weeks of Day 1
Oral analgesics (including opioids) for non-HS-related pain, unless specified as permitted in Section 6.5.1	2 weeks of Day 1 (except stable use of ibuprofen and acetaminophen as indicated in Exclusion Criterion 17)
Systemic antibiotic treatment for HS. Note: Systemic antibiotic use (including oral or IV) is allowed for treatment of acute bacterial, fungal, or viral infections.	4 weeks of Day 1
Systemic non-biologic therapies with potential therapeutic impact for HS, including MTX, cyclosporine, retinoids, and fumaric acid esters, and oral or injectable corticosteroids (unless clearly specified as permitted; see Section.6.5.1).	4 weeks of Day 1
Surgical, laser, or IPL intervention in area with HS lesion except as outlined in Section.6.5.1	4 weeks of Day 1
Phototherapy (PUVA and/or UVB)	4 weeks of Day 1
Nonbiologic investigational drugs	4 weeks or 5 half-lives (whichever is longer) prior to Day 1
Biologics that have a potential to impact HS (eg, adalimumab).	12 weeks or 5 half-lives prior to Day 1, whichever is longer
Live or live-attenuated vaccines. Note: Currently authorized nonlive and nonlive-attenuated vaccines for COVID-19 (eg, RNA-based vaccines, protein-based vaccines, nonreplicating viral vector-based vaccines) are allowed during the study.	12 weeks of Day 1
Drospirenone, chlormadinone acetate, or cyproterone acetate, unless part of a stable contraceptive regimen as described in Section 6.5.1	12 weeks prior to Day 1

6.6 RESCUE TREATMENT

In the event that an intolerable painful lesion occurs that requires an immediate intervention, at Week 8 or later, physicians will have the option to perform protocol-allowed interventions. Only

two types of interventions are allowed: injection with intralesional triamcinolone acetonide suspension (at a concentration of up to 5 mg/mL, up to 1 cc) and incision and drainage. If incision and drainage is performed, the required over-the-counter antiseptic wash should continue to be used. New systemic and topical therapies following incision and drainage (including antibiotics) are prohibited. Concomitant use of wound care dressings is allowed; however, options are limited to alginates, hydrocolloids, and hydrogels. If a subject requires more than 2 lesion interventions during each of the double-blind phases of the study, they must be discontinued from the study.

All study visit evaluations must occur before any interventions are performed. Any lesion that undergoes an intervention will be documented in the source. The study site will be required to count any lesion that undergoes an intervention as permanently present from the date of the intervention and must account for it in the source and on the appropriate eCRF. All interventions (including local anesthetics) should be recorded in the eCRF for tracking purposes.

6.7 DOSE MODIFICATION

No dose modification is allowed in this study. Study treatment can be interrupted temporarily or permanently if deemed necessary as per the Investigator's discretion.

6.8 TREATMENT AFTER THE END OF THE STUDY

All subjects will return to the study site for the EOS (Day 281/Week 40) or ET visit for final safety and EOS assessments. After this visit, subjects should be treated according to the clinical judgment of the subject's physician. Care after EOS/ET will not be provided by AnaptysBio, Inc. Any SAE or pregnancy occurring through the EOS visit should be reported to the pharmacovigilance unit (Section 8.2.1) and followed up until an outcome is determined.

7 STUDY TREATMENT DISCONTINUATION AND SUBJECT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY TREATMENT

The subject's eligibility criteria will be checked prior to administration of the study treatment on Day 1. If a clinically significant finding or AE/SAE is identified after enrollment, the Investigator or qualified designee will determine if the subject can receive the study treatment and continue in the study and if any change in subject management is needed.

Discontinuation from study treatment does not mean discontinuation from the study, and remaining study procedures should be completed as indicated by the study protocol. In case of early withdrawal from the study treatment and study, the subject will be required to attend the ET visit.

7.1.1 TEMPORARY INTERRUPTION

Study treatment can be interrupted temporarily for any individual subject in case of an AE as per the Investigator's discretion. The Medical Monitor should be informed. Re-starting of study treatment can be done after discussion with the Medical Monitor.

7.1.2 RE-CHALLENGE

The study treatment can be reintroduced at the next scheduled administration visit at the Investigator's discretion and after discussion with the Medical Monitor. Study treatment will be reintroduced at the maintenance dose (200 mg imsidolimab, 100 mg imsidolimab, or placebo). In case of positive re-challenge, the study treatment should be withdrawn permanently.

7.2 SUBJECT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

A subject may withdraw from the study at any time at his or her own request or may be withdrawn at any time at the discretion of the Investigator for safety, behavioral, compliance, or administrative reasons.

In case of early withdrawal from the study treatment, the subject will be required to attend an ET visit at the time the decision is made to stop study treatment early (see the SoA in Section 1.3). After completion of the ET visit, the subject should then return for a final follow-up EOS/ET visit approximately 12 weeks after receiving their last dose of study treatment. Subjects must be withdrawn from the study under the following circumstances, any SAE or AE which, in the opinion of the Investigator, warrant study discontinuation for safety reasons, or pregnancy occurring through the EOS, which should be followed up until outcome.

The following events are considered sufficient reasons for discontinuing a subject from the study treatment and/or the study:

- Pregnancy (refer to Appendix 1 and Section 8.2.1.8)
- Significant deviation/lack of compliance with protocol
- Any significant AE, laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the subject in the opinion of the Investigator
- Disease progression which requires discontinuation of the study treatment
- Withdrawal of consent
- Lost to follow-up
- Use of any prohibited medication or treatment that in the opinion of the Investigator necessitates the subject being withdrawn (refer to Section 6.5.2)
- Termination of the subject's participation by the Investigator or AnaptysBio

The reason for subject discontinuation or withdrawal from the study will be recorded on the eCRF.

If a subject withdraws from the study, he or she may request destruction of any samples taken and not tested, and the Investigator must document this in the study site study records.

See SoA (Section 1.3) for data to be collected at the time of study discontinuation and follow-up and for any further evaluations that need to be completed.

7.3 LOST TO FOLLOW-UP

A subject will be considered lost to follow-up if he or she repeatedly fails to return for scheduled visits and is unable to be contacted by the study site.

The following actions must be taken if a subject fails to return to the clinic for a required study visit (unless this is required by the COVID-19 situation and virtual visits are scheduled instead):

- The study site must attempt to contact the subject and reschedule the missed visit as soon as possible and counsel the subject on the importance of maintaining the assigned visit schedule and ascertain whether or not the subject wishes to and/or should continue in the study. If the re-scheduled visit falls within the next visit's window, then the visit should be considered a missed visit and the subject should come in for the next scheduled visit as planned. Missed visits must be captured in the eCRFs and will be recorded as a protocol deviation.
- Before a subject is deemed lost to follow-up, the Investigator or designee must make every effort to regain contact with the subject (where possible, 3 telephone calls and, if necessary, a certified letter to the subject's last known mailing address or local equivalent methods). These contact attempts should be documented in the subject's medical record or study file.
- Should the subject continue to be unreachable, he or she will be considered to have withdrawn from the study.

8 STUDY ASSESSMENTS AND PROCEDURES

Study procedures and their timing are summarized in the SoA (Section 1.3). Assessments scheduled on the day of study treatment administration must be performed prior to the study treatment administration unless otherwise noted. There are visits where the protocol requires more than 1 procedure to be completed at the same time point. When indicated, the procedures should follow the recommended order of events; see Section 1.3 for instructions.

Protocol waivers or exemptions are not allowed.

Immediate safety concerns should be discussed with the Medical Monitor immediately upon occurrence or awareness to determine if the subject should continue or discontinue in the study.

Adherence to the study design requirements, including those specified in the SoA, is essential and required for study conduct.

All screening evaluations must be completed and reviewed to confirm that potential subjects meet all eligibility criteria. The Investigator will maintain a screening log to record details of all subjects screened and to confirm eligibility or record reasons for screening failure, as applicable.

Procedures conducted as part of the subject's routine clinical management (eg, blood count) and obtained before signing of the ICF may be utilized for screening purposes provided the procedures met the protocol specified criteria and were performed within the time frame defined in the SoA (Section 1.3).

Repeat or unscheduled samples may be taken for safety reasons or for technical issues with the samples.

8.1 EFFICACY ASSESSMENTS

Clinical evaluations of HS will be performed by an experienced and qualified dermatologist (board certified or equivalent) or other suitably qualified and experienced designee. To assure consistency and reduce variability, the same assessor should perform all assessments on a given subject, whenever possible (especially at Day 1 and Week 16).

8.1.1 HIDRADENITIS SUPPURATIVA PAIN NUMERIC RATING SCALE

The HS Pain NRS will be completed at the visits specified in the SoA (Section 1.3) using worst and average HS Pain NRSs. The subject will be asked to assign a numeric score representing the worst intensity over the last 24 hours and the average intensity over the last 7 days of their pain on a scale from 0 to 10, with 0 indicating no pain and 10 indicating the worst imaginable pain symptoms.

These assessments will be completed by the subject on a worksheet prior to any safety and efficacy evaluations at every study visit. Worst HS Pain NRSs should be performed before average HS Pain NRSs. The scales are presented in Appendix 2.

8.1.2 PATIENT GLOBAL IMPRESSION OF SEVERITY

The PGIS will be assessed at the visits specified in the SoA (Section 1.3). It is a single-item question, which asks the subject to rate the current severity of their symptoms. The response options are “No activity”, “Mild”, “Moderate”, “Severe”.

The PGIS will be completed by the subject on a worksheet prior to any safety and efficacy evaluations. The questionnaire is self-explanatory and handed to the subject who is asked to fill it in without the need for a detailed explanation. The PGIS (modified from Yalcin 2003) is presented in Appendix 3.

8.1.3 PATIENT GLOBAL IMPRESSION OF BOTHER

The PGIB will be assessed at the visits specified in the SoA (Section 1.3). It is a single-item questionnaire, which asks the subject to rate how bothered they are by the signs and symptoms of HS.

The PGIB will be completed by the subject on a worksheet prior to any safety and efficacy evaluations. The questionnaire is self-explanatory and handed to the subject, who is asked to fill it in without the need for a detailed explanation. The PGIB (modified from Yalcin 2003) is presented in Appendix 4.

8.1.4 PATIENT GLOBAL IMPRESSION OF CHANGE

The PGIC will be assessed at the visits specified in the SoA (Section 1.3). The PGIC is a single-item, self-administered questionnaire, which asks the subject to rate the change in their symptom severity (“Very much better” to “Very much worse”).

The PGIC will be completed by the subject on a worksheet prior to any safety and efficacy evaluations. The questionnaire is self-explanatory and handed to the subject who is asked to fill it in without the need for a detailed explanation. The PGIC (modified from Yalcin 2003) is presented in Appendix 5.

8.1.5 HIDRADENITIS SUPPURATIVA PATIENT’S GLOBAL ASSESSMENT

The HS-PtGA asks the subject to assess how HS has influenced their quality of life. Scores are on a 5-point scale from ‘not at all’ to ‘extremely’, with higher scores indicating more severe impact on quality of life (Kirby 2021). The HS-PtGA is shown in Appendix 6.

8.1.6 DERMATOLOGY LIFE QUALITY INDEX QUESTIONNAIRE

The DLQI questionnaire will be assessed at the visits specified in the SoA (Section 1.3). It is a simple 10-question validated questionnaire (Finlay 1994; Lewis-Jones 1995). The DLQI score ranges from 0 (no effect on the subject’s life) to 30 (extremely large effect on the subject’s life), with higher score indicating greater impairment of quality of life.

The DLQI will be completed by the subject on a worksheet prior to any safety and efficacy evaluations. The questionnaire is self-explanatory and will be filled in by the subject without the need for a detailed explanation. The DLQI is presented in Appendix 7.

8.1.7 HIDRADENITIS SUPPURATIVA QUALTY OF LIFE

The HiSQOL questionnaire is a 17-item questionnaire scored from 0 to 68 with domains for symptoms, activity-adaptation, and psychosocial impact with higher scores representing a more severe disease impact (Kirby 2020). Each domain may also be scored on the following subscores: symptoms (0-16), activity-adaptation (0-32) and psychosocial (0-20). The questionnaire is presented in Appendix 8.

The HiSQOL will be completed by the subject on a worksheet prior to any safety and efficacy evaluations. The questionnaire is self-explanatory and will be filled in by the subject without the need for a detailed explanation.

8.1.8 HIDRADENITIS SUPPURATIVA PHYSICIAN'S GLOBAL ASSESMENT

The HS-PGA (refer to Appendix 9) documents the physician's assessment of the subject's overall HS activity at a given timepoint based on the presence and relative number of HS lesions, drainage and pain and/or tenderness across all HS involved areas. Using the descriptors provided for each distinct category, the subject's HS is assessed as inactive (0), almost inactive (1), mild (2), moderate (3), or severe (4). A higher score indicates more severe disease.

8.1.9 HURLEY STAGES OF HIDRADENITIS SUPPURATIVA

The Hurley system describes 3 clinical stages of HS (Hurley 1989; Kimball 2014):

- Stage 1 – abscess formation, single or multiple, without sinus tracts and cicatrization
- Stage 2 – single or multiple, widely separated, recurrent abscesses with tract formation and cicatrization
- Stage 3 – diffuse or near-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area.

The participant is assigned Hurley Stage corresponding to the Hurley Stage of his or her worst involved anatomic region.

8.1.10 ABSCESS, INFLAMMATORY NODULE, AND DRAINING FISTULA COUNT

Abscess (fluctuant, with or without drainage, tender or painful), inflammatory nodules (tender, erythematous, pyogenic granuloma lesion), draining fistulas, sinus tracts with communications to skin surface, draining purulent fluid, and other lesions (noninflammatory nodules, non-draining fistulas) will all be individually counted on the entire body at each visit. The AN count will be calculated based on the sum of the abscesses and inflammatory nodules. See the Study Manual for additional details.

The location of existing lesions and draining fistulas and new occurrences should be documented in the eCRF.

8.1.11 HIDRADENITIS SUPPURATIVA CLINICAL RESPONSE

HiSCR50 is defined as a ≥ 50% and HISCR75 is defined as a ≥ 75% reduction in inflammatory lesion count (abscesses plus inflammatory nodules), and no increase in abscesses or draining fistulas in comparison to Baseline. It has been recently used to assess the effectiveness of treatment with biologics (Kimball 2014).

8.1.12 INTERNATIONAL HIDRADENITIS SUPPURATIVA SEVERITY SCORE SYSTEM

This IHS4 scores consider the number of nodules, number of abscesses, and number of draining tunnels (fistulae/sinuses). The scoring system is shown in Appendix 10. An IHS4 score of ≤ 3 signifies mild HS, 4–10 signifies moderate HS, and ≥ 11 signifies severe HS (Zouboulis 2017).

8.2 SAFETY ASSESSMENTS

8.2.1 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.2.1.1 DEFINITION OF ADVERSE EVENTS

An AE is any untoward medical occurrence in a subject temporally associated with the use of a study treatment, whether or not considered related to the study treatment.

An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment that does not necessarily have a causal relationship with this treatment.

8.2.1.1.1 EVENTS MEETING THE ADVERSE EVENT DEFINITION

Events meeting the AE definition include:

- Any abnormal laboratory test results (hematology, biochemistry, or urinalysis) or other safety assessments (eg, ECG, vital signs measurements), including those that worsen from Day 1, considered clinically significant in the medical and scientific judgment of the Investigator (ie, not related to progression of underlying disease).
- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.
- New conditions detected or diagnosed after study treatment administration even though it may have been present before the start of the study.
- Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either study treatment or a concomitant medication. Overdose per se will not be reported as an AE/SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae.

"Lack of efficacy" or "failure of expected pharmacological action" per se will not be reported as an AE or SAE. Such instances will be captured in the efficacy assessments. However, the signs, symptoms, and/or clinical sequelae resulting from lack of efficacy will be reported as AE or SAE if they fulfill the definition of an AE or SAE.

8.2.1.1.2 EVENTS NOT MEETING THE ADVERSE EVENT DEFINITION

Events not meeting the AE definition include:

- Any clinically significant abnormal laboratory findings or other abnormal safety assessments which are associated with the underlying disease, unless judged by the Investigator to be more severe than expected for the subject's condition.
- The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the subject's condition.
- Medical or surgical procedure (eg, endoscopy, appendectomy): the condition that leads to the procedure is the AE.
- Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).
- Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the study that do not worsen.

8.2.1.2 DEFINITION OF SERIOUS ADVERSE EVENTS

An AE or suspected adverse reaction is considered "serious" if, in the view of either the Investigator or AnaptysBio, it results, at any dose, in any of the following outcomes:

- **Death**
- **Life-threatening adverse event** – The term 'life-threatening' in the definition of "serious" refers to an event in which the subject was at 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.
- **Inpatient hospitalization or prolongation of existing hospitalization** – In general, hospitalization signifies that the subject has been admitted (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE should be considered serious. Hospitalization for elective treatment of a pre-existing condition that did not worsen from Baseline is not considered an AE.
- **Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions** – The term disability means a substantial disruption of a person's ability to conduct normal life functions. This definition is not intended to include

experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (eg, sprained ankle) which may interfere with or prevent everyday life functions but do not constitute a substantial disruption.

- **Congenital anomaly/birth defect**
- **Other important medical events** – Events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include invasive or malignant cancers, allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

8.2.1.3 CLASSIFICATION OF AN ADVERSE EVENT

8.2.1.3.1 SEVERITY OF EVENT

The intensity of an AE is an estimate of the relative severity of the event. The Investigator will make an assessment of intensity for each AE and SAE reported during the study based on his or her clinical experience and familiarity with the literature. The following definitions are to be used to rate the severity of an AE:

- **Mild** – Events require minimal or no treatment, are easily tolerated by the subject, causing minimal discomfort, and do not interfere with the subject's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning and sufficient discomfort to the subject.
- **Severe** – Events interrupt a subject's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious". An AE that is assessed as severe should not be confused with a SAE. Severe is a category utilized for rating the intensity of an event, and both AEs and SAEs can be assessed as severe. An event is defined as 'serious' when it meets at least 1 of the predefined outcomes as described in the definition of an SAE, NOT when it is rated as severe.

8.2.1.3.2 RELATIONSHIP TO STUDY TREATMENT

All AEs must have their relationship to study treatment assessed by the Investigator who examines and evaluates the subject based on temporal relationship and his or her clinical judgment. Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study treatment administration will be considered and investigated. The Investigator will also consult the IB in his or her assessment. The degree of certainty about causality will be graded using the categories below. In a clinical study, the study treatment must always be suspect.

- **Unrelated** – Clinical event incontrovertibly not related to the study treatment.
- **Unlikely to be related** – Clinical event with an incompatible time relationship to study treatment administration which makes a causal relationship improbable, and in which an underlying condition or other drugs or chemicals provides plausible explanations.
- **Possibly related** – Clinical event with a reasonable time relationship to study treatment administration, and that is unlikely to be attributed to concurrent condition or other drugs or chemicals.
- **Related** – Clinical event with plausible time relationship to study treatment administration and that cannot be explained by concurrent condition or other drugs or chemicals.

For each AE/SAE, the Investigator must document in the medical notes that he or she has reviewed the AE/SAE and has provided an assessment of causality.

There may be situations in which an SAE has occurred, and the Investigator has minimal information to include in the initial report to the pharmacovigilance unit. However, it is very important that the Investigator always make an assessment of causality for every event before the initial transmission of the SAE data to the pharmacovigilance unit within 24 hours of awareness of the event.

The Investigator may change his or her opinion of causality in light of follow-up information and send a SAE follow-up report with the updated causality assessment.

The causality assessment is one of the criteria used when determining regulatory reporting requirements.

8.2.1.3.3 EXPECTEDNESS

The pharmacovigilance unit will be responsible for determining whether an AE is expected or unexpected as interpreted through the IB. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study treatment.

8.2.1.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an AE or SAE may come to the attention of study personnel during study visits and interviews of a study subject presenting for medical care, or upon review by a study monitor.

All AEs including local and systemic reactions will be captured on the appropriate eCRF. Information to be collected includes event description, date of onset, clinician's assessment of severity, seriousness, relationship to study treatment (assessed only by those with the training and authority to make a diagnosis), action taken, and outcome of the event. All AEs occurring while on study must be documented appropriately regardless of relationship (see Section 8.2.1.3.2). All AEs will be followed to adequate resolution or stabilization.

Study site personnel will note the occurrence and nature of each subject's medical condition(s) present prior to the informed consent signature in the appropriate section of the source document and eCRF. During the study, study site personnel will note any change in the condition(s) and the occurrence and nature of any AE. Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and nonleading verbal questioning of the subject is the preferred method to inquire about AE occurrences.

Should a subject experience an AE at any time after the screening visit informed consent signature until the end of participation in the study, the event will be recorded as an AE in the source document and eCRF. Any SAE related to the study participation (eg, screening procedure) will be recorded in the source document and eCRF from the time consent is given to participate in the study until the end of participation in the study (EOS/ET visit).

Investigators are not obligated to actively seek AEs or SAEs after conclusion of the study participation. However, if the Investigator learns of any SAE, including a death, at any time after a subject has been discharged from the study, and he or she considers the event to be reasonably related to the study treatment or study participation, the Investigator must promptly notify the pharmacovigilance unit.

Any medical condition that is present at the time that the subject is screened will be considered as medical history and not reported as an AE. However, if the study subject's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE/SAE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

The Investigator is responsible for appropriate medical care of subjects during the study. After the initial AE/SAE report, the Investigator is required to proactively follow each subject at subsequent visits/contacts. The Investigator also remains responsible for following through with an appropriate health care option for all AEs that are ongoing at the end of the study. The subject should be followed until the event is resolved or stable. If an AE is ongoing at the end of study, the follow-up duration is left to the discretion of the Investigator. Follow-up frequency will be performed at the discretion of the Investigator.

Whenever possible, clinically significant abnormal laboratory results are to be reported using the diagnostic that resulted in the clinically significant abnormal laboratory results and not the actual abnormal test.

8.2.1.5 ADVERSE EVENT REPORTING

When an AE/SAE occurs, it is the responsibility of the Investigator to review all documentation (eg, hospital progress notes, laboratory reports, and diagnostics reports) related to the event.

The Investigator will then record all relevant AE/SAE information (including event term, start and stop dates, severity, relationship to study treatment, outcome, if serious or non-serious) in the eCRF. Each event must be recorded separately.

It is not acceptable for the Investigator to send photocopies of the subject's medical records to the pharmacovigilance unit in lieu of completion of the AE/SAE eCRF page.

There may be instances when copies of medical records for certain cases are requested by the pharmacovigilance unit. In this case, all subject identifiers, with the exception of the subject number, will be redacted on the copies of the medical records before submission to the pharmacovigilance unit.

The Investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE/SAE.

The Investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as medically indicated or as requested by the pharmacovigilance unit to elucidate the nature and/or causality of the AE or SAE as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals.

New or updated information will be recorded in the originally completed eCRF.

8.2.1.6 SERIOUS ADVERSE EVENT REPORTING

Prompt notification by the Investigator to the pharmacovigilance unit of an SAE is essential so that legal obligations and ethical responsibilities towards the safety of subjects and the safety of a study treatment under clinical investigation are met. All SAEs will be recorded and reported to the pharmacovigilance unit within 24 hours of awareness. The Investigator will submit any updated SAE data to the pharmacovigilance unit within 24 hours of receipt of the information as outlined in the Safety Reporting Instructions that will be provided to the study sites and in the study Safety Management Plan.

The pharmacovigilance unit will inform the Medical Monitor, AnaptysBio, and Innovaderm within 1 business day of awareness of a new SAE. The pharmacovigilance unit will process and evaluate all SAEs as soon as the reports are received. For each SAE received, the pharmacovigilance unit, in consultation with AnaptysBio if needed, will make a determination as to whether the criteria for expedited reporting to relevant regulatory authorities have been met.

AnaptysBio or designee has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study treatment under clinical investigation. or designee will comply with country specific regulatory requirements relating to safety reporting to the regulatory authority, IRB/EC, and Investigators.

Investigator safety reports must be prepared for suspected unexpected SAEs according to local regulatory requirements and pharmacovigilance unit policy, and forwarded to Investigators as necessary.

An Investigator who receives an Investigator safety report describing an SAE or other specific safety information (eg, summary or listing of SAEs) from the pharmacovigilance unit will review and then file it along with the IB and will notify the IRB/EC, if appropriate according to local requirements.

If a subject dies while participating in the study, the Investigator will provide the pharmacovigilance unit with a copy of any postmortem findings.

8.2.1.6.1 REPORTING VIA AN ELECTRONIC DATA COLLECTION TOOL

The primary mechanism for reporting an SAE to the pharmacovigilance unit will be the electronic data capture (EDC) clinical database.

If the electronic system is unavailable, then the study site will use the back-up paper SAE Report Form. The study site will then enter the SAE data into the EDC system as soon as it becomes available.

After the study is completed and the database is locked, the tooled system will be taken off-line to prevent the entry of new data or changes to existing data.

If a study site receives a report of a new SAE from a subject or receives updated data on a previously reported SAE after the EDC system is locked, then the study site can report this information on a paper SAE form and email the form to the pharmacovigilance unit.

Contacts for SAE reporting can be found in SAE form and Safety Reporting Instructions that will be provided to the study sites.

8.2.1.6.2 REPORTING VIA PAPER CASE REPORT FORM

In rare circumstances, and in the absence of EDC or email, notification by telephone is acceptable for notifying the pharmacovigilance unit of an SAE. Once the EDC is available, the SAE must be reported in the system within 24 hours of it becoming available.

Initial notification via telephone does not replace the need for the Investigator to complete and sign the SAE CRF pages within the designated reporting time frames.

Contacts for SAE reporting can be found in Safety Reporting Instructions that will be provided to the study sites.

8.2.1.7 REPORTING EVENTS TO SUBJECTS

Not applicable.

8.2.1.8 REPORTING OF PREGNANCY

If a female subject or a female partner of a male subject becomes pregnant during the study and up to 28 days after the end of the study, the subject should inform the study site as soon as possible.

If a pregnancy is reported, the Investigator should inform the pharmacovigilance unit within 24 hours of learning of the pregnancy and should follow the procedures outlined in Appendix 1.

If a pregnancy occurs, it will be followed up to determine the outcome, but no longer than 6 to 8 weeks after the estimated delivery date, where consent has been obtained to do so.

Abnormal pregnancy outcomes (eg, spontaneous abortion, fetal death, stillbirth, congenital anomalies, and ectopic pregnancy) are considered SAEs and must be reported within 24 hours of awareness as described in Section 8.2.1.6.

8.2.1.9 TREATMENT OF OVERDOSE

For this study, any dose of imsidolimab or placebo administered in a volume exceeding the planned dosing detailed in Table 3 (Dose Strength[s]/Dosage Level[s]) will be considered an overdose.

In the improbable event of a suspected overdose, the following procedures should be executed:

- Administration is to be discontinued.
- The subject is to be monitored clinically.
- Supportive measures are to be undertaken as clinically indicated.
- Electrocardiography and clinical laboratory evaluations (ie, blood glucose, hepatic enzymes, creatinine, blood urea nitrogen, creatine kinase (CK), and complete blood count) are to be performed and followed until all values return to Baseline levels and AEs subside, if applicable.

No information on overdose, maximum tolerated dose, or dose-limiting toxicities for imsidolimab has been established at this time and since there are no known antidotes for imsidolimab, the treatment of overdose is at Investigator's discretion.

In the event of an overdose, the Investigator should:

1. Contact the Medical Monitor immediately.
1. Closely monitor the subject for any AE/SAE and laboratory abnormalities and follow-up until resolution.
2. Obtain a serum sample for PK analysis soon after the dose for SC administration.
3. Document the quantity of the excess dose as well as the duration of the overdose in the eCRF.

Decisions regarding dose interruptions will be made by the Investigator in consultation with the Medical Monitor based on the clinical evaluation of the subject.

8.2.2 HEIGHT AND WEIGHT

Height (cm) and weight (kg) will be collected to calculate the body mass index (BMI). Height and weight will be measured at the time points specified in the SoA (Section 1.3).

8.2.3 CHEST X-RAY

Bidirectional posterior-anterior and lateral view chest X-ray will be performed at screening (Section 1.3). If a chest X-ray was performed within 6 months of screening and no clinically significant abnormality was observed, it can be skipped at screening.

8.2.4 PHYSICAL EXAMINATIONS

Complete physical examinations will be performed at the time points indicated in the SoA (Section 1.3).

A complete physical examination will include assessments of general appearance; skin; head/neck; pulmonary, cardiovascular, gastrointestinal, lymphatic, and musculoskeletal system; extremities; eyes; nose; throat; and neurologic status. The indication under study, hidradenitis suppurativa, should not be reported as part of the physical examination.

A detailed examination of the skin should be performed at the time points indicated in the SoA for the efficacy assessments (eg, AN count).

Investigators should pay special attention to clinical signs related to previous serious illnesses.

8.2.5 VITAL SIGNS

Body temperature (°C), pulse rate (bpm), blood pressure (mmHg), and respiratory rate (breath/min) will be assessed at the time points specified in SoA (Section 1.3).

Blood pressure and pulse rate will be assessed in a seated position with a completely automated device. Manual techniques will be used only if an automated device is not available.

Assessments should be preceded by at least 5 minutes of rest for the subject in a quiet setting without distractions (eg, television, cell phones).

Vital signs including body temperature, respiratory rate, and pulse rate (after at least 5 minutes rest) should be measured once. Arterial blood pressure should be measured once, using a validated device, and recorded in the eCRF.

8.2.6 ELECTROCARDIOGRAMS

A single 12-lead ECG will be obtained at the time points specified in the SoA (see Section 1.3) using a validated ECG machine that automatically calculates the heart rate and measures RR, PR, QRS, QT, and QTcF intervals.

Additional information will be provided in a separate manual.

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.

The ECG individual data (including clinical significance that will be reported as AE) will be entered into the electronic data capture (EDC).

8.2.7 CLINICAL SAFETY LABORATORY ASSESSMENTS

See Appendix 11 for the list of clinical laboratory tests to be performed and the SoA (Section 1.3) for the timing and frequency of the tests.

A central laboratory will be used to perform all laboratory tests except urine pregnancy dipstick which will be assessed by the study site staff. However, local laboratory tests will be allowed in the event that the central laboratory results will not be available immediately and the Investigator needs to make an immediate decision for any safety concerns based on laboratory results. If a local sample is required, it is important that the sample for central analysis is obtained at the same time.

The Investigator must review the laboratory report, document this review, and record any clinically relevant changes occurring during the study in the AE section of the eCRF. The laboratory reports must be filed with the source documents. Clinically significant abnormal laboratory findings are those that are not associated with the underlying disease, unless judged by the Investigator to be more severe than expected for the subject's condition.

All laboratory tests with values considered clinically significantly abnormal during the study and including the subject's last study visit (EOS) should be repeated until the values return to normal or Baseline or are no longer considered clinically significant or judged medically stabilized by the Investigator or Medical Monitor.

If such values do not return to normal/Baseline within a period of time judged reasonable by the Investigator, the etiology should be identified, and AnaptysBio notified.

All protocol-required laboratory assessments, as defined in Appendix 11, must be conducted in accordance with the Laboratory Manual and the SoA.

If laboratory values from non-protocol specified laboratory assessments performed at the institution's local laboratory require a change in subject management or are considered clinically significant by the Investigator (eg, SAE or AE), then the results must be recorded in the eCRF.

8.3 OTHER ASSESSMENTS

8.3.1 FITZPATRICK SKIN TYPE CLASSIFICATION

The Fitzpatrick skin type (Attwa 2016; Fitzpatrick 1988; Wallace 2017; Zalaudek 2007) will be evaluated at screening as described in Appendix 12. Fitzpatrick skin type may be collected after the screening if missed during this visit.

8.3.2 PHOTOGRAPHY

Photography (of representative lesion[s], fistulas, and scarring) is an optional procedure for all subjects at each of the specified visits at selected site.

Additional information on photography will be described in the photography manual provided to study sites.

8.3.3 PHARMACOKINETICS

Whole blood will be obtained for the determination of imsidolimab concentration in human serum. Samples will be collected according to the SoA (Section 1.3) and Table 5. Whole blood

will be obtained from each subject for PK assessments during the study. Each serum sample will be divided into 2 aliquots (1 each for primary and a back-up). Samples collected for analyses of imsidolimab serum concentration also may be used to correlate exposure to safety or efficacy as well as supportive analysis for dose justification.

The actual date and time (24-hour clock) of the blood sample collection will be recorded in the subject's eCRF. The details of blood sample collection, sample tube labeling, sample preparation, storage, and shipping procedures will be described in a separate laboratory manual.

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

Only samples within the stability window of the assay will be analyzed.

While PK samples must be collected from subjects randomized to the placebo arm to maintain the blinding of treatment assignment, PK assay results for these subjects are not needed for the safe conduct or proper interpretation of this study. These samples may not be analyzed unless needed to investigate if a dosing error has occurred. Personnel at the bioanalytical laboratory performing PK assays will be unblinded, the clinical study team members, and study site staff (with the exception of the unblinded Pharmacist) will remain blinded to treatment for the duration of the study. Data may be de-identified for quality review. Additional details on de-identification or unblinding of the PK data, if applicable, will be described in a separate plan.

Drug concentration information that may unblind the study will not be reported to study sites or blinded personnel until the study has been unblinded.

Table 5: Pharmacokinetic and Anti-drug Antibody Collection Schedule

Study Visit	PK Sample Time Point	ADA Sample Time Point
Day 1	Predose	Predose
Day 29	Predose	Predose
Day 57	Predose	Predose
Day 85	Predose	Predose
Day 113	Predose	Predose
Day 141	Predose	Predose
Day 169	Predose	-
Day197	Predose	-
Day 225	Anytime	Anytime
Day 253	Anytime	-
Day 281	Anytime	Anytime

Abbreviations: ADA, anti-drug antibody; hr, hours; min, minutes; PK, pharmacokinetic

8.3.4 IMMUNOGENICITY ASSESSMENTS

Anti-drug antibodies to imsidolimab will be evaluated in serum samples collected from all subjects according to the SoA (Section 1.3) and Table 5. Additionally, serum samples also should also be collected at the final visit from subjects who discontinued study treatment or were

withdrawn from the study. These samples will be tested by AnaptysBio or its designee. Each serum sample will be divided into 2 aliquots (1 each for primary and a back-up).

The detection and characterization of antibodies to imsidolimab will be performed using a validated assay method by or under the supervision of AnaptysBio.

Serum samples will be tested in a multi-tiered approach. A validated screening assay for antibodies binding to imsidolimab initially will be used to assess serum samples. Samples that are determined putative positive in the screening assay then will be subjected to a confirmatory assay to demonstrate that antibodies are specific to imsidolimab. Samples that are identified as positive in the confirmatory assay will be further characterized in a validated titer assay and the titer of confirmed positive samples will be reported. Other analyses may be performed to verify the stability of antibodies to study treatment and/or to further characterize the immunogenicity of study treatment.

Samples that are confirmed positive for antibodies binding to imsidolimab may be further characterized for their ability to neutralize the activity of the study treatment using a validated neutralizing antibody assay method and the presence and/or titer of ADA may be correlated to safety and PK data.

8.3.5 BIOMARKER ANALYSIS

The actual date and time of the biomarker sample collection will be recorded in the subject's eCRF. The details of sample collection, sample tube labeling, sample preparation, storage, and shipping procedures will be described in a separate Laboratory Manual.

The measurement of biomarkers may be performed by an additional third party (eg, a university Investigator) designated by AnaptysBio.

8.3.5.1 TAPE STRIPPING

Tape strip samples will be collected from non-lesional and lesional skin according to the SoA (Section 1.3) to measure cutaneous biomarkers including but not limited to IL-36R, Th-17 cytokines such as IL-17A, and markers of neutrophils and dendritic cell infiltration.

8.3.5.2 DRAINAGE FLUID COLLECTION

Optional noninvasive collection of drainage fluid to assess biomarkers may be conducted at any visit after screening. Drainage fluid should be collected where present from areas that are draining the most.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

The primary analysis for this study is to compare the mean AN count for imsidolimab with placebo during the double-blind treatment period, at a two-sided alpha = 0.10 level. Any testing being performed for secondary or exploratory endpoints will be considered exploratory in nature based on a 2-sided alpha = 0.10

H_0: $\mu_{imsidolimab} - \mu_{Placebo} = 0$ vs. H_A: $\mu_{imsidolimab} - \mu_{Placebo} \neq 0$

9.2 SAMPLE SIZE DETERMINATION

Approximately 120 subjects will be randomized in a 1:1:1 ratio to receive one of the following study treatments:

1. Imsidolimab 400 mg on Day 1 followed by 200 mg on Days 29, 57, and 85
2. Imsidolimab 200 mg on Day 1, followed by 100 mg on Days 29, 57, and 85
3. Placebo on Days 1, 29, 57, and 85

For this phase 2 study, the sample size was chosen empirically. Assuming a total of 10% of subjects will discontinue prior to Week 16, there will be approximately 108 evaluable subjects (36 subjects in each arm) at the end of Week 16. The study has 80% power to detect a between-group treatment difference of 4.9 lesions in the primary endpoint of mean change from Baseline in the AN count at Week 16, using a two-sided, equal-variance two-sample t-test at the $\alpha = 0.10$ level, with the assumption of a common standard deviation (SD) of 8.2 lesions. The assumption was based on PIONEER 1 study (Kimball 2016). Table 6 shows more information on power from a set of scenarios of variability and between-group mean differences.

Table 6: Power Exploration for Different Scenarios of Variability and Between-Group Mean Differences

Common standard deviation	Between-group mean difference	Power (%)	
		1-sided test	2-sided test
7.2	2	46	32
	3	68	54
	4	86	76
	5	95	90
8.2	2	40	27
	3	60	46
	4	78	66
	5	90	82
9.2	2	36	24
	3	54	39
	4	71	57
	5	84	74

Note: An equal variance two-sample t-test at alpha=0.10 is used for the power calculations.

9.3 POPULATIONS FOR ANALYSES

The analysis sets are defined in Table 7.

Table 7: Analysis Sets

Analysis Set	Description
ITT Analysis Set	The ITT analysis set will include all randomized subjects. In this analysis set, treatment will be assigned based upon the treatment arm to which subjects were randomized regardless of which treatment they receive. ITT analysis set will be used for primary, secondary, and exploratory efficacy analyses.
Safety Analysis Set	The Safety Analysis Set will include all randomized subjects who receive at least 1 dose of imsidolimab or placebo. The Safety Analysis Set will be used for all safety analyses. Subjects will be analyzed as treated.
Extension Analysis Set	The Extension Analysis Set is a subset of the Safety Analysis Set who receive at least 1 dose of imsidolimab in the extension period. The Extension Analysis Set will be used for summarizing both efficacy and safety data for those subjects who entered the extension period. Subjects will be analyzed as treated.
Per Protocol Analysis Set	The per protocol analysis set will include all subjects in the ITT analysis set who do not have major protocol violations that would affect the evaluation of the primary efficacy endpoint.
PK Analysis Set	The PK analysis set will include all imsidolimab-treated subjects in the Safety Analysis Set who have at least 1 quantifiable postdose PK sample available and who do not have events or protocol deviations or events with the potential to affect PK concentrations. The PK analysis set will be used for all PK analyses.

Abbreviations: ITT, intent-to-treat; PK, pharmacokinetic

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

The statistical analysis will be performed using SAS® Version 9.4 or higher. All details regarding the statistical analysis and the preparation of tables, listings, and figures will be described in the Statistical Analysis Plan (SAP).

The default summary statistics for continuous variables include number of contributing observations, mean, SD, median, minimum, and maximum. For PK parameters, coefficient of variation (CV) and geometric mean will also be presented, as appropriate.

For categorical variables, the number and percentage (percentage of subjects in each category relative to the total number of subjects in the relevant analysis set or relative to the total number

of subjects in the relevant analysis set with assessments available [where appropriate]) in each category will be the default summary presentation.

Unless otherwise specified, "Baseline" is defined as the last observed value of the parameter of interest prior to the first intake of study treatment (this includes unscheduled visits). For numerical variables, change from Baseline will be calculated as the difference between the value of interest and the corresponding Baseline value. In the analysis of extension study subjects using the Extension Analysis Set, for those subjects who received placebo initially, their baseline will be re-calculated based on the latest data prior to receiving imsidolimab.

Unless otherwise specified, all formal statistical tests will be 2-sided at the 10% significance level. Point estimates of treatment differences will be accompanied with 2-sided 90% confidence intervals (CIs), where applicable.

In the case of normality assumption violations, appropriate nonparametric methods may be used for analysis.

All data will be presented in by-subject listings.

9.4.2 SUBJECT DISPOSITION

A tabular presentation of the subject disposition will be provided. It will include the number of subjects screened, randomized, treated, 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 subject. A list of protocol deviations/violations will be identified and discussed with the Investigator/AnaptysBio in dry run to categorize as major or minor with decisions of exclusion from analysis sets prior to unblinding.

During the COVID-19 pandemic, protocol deviations related to COVID-19 will be documented and information on how they will be handled in the analyses will be detailed in the SAP.

9.4.3 BASELINE DESCRIPTIVE STATISTICS

Subject characteristics obtained at Baseline will be summarized for all subjects taking imsidolimab or placebo.

Summaries will include descriptive statistics for continuous variables (sample size [n], mean, SD, median, minimum, and maximum) and for categorical variables (n, frequency, and percentage).

Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) latest version and listed for all subjects.

9.4.4 CONCOMITANT MEDICATION

All medications will be coded using the World Health Organization Drug Dictionary and Anatomical Therapeutic Chemical system. Each medication will be classified as prior medication if it is stopped prior to the first dose of study treatment, or as concomitant medication if it is ongoing at the time of the first dose or is started after the first dose of study treatment. Prior, concomitant, and rescue medications will be summarized descriptively with a by-subject listing.

To handle the issue of rescue medication use, the efficacy data on and after the use rescue medication will be set to missing in the efficacy analysis.

9.4.5 ANALYSIS OF THE PRIMARY EFFICACY ENDPOINT

The primary efficacy endpoint is the change from Baseline in AN count at Week 16.

The primary estimand, comprising four components, is defined as follows:

a) The target population consists of subjects with hidradenitis suppurativa who are eligible to be included in the clinical trial based on the inclusion/exclusion criteria in the protocol. The ITT analysis set will include all randomized subjects. For the analysis, treatment will be assigned based upon the treatment arm to which subjects are randomized regardless of which treatment they receive.
b) The primary variable is the change from baseline in AN count of an individual subject at Week 16.
c) To handle intercurrent events such as use of rescue medications, the hypothetical strategy for estimand will be used. Data collected following receipt of rescue medication (if any) will be considered missing in the analysis.
d) The population-level summary measures will be the population mean differences in the primary variable between each dose of imsidolimab and placebo at Week 16.

A general linear mixed effects model for repeated measures (MMRM) analysis will be used to estimate the least squares means (LSM) and associated standard errors for the change from Baseline in AN count to Week 16. The model will include change from Baseline in AN count at Week 16 as the dependent variable, fixed effects for treatment arm, categorical time point, and the treatment by time point interaction, and the Baseline AN count and stratification factor (ie, Hurley Stage at baseline (Stage II or III)) as covariates. An unstructured covariance structure will be used. The difference between LSMs (imsidolimab – placebo) at Week 16 will be presented along with the associated 90% CI and p-value. The ITT analysis set will be used for the primary efficacy analysis.

9.4.6 ANALYSIS OF THE SECONDARY EFFICACY ENDPOINTS

The ITT analysis set will be used for analysis of secondary efficacy endpoints. Following are the secondary efficacy endpoints:

- Percent change from Baseline in AN count at Week 16
- Proportion of subjects achieving HiSCR50 at Week 16

- Change from Baseline in HS Pain NRS at Week 16
- Percent change from Baseline in HS Pain NRS at Week 16

9.4.6.1 CATEGORICAL ENDPOINTS

Frequency and percentages for each response Yes/No for categorical endpoints will be presented separately by visit for each treatment arm. Subjects with missing scores at a given visit will be considered to have not met the criteria of interest (ie, nonresponse). Estimates of the difference between treatments (imsidolimab – placebo) will be presented along with exact 90% CIs. Treatment arms will be compared using Cochran–Mantel–Haenszel chi-squared test, adjusted for stratification factor (Hurley Stage at baseline (Stage II or III)).

9.4.6.2 CONTINUOUS ENDPOINTS

Summary statistics will be provided by visit and treatment arm. A by-subject listing will be presented for each assessment, by visit. Mixed model for repeated measures (MMRM) method for longitudinal continuous data will be used for testing, with treatment group as main effect, with visit and interaction of treatment by visit as factors, and with baseline values and stratification factor (Hurley Stage at baseline [Stage II or III]) as covariates.

9.4.7 ANALYSIS OF THE EXPLORATORY ENDPOINTS

Following are the exploratory endpoints:

- Change from Baseline in AN count at visits other than Week 16
- Percent change from Baseline in AN count at visits other than Week 16
- Proportion of subjects achieving AN50 and AN75 responses
- Percentage of subjects experiencing flare, defined as a ≥25% increase in AN count with an absolute increase in AN count of ≥2 relative to Baseline at each visit
- Change from Baseline in abscess count at each visit
- Change from Baseline in inflammatory nodule count at each visit
- Change from Baseline in draining fistula count at each visit
- Proportion of subjects achieving HiSCR50 at visits other than Week 16
- Proportion of subjects achieving HiSCR75 at each visit
- Proportion of subjects achieving 0 (inactive) or 1 (almost inactive) on HS-PGA at each visit
- Proportion of subjects with ≥ 2-point reduction from Baseline on HS-PGA at each visit
- Change from Baseline in HS-PGA
- Change from Baseline in calculated composite of abscesses, draining fistulas, and inflammatory and non-inflammatory nodules
- Change from Baseline in HS Pain NRS at visits other than Week 16
- Percent change from Baseline in HS Pain NRS at visits other than Week 16

- Proportion of subjects achieving a ≥ 3-point reduction on the HS Pain NRS for subjects with Baseline HS Pain NRS of at least 3
- Proportion of subjects requiring rescue medication or treatment at each visit
- Change from Baseline in DLQI score at each visit
- Change from Baseline in IHS4 at each visit
- Change from Baseline in HiSQoL at each visit
- Change from Baseline in HS-PtGA at each visit
- Proportion of subjects in each response category for the HS-PtGA at each visit
- Proportion of subjects in each response category for the PGIC at each visit
- Proportion of subjects achieving improvement ("Much better" or "Very much better") according to the PGIC at each visit
- Proportion of subjects achieving improvement ("A little better", "Much better" or "Very much better") according to the PGIC at each visit
- Proportion of subjects in each response category for the PGIB at each visit
- Change from Baseline in PGIB at each visit
- Proportion of subjects achieving "A little bothered" or "Not at all bothered" for the PGIB at each visit
- Proportion of subjects in each response category for the PGIS at each visit
- Proportion of subjects achieving "Mild" or "No activity" according to the PGIS at each visit
- Change from Baseline in PGIS at each visit
- Proportion of subjects in each category of Hurley Stage at each visit
- Change from Baseline in Hurley Stage at Weeks 16, 32, and 40
- Proportion of subjects achieving at least a 1-stage improvement in Hurley stage
- Skin tape strip and drainage fluid biomarkers analysis including, but not limited to, IL-36 and Th-17
- Presence of ADAs to imsidolimab
- Serum concentration following imsidolimab administration and other parameters as appropriate will be determined to describe the PK profile of imsidolimab

Methods for analyzing the above categorical and continuous efficacy endpoints will mirror the methods described in Section 9.4.6.1 and 9.4.6.2, respectively. ITT analysis set will be used for analysis of exploratory efficacy endpoints.

As further additional exploratory analyses, the primary efficacy endpoint, all secondary efficacy endpoints, and some of the exploratory endpoints will be summarized using the Extension analysis population.

9.4.8 SAFETY ANALYSES

Following are the primary safety and tolerability endpoints:

- Assessment of AEs, SAEs, and AEs leading to treatment discontinuation and study withdrawal.
- Vital signs.
- 12-Lead ECG.
- Clinical safety laboratory tests (hematology, biochemistry, and urinalysis).

All safety analyses will be performed on the Safety Analysis Set. In addition, the safety data for the subjects who entered the extension period will also be analyzed by the Extension Analysis Set.

9.4.8.1 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

A TEAE is defined as:

- A new event that occurs during or after first dose of study treatment or,
- Any event present at Baseline that worsens in either intensity or frequency after first dose of study treatment.

Adverse events will be coded using the MedDRA and only TEAEs will be summarized. Number of events and percentage will be tabulated by preferred term (PT) and primary system organ class (SOC). Multiple occurrences of an AE for a subject will only be counted once per primary SOC and PT. Percentages will be determined relative to the subjects in the Safety Analysis Set for the given treatment arm.

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 TEAEs, SAEs, TEAEs leading to treatment discontinuation, and TEAEs leading to withdrawal of subject will be tabulated for each treatment arm.

All AE data will be listed for each subject.

Summaries over SOC and PT of TEAEs, TEAEs leading to death, SAEs, and TEAEs that led to discontinuation from the study or study treatment will be presented by treatment. Summaries will also be presented by relatedness to the study treatment and the severity of the TEAE.

9.4.8.2 12-LEAD ELECTROCARDIOGRAM, VITAL SIGNS, AND CLINICAL SAFETY LABORATORY TESTS

Summaries and listings of data for vital signs and safety laboratory tests result (hematology, biochemistry, and urinalysis) 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 biochemistry tests, listings of subject 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 biochemistry data will be reported in System International units.

Descriptive statistics will be used to present the safety outcomes including, weight, BMI, 12-Lead ECG, vital signs, and clinical laboratory test results.

Change from Baseline will also be summarized for vital signs, and clinical laboratory tests results.

All ECG data results (normal/abnormal) will be summarized using frequency and percentage, and parameter values will be summarized descriptively. Clinically significant abnormalities will be presented in by-subject listings.

9.4.9 PHARMACOKINETIC ANALYSES

Limited imsidolimab PK analysis will be evaluated by assessment of drug concentrations in serum. These drug concentrations will be listed and summarized for each sampling time point using appropriate descriptive statistics. Due to limited PK sampling, noncompartmental analysis (NCA) will not be conducted in this study.

9.4.9.1 DERIVATION OF PHARMACOKINETIC PARAMETERS

Due to limited PK sampling, NCA will not be conducted in this study. Thus, PK parameters will not be derived.

9.4.9.2 PHARMACOKINETIC CONCENTRATION DATA ANALYSIS

A subject listing of all concentration-time data following SC injections will be presented by subject and scheduled sample collection time.

Concentration data of imsidolimab will be summarized by day and nominal time point using the number of observations, arithmetic mean, SD, CV, minimum, median, maximum, and geometric mean.

Graphs for mean concentration-time data following SC administration will be presented. Individual subject concentration-time plots will also be presented.

Mean trough concentrations-time data will be graphically displayed for samples collected at the visits specified in the SoA (Section 1.3) to visually assess time to attainment of steady state. Time to steady state may also be explored by using inferential statistics, if deemed appropriate. Other presentations of data may be added at the discretion of the PK scientist, as appropriate, and will be described in detail in a separate analysis plan.

9.4.9.3 PHARMACOKINETIC PARAMETER DATA ANALYSIS

No analysis will be performed on PK parameters.

9.4.9.4 POPULATION PHARMACOKINETICS ANALYSIS

Pharmacokinetic data from the study may also be used for population PK and/or exposure-response analyses. The data may be combined with PK data from other ANB019 studies, if

needed, to conduct the population PK analysis. If done, a separate analysis plan will be prepared, and results will be reported separately from the Clinical Study Report.

9.4.9.5 IMMUNOGENICITY ANALYSES

Observed values for ADA levels/status will be listed by-subject and summarized with descriptive statistics based on the Safety Analysis Set. If data permits, potential correlation may be analyzed between ADA levels, serum concentration, and safety and efficacy endpoints.

In addition, ADA incidences (overall, treatment-emergent, and treatment-boosted) will be listed and summarized.

9.4.10 BIOMARKER ANALYSES

Tape strip biomarkers (including but not limited to IL-36R and Th-17 cytokine) analysis will be performed by a third party designated by AnaptysBio. A separate analysis plan will be created for the biomarker analyses.

9.4.11 PLANNED INTERIM ANALYSIS

Interim analyses (IA) may be performed for assessment of all primary and secondary efficacy endpoints, and evaluation of all safety data available.

The rationale for these analyses is to assist in making decisions for potential future development of this treatment. No adjustments to the current protocol are planned as a result of the interim analyses; therefore, overall alpha in the analyses of the primary analysis is expected to be maintained at 0.10, two-sided.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

After reading the protocol, each Investigator will sign the protocol signature page and send a copy of the signed page to AnaptysBio or representative. The study will not start at any study site at which the Investigator has not signed the protocol.

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO SUBJECTS

An ICF describing in detail the study treatments, study procedures, and risks will be given to the subjects, and written documentation of informed consent is required prior to starting any study-related procedures. The following materials will be submitted to the IRB/EC with this protocol: subject self-reported questionnaires, ICF, IB, and other relevant documents (eg, advertisements).

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Each informed consent document must adhere to the ethical principles stated in the Declaration of Helsinki and will include the elements required by FDA regulations in 21 CFR Part 50, as well as the elements required by the ICH GCP guideline, and applicable federal and local regulatory requirements. The consent form will be IRB/EC -approved, and the subject will be asked to read and review the document.

The Investigator or his/her representative will explain the research study to the subject and answer any questions that may arise. A verbal explanation will be provided in terms suited to the subject's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research subjects. Subjects will have the opportunity to carefully review the written consent form and ask questions prior to signing. The subjects should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The subject will sign the informed consent document prior to any procedures being done specifically for the study.

Subjects must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the subjects for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the subject undergoes any study-specific procedures. The rights and welfare of the subjects will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

The medical record must include a statement that written informed consent was obtained before the subject was entered in the study and the date the written consent was obtained. The authorized person obtaining the informed consent must also sign the ICF.

Subjects must be re-consented to the most current version of the ICF(s) during their participation in the study. Subjects who are rescreened are required to sign a new ICF.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study subjects, Investigator, the IND Sponsor, and regulatory authorities, as applicable. If the study is prematurely terminated or suspended, the Investigator will promptly inform study subjects and the IRB/EC and will provide the reason(s) for the termination or suspension. Study subjects will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to subjects
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Scientific or corporate reasons

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the AnaptysBio, IRB/EC and/or regulatory authorities.

10.1.3 CONFIDENTIALITY AND PRIVACY

Subject confidentiality and privacy are strictly held in trust by the participating Investigators, their staff, and AnaptysBio and their interventions. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to subjects. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of AnaptysBio.

All research activities will be conducted in a setting as private as possible. The Investigator must assure that the subjects' anonymity will be maintained and that subjects' identities are protected from unauthorized parties. On CRFs or other documents submitted to AnaptysBio, subjects should not be identified by their names, but by an identification code. The Investigator should keep a subject log relating codes with the names of subjects. The Investigator should maintain in strict confidence documents not for submission to AnaptysBio (eg, subjects' written consent forms).

The study monitor, other authorized representatives of AnaptysBio, and representatives of the IRB/EC, regulatory agencies, or pharmaceutical company supplying study treatment may inspect all documents and records required to be maintained by the Investigator, including but not

limited to, medical records (office, clinic, or hospital) and pharmacy records for the subjects in this study. The clinical study site will permit access to such records.

The study subject's contact information will be securely stored at each clinical study site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the applicable legal or regulatory requirements, the reviewing IRB/EC, Institutional policies, or AnaptysBio requirements.

Study subject research data, which are for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the data management company responsible for data management, analysis, and reporting. This will not include the subject's contact or identifying information. Rather, individual subjects and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical study sites and by data management research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived by AnaptysBio.

All information generated in this study must be considered highly confidential and must not be disclosed to any persons not directly concerned with the study without written prior permission from AnaptysBio. Authorized regulatory officials and AnaptysBio personnel (or their representatives) will be allowed full access to inspect and copy the records. All study investigational product, subject bodily fluids, and/or other materials collected shall be used solely in accordance with this protocol, unless otherwise agreed to in writing by AnaptysBio. Subjects will only be identified by unique subject numbers on eCRFs. Every subject will be given a copy of each version of the ICF that he or she signs before and during the study. Each ICF may also include authorization allowing the institution, Investigator, and AnaptysBio to use and disclose personal health information in compliance with the Health Information Portability and Accountability Act (HIPAA).

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

With the subject's approval and approval by IRB/EC, de-identified biological samples will be stored at a certified, licensed central laboratory. During the conduct of the study, a subject may choose to withdraw consent to have biological specimens stored for future research. Once samples have been analyzed specimens will be destroyed. If no analyses have been completed within 5 years following EOS, samples will be destroyed.

Any remaining serum/plasma from samples collected for PK/PD immunogenicity endpoints may be retained for assay method development, troubleshooting, or validation. These samples may also be used for research purposes, but will not be used for any type of genetic analyses.

10.1.5 MEDICAL MONITOR

Medical monitoring will be conducted to ensure the early recognition, identification and reporting of issues impacting on subjects' health and well-being throughout the trial. Details of medical monitoring with contact information of the Medical Monitors will be documented in a Medical Monitoring Plan.

10.1.6 SAFETY OVERSIGHT

No Data and Safety Monitoring Board is required as part of this study.

10.1.7 CLINICAL MONITORING

All aspects of the study will be monitored by AnaptysBio or authorized representatives of AnaptysBio according to GCP and Standard Operating Procedures (SOPs) for compliance with applicable government regulations, (ie, Informed Consent Regulations [US 21CFR, Part 50] and Institutional Review Board regulations [US 21CFR, Part 56.103]).

Access to all records, both during the study and after study completion, should be made available to AnaptysBio at any time for review and audit to ensure the integrity of the data. The Investigator must notify AnaptysBio immediately if the responsible IRB/EC has been disqualified or if proceedings leading to disqualification have begun.

The Investigator must conduct the protocol in accordance with applicable GCP regulations and guidelines; applicable informed consent regulations (US 21CFR, Part 50); and in compliance with the Declaration of Helsinki. Every attempt must be made to follow the protocol and to obtain and record all data requested for each subject at the specified times. If data are not recorded per protocol, the reasons must be clearly documented on the eCRF/records.

Before study initiation, at a study site initiation visit or at a meeting with the Investigator(s), a representative from AnaptysBio will review the protocol and study eCRFs with the Investigator(s) and their staff. During the study, the study monitor will visit the study site regularly to check the completeness of subject records, the accuracy of entries on the eCRFs, the adherence to the protocol and to GCP, the progress of enrollment, and to ensure that consent is being sought and obtained in compliance with applicable regulations, and that the study drug is being stored, dispensed and accounted for according to specifications.

The Investigator and key study personnel must be available to assist the monitor during these visits. The Investigator must give the monitor access to relevant hospital or clinical records, to confirm their consistency with the eCRF entries. No information in these records about the identity of the subjects will leave the study site.

Monitoring standards require full verification for the presence of informed consent, adherence to the inclusion/exclusion criteria, documentation of SAEs, and the recording of primary efficacy and safety variables. Additional checks of the consistency of the source data with the eCRFs will be performed according to the study-specific Monitoring Plan.

The Investigator must promptly complete the eCRFs after the subject’s visit. The monitor is responsible for reviewing them and clarifying and resolving any data queries. A copy of the eCRFs will be retained by the Investigator who must ensure that it is stored in a secure place with other study documents, such as the protocol, the IB, and any protocol amendments.

The Investigator must provide AnaptysBio and the responsible IRB/EC with a study summary shortly after study completion, or as designated by AnaptysBio.

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

Each clinical study site will perform internal quality management of study conduct, data and biological specimen collection, documentation, and completion.

Quality control (QC) procedures will be implemented beginning with the data entry system, and data QC checks, which will be run on the database, will be generated. Any missing data or data anomalies will be communicated to the study site(s) for clarification/resolution.

Following written SOPs, the monitors will verify that the clinical trial is conducted and data are generated and biological specimens are collected, documented (recorded), and reported in compliance with the protocol, ICH GCP, and applicable regulatory requirements (eg, GLP, Good Manufacturing Practices).

The investigational site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by AnaptysBio, and inspection by IRB/EC and local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

All protocol-specified data will be recorded in site source documents. Study data will be entered within the clinical database eCRFs from the original source documents. Upon each subject's completion of the study, the Investigator is required to sign and affirm the data entered in the subject CRF along with a statement attesting that all pages of the subject's case report have been reviewed. All Investigator data attestation signatures will be made through the 21 CFR Part 11 compliant EDC system. Signature stamps and "per signatures" are not acceptable.

It is AnaptysBio's policy that study data be verifiable with the source data which necessitates access to all original recordings, laboratory reports, and other records for each subject. The Investigator must therefore agree to allow access to subjects' records, and source data must be made available for all study data. Subjects (or their legal representatives) must also allow access to their medical records. Subjects will be informed of the importance of increased record access and permission granted by signature on the informed consent document prior to screening.

Checks will be performed to ensure quality, consistency, and completeness of the data. Instances of missing or uninterpretable data will be resolved with the Investigator or study coordinator. Data queries, documented within the clinical database, will be accessible to the research facility through the EDC system. Study site personnel will be responsible for providing resolutions to the data queries and for correcting the eCRFs, as appropriate.

The Investigator must keep written or electronic source documents for every subject participating in the clinical study. For the appropriate document retention period. The subject file that identifies the study in which the subject is participating must include the subject's available demographic and medical information including:

- Name
- Contact information
- Year of birth
- Sex
- Fitzpatrick skin type
- Medical historySmoking history
- Concomitant therapies/medication
- Study visit dates
- Performed examinations, evaluations, and clinical findings
- Investigational product administration
- AEs, SAEs, or pregnancy (as applicable)

Additionally, any other documents with source data, especially original printouts of data that were generated by technical equipment must be included in the subject's source document (eg, laboratory value listings). All these documents must have at least the subject's study number, and the date of the evaluation.

The data recorded during the course of the study will be documented in the eCRF and/or the study-specific forms. Before or at study termination, all data must be forwarded to AnaptysBio. The data will then be recorded, evaluated, and stored in anonymous or coded form in accordance with data-protection regulations.

Subjects will authorize the use of their protected health information during the informed consent process in accordance with the applicable privacy requirements. Subjects who deny permission to use and disclose protected health information will not be eligible to participate in the study.

The Investigator will ensure that the study documents forwarded to AnaptysBio, and any other documents, contain no mention of subject names. Any amendments and corrections necessary will be undertaken in both the source documents and eCRFs (as appropriate), and countersigned by the Investigator, or documented designee, stating the date of the amendment/correction. Errors must remain legible and may not be deleted with correction aids. The Investigator must state his/her reason for the correction of any data. In the case of missing data/remarks, the entry spaces provided in the eCRF should be cancelled out so as to avoid unnecessary follow-up inquiries.

Electronic CRFs will be kept by AnaptysBio or an authorized designee in a secured area. Clinical data will be recorded in a computer format for subsequent statistical analyses. Data files will be stored on electronic media with a final master data file kept by AnaptysBio after descriptive and statistical analyses and reports have been generated and are complete.

It is the responsibility of the Investigator to ensure that the study site file is maintained in accordance with the ICH Guidance for Industry E6(R2) GCP: Consolidated Guidance, Section 8 – Essential Documents for the Conduct of a Clinical Trial.

10.1.9.2 STUDY RECORDS RETENTION

Study documents should be retained for a minimum of 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 until at least 2 years have elapsed since the formal discontinuation of clinical development of the study treatment. These documents should be retained for a longer period, however, if required by local regulations or as specified in the study agreement, whichever retention period is longer.

If the Investigator withdraws from the study (eg, relocation, retirement) all study-related records should be transferred to a mutually agreed upon designee. Notice of such transfer will be provided to AnaptysBio in writing. No records will be destroyed without the written consent of AnaptysBio, if applicable. It is the responsibility of AnaptysBio to inform the Investigator when these documents no longer need to be retained.

10.1.10 PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical trial protocol or ICH GCP requirements. The noncompliance may be either on the part of the subject, the Investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the study site and implemented promptly. Protocol deviations related to COVID-19 pandemic will be identified and documented accordingly.

These practices are consistent with ICH GCP:

- 4.5 Compliance with Protocol, Sections 4.5.1, 4.5.2, and 4.5.3
- 5.1 Quality Assurance and Quality Control, Section 5.1.1
- 5.20 Noncompliance, Sections 5.20.1, and 5.20.2.

It is the responsibility of the Investigator to use continuous vigilance to identify and report deviations as soon as possible. All deviations must be addressed in study source documents, and applicable deviations must be sent to the reviewing IRB/EC per their policies. The Investigator is responsible for knowing and adhering to the reviewing IRB/EC requirements. Further details about the handling of protocol deviations will be included in the Protocol Deviation Management Plan, Data Management Plan, Medical Monitoring Plan, blind data review documentation, and SAP.

This study will be conducted as described in this protocol, except for an emergency situation in which the protection, safety, and well-being of the subject requires immediate intervention, based on the judgment of the Investigator (or a designee, appropriately trained professional designated by the Investigator). In the event of a significant deviation from the protocol due to an emergency, accident, or mistake, the Investigator or designee must contact the Medical Monitor and AnaptysBio at the earliest possible time by telephone. This will allow an early joint decision regarding the subject's continuation in the study. This decision will be documented by the Investigator and the Medical Monitor. Please refer to Section 4.5 for allowable, as necessary, modifications to the protocol due to COVID-19 restrictions.

The monitor must ensure that a prompt action is taken to secure compliance. If a noncompliance that significantly affects or has the potential to significantly affect human subject protection or reliability of trial results is discovered, the CRO and AnaptysBio should perform a root cause analysis and implement appropriate corrective and preventive actions.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations: It is understood by the Investigator that the information generated in this study will be used by AnaptysBio in connection with the development of the product. To allow for the use of information derived from the study, it is understood that the Investigator is obliged to provide AnaptysBio with complete test results, all study data, and access to all study records.

Any results of medical investigations with AnaptysBio's products and/or publication/lecture/manuscripts based thereon, shall be exchanged and discussed by the Investigator and AnaptysBio representative(s), 30 days before submission for publication or presentation. Due regard shall be given to AnaptysBio's legitimate interests for example, manuscript authorship, obtaining optimal patent protection, coordinating and maintaining the proprietary nature of submissions to health authorities, coordinating with other ongoing studies in the same field, and protecting confidential data and information. AnaptysBio, Inc. shall be furnished with a copy of any proposed publication. Comments shall be rendered without undue delay.

In cases of publications or presentations of material arising from multicenter clinical investigations, AnaptysBio is to serve as coordinator and referee. Individual Investigators who are part of a multicenter investigation may not publish or present data that are considered common to a multicenter investigation without the consent of the other participating Investigators and the prior review of AnaptysBio.

Results from investigations shall not be made available to any third party by the investigating team outside the publication procedure as outlined previously. AnaptysBio, Inc. will not quote from publications by Investigators in its scientific information and/or promotional material without full acknowledgment of the source (ie, author and reference).

10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, financial interest, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this study. AnaptysBio has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

10.2 ADDITIONAL CONSIDERATIONS

10.2.1 ETHICS AND RESPONSIBILITY

This study must be conducted in compliance with the protocol, the ICH Guidance for Industry E6(R2) GCP: Consolidated Guidance, the Declaration of Helsinki, IRB/EC requirements, and all applicable national and local regulatory requirements. Investigators must submit all essential regulatory documentation, as required by local and national regulations (including approval of the protocol and ICF by a Health and Human Services [HHS]-registered IRB/EC) to AnaptysBio before investigational product will be shipped to the respective study sites.

10.2.2 AMENDMENT POLICY

Only AnaptysBio (or designee) may modify the protocol. Amendments must be approved by all applicable national and local committees including, but not limited to, the government regulatory authorities and/or regional IRB/EC before implementation. The only exception is when an Investigator considers that a subject may be harmed, and immediate action is necessary. Under these circumstances, approval of the chairman of the IRB/EC, or an authorized designee, must be sought immediately. The Investigator should inform AnaptysBio, and the full IRB/EC, no later than 5 working days after the emergency occurs. Protocol-specified safety reporting requirements must be adhered to, independent of any other variables.

10.2.3 INSURANCE

AnaptysBio, Inc. will provide insurance in accordance with local guidelines and requirements for the subjects in this study. The terms of the insurance will be kept in the study files.

11 REFERENCES

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12 APPENDICES

APPENDIX 1: CONTRACEPTIVE GUIDANCE AND COLLECTION OF PREGNANCY INFORMATION

Definitions:

Woman of childbearing potential (WOCBP)

A woman is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

If fertility is unclear (eg, amenorrhea in athletes) and a menstrual cycle cannot be confirmed before first dose of study treatment, additional evaluation should be considered.

Women in the following categories are not considered WOCBP

1. Premenarchal
2. Premenopausal female with 1 of the following:
   a) Documented hysterectomy.
   b) Documented bilateral salpingectomy.
   c) Documented bilateral oophorectomy.
   Note: For individuals with permanent infertility due to an alternate medical cause other than the above, (eg, mullerian agenesis, androgen insensitivity), Investigator discretion should be applied to determining study entry.
   Note: Documentation can come from the study site personnel's review of the subject's medical records, medical examination, or medical history interview.
3. Postmenopausal female:
   d) A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high FSH level in the postmenopausal range will be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy (HRT). However, in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient.
   e) Females on HRT and whose menopausal status is in doubt will be required to use 1 of the non-estrogen hormonal highly effective contraception methods if they wish to continue their HRT during the study. Otherwise, they must discontinue HRT to allow confirmation of postmenopausal status before study enrollment.

Contraception Guidance:

Male subjects

Male subjects with female partners of childbearing potential are eligible to participate if they agree to ONE of the following (during the protocol-defined time frame in Section 5.1):

- Are abstinent from penile-vaginal intercourse as their usual and preferred lifestyle (abstinent on a long-term and persistent basis) and agree to remain abstinent.

- Agree to use a male condom plus partner use of a contraceptive method with a failure rate of < 1% per year when having penile-vaginal intercourse with a WOCBP who is not currently pregnant.

In addition, male subjects must refrain from donating sperm for the duration of the study and for 220 days (which includes the duration of relevant exposure plus the duration of sperm cycle) after the last dose of study treatment.

Male subjects with a pregnant or breastfeeding partner must agree to remain abstinent from penile-vaginal intercourse or use a male condom during each episode of penile penetration for the duration of the study and for 220 days (which includes the duration of relevant exposure plus the duration of sperm cycle) after the last dose of study treatment.

Female subjects

Female subjects of childbearing potential are eligible to participate if they agree to use highly effective methods of contraception consistently and correctly as described in the table below and during the protocol-defined time frame in Section 5.1, and refrain from donating oocytes for assisted reproduction during this period. For WOCBP, hormonal contraceptives must be used without schedule changes and in steady doses during the study treatment. Starting hormonal contraceptives during the study is not permitted.

Highly Effective Contraceptive Methods:

Highly Effective Contraceptive Methods That Are User Dependent [a]

Failure rate of <1% per year when used consistently and correctly.

- Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation
  - Oral
  - Intravaginal
  - Transdermal
- Progestogen only hormonal contraception associated with inhibition of ovulation
  - Oral
  - Injectable

Highly Effective Methods That Are User Independent [a]

- Implantable progestogen only hormonal contraception associated with inhibition of ovulation
  - Intrauterine device (IUD)
  - Intrauterine hormone-releasing system (IUS)
  - Implants inserted beneath the skin
- Bilateral tubal ligation or occlusion

Vasectomized Partner

A vasectomized partner is a highly effective birth control method provided that the partner is the sole male sexual partner of the WOCBP and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used.

Sexual Abstinence

Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatment. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the subject.

[a] Typical use failure rates may differ from those when used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for subjects participating in clinical studies.

Pregnancy Testing:

Women of childbearing potential should only be included after a confirmed menstrual period and a negative highly sensitive serum pregnancy test at screening and urine pregnancy test on Day 1 (prior to study treatment administration).

Additional pregnancy testing should be performed as mentioned in the SoA (Section 1.3).

Pregnancy testing will be performed whenever a menstrual cycle is missed or when pregnancy is otherwise suspected. Positive urine pregnancy test result should be confirmed with serum test.

Collection of Pregnancy Information

Male subjects with partners who become pregnant

The Investigator will attempt to collect pregnancy information on any male subject's female partner who becomes pregnant while the male subject is in this study. This applies only to male subjects who receive study treatment.

After obtaining the necessary signed informed consent from the pregnant female partner directly, the Investigator will record pregnancy information on the appropriate pregnancy form and submit it to the pharmacovigilance unit within 24 hours of learning of the partner's pregnancy. The female partner will also be followed to determine the outcome of the pregnancy. Information on the status of the mother and child will be forwarded to AnaptysBio. Generally, the follow-up will be no longer than 6 to 8 weeks following the estimated delivery date. Any termination of the pregnancy will be reported regardless of fetal status (presence or absence of anomalies) or indication for the procedure.

Any SAEs associated with the pregnancy in the male subject's partner should also be reported to the pharmacovigilance unit within 24 hours of the event using the back-up Paper Report Form.

Female subjects who become pregnant

The Investigator will collect pregnancy information on any female subject who becomes pregnant while participating in this study. Information will be recorded on the appropriate form and submitted to the pharmacovigilance unit within 24 hours of learning of a subject's pregnancy. The subject will be followed to determine the outcome of the pregnancy. The Investigator will collect follow-up information on the subject and the neonate and the information will be forwarded to AnaptysBio. Generally, follow-up will not be required for longer than 6 to 8 weeks after the delivery date. Any termination of pregnancy will be reported, regardless of fetal status (presence or absence of anomalies) or indication for the procedure.

While pregnancy itself is not considered to be an AE or SAE, any pregnancy complication or elective termination of a pregnancy will be reported as an AE or SAE. A spontaneous abortion is always considered to be an SAE and will be reported as such.

Any poststudy pregnancy related SAE considered reasonably related to the study treatment by the Investigator will be reported to AnaptysBio as described in Section 8.2.1.8. While the Investigator is not obligated to actively seek this information in former subjects, he or she may learn of an SAE through spontaneous reporting.

Any female subject who becomes pregnant while participating in the study will be withdrawn from the study.

APPENDIX 2: PAIN NUMERIC RATING SCALES

Worst Pain Numeric Rating Scale:

Select the number that best describes your *WORST* pain (with regards to your HS) during the past 24 hours? Please select one number.

Numeric Rating Scale										
0	1	2	3	4	5	6	7	8	9	10
No pain										Worst imaginable pain

Source: modified from Farrar 2001

Average Pain Numeric Rating Scale:

In the past 7 days, how would you rate your pain on average?

Numeric Rating Scale										
0	1	2	3	4	5	6	7	8	9	10
No pain										Worst imaginable pain

PROMIS® Numeric Rating Scale v.1.0 – Pain Intensity 1a
5 October 2017

https://www.healthmeasures.net/index.php?option=com_instruments&view=measure&id=896&Itemid=992

APPENDIX 3: PATIENT GLOBAL IMPRESSION OF SEVERITY

Overall, how would you rate the **severity** of your HS now?

1. ☐ No activity
2. ☐ Mild
3. ☐ Moderate
4. ☐ Severe

APPENDIX 4: PATIENT GLOBAL IMPRESSION OF BOTHER

Please choose the ONE response that best describes how bothered you are ***by your hidradenitis suppurativa*** right now.

- ☐ Not at all bothered
- ☐ A little bothered
- ☐ Moderately bothered
- ☐ Very bothered
- ☐ Extremely bothered

Source: modified from Yalcin 2003

APPENDIX 5: PATIENT GLOBAL IMPRESSION OF CHANGE

Overall, how would you rate the change in severity of your HS compared with how it was before you started taking the medication in this study?

1. ☐ Very much better
2. ☐ Much better
3. ☐ A little better
4. ☐ No change
5. ☐ A little worse
6. ☐ Much worse
7. ☐ Very much worse

APPENDIX 6: HIDRADENITIS SUPPURATIVA PATIENT'S GLOBAL ASSESSMENT

In the past 7 days, how much has HS influenced your quality of life?

Response	**Score**
Not at all	0
Slightly	1
Moderately	2
Very much	3
Extremely	4

APPENDIX 7: DERMATOLOGY LIFE QUALITY INDEX

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick ☑ one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful,** or **stinging** has your skin been?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
2.	Over the last week, how **embarrassed** or **self-conscious** have you been because of your skin?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **yard?**	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	☐ ☐	Not relevant ☐
	If "No," over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	☐ ☐ ☐	
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐

9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
10	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐

Please check you have answered EVERY question. Thank you.

If two or more questions are left unanswered the questionnaire is not scored. If two or more response options are ticked, the response option with the highest score should be recorded. If there is a response between two tick boxes, the lower of the two score options should be recorded.

Scoring:

Very much 3 points

A lot 2 points

A little 1 point

Not at all 0 points

Not relevant 0 points

Question 7, 'prevented work or studying' 3 points

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.

APPENDIX 8: HIDRADENITIS SUPPURATIVA QUALITY OF LIFE

Please select the single best option for each item

In the past 7 days, how much has your HS caused problems with:	**UNABLE TO DO** due to my HS	Extremely	Very much	Moderately	Slightly	Not at all
1. Walking (not for exercise)	[ ]					
2. Exercising (for example: swimming, jogging, biking, yoga, aerobics)	[ ]					
3. Sleeping						
4. Washing yourself						
5. Getting dressed						
6. Your concentration						

In the past 7 days, how have your current or potential new HS lesions influenced:	Extremely	Very much	Moderately	Slightly	Not at all
7. What you wear to avoid discomfort					

In the past 7 days, how bothered have you been by:	Extremely	Very much	Moderately	Slightly	Not at all
8. Pain					
9. Itch					
10. Drainage					
11. Odor					

In the past 7 days, how much has HS caused you to feel:	Extremely	Very much	Moderately	Slightly	Not at all
12. Down or depressed					
13. Embarrassed					
14. Anxious or nervous					

In the past 7 days, how much has HS:			Extremely	Very much	Moderately	Slightly	Not at all
15. Made sexual activity difficult	I am not sexually active [ ]	UNABLE TO DO **due to my HS** [ ]					
16. Affected your desire for sexual activities							

In the past 7 days, how much has HS:			Extremely	Very much	Moderately	Slightly	Not at all
17. Influenced your ability to work or study	I do not work or study [ ]	UNABLE TO DO due to my HS [ ]					

Source: Kirby 2020

APPENDIX 9: HIDRADENITIS SUPPURATIVA PHYSICIAN'S GLOBAL ASSESSMENT

Select the single unique category that best captures the global assessment of subject's HS activity at the given time point:

Category (Score)	Description
Inactive (0)	No nodules or abscesses; no drainage and areas are dry following palpation; no pain and/or tenderness with palpation
Almost inactive (1)	Few scattered nodules and/or abscesses; none or little drainage or discharge with palpation; slight pain and/or tenderness with palpation
Mild (2)	Several nodules and/or abscesses; small amount of spontaneous drainage; mild pain and/or tenderness with palpation
Moderate (3)	A moderate number of nodules and/or abscesses; moderate amount of spontaneous drainage; moderate pain and/or tenderness with palpation, subject may wince with palpation
Severe (4)	Many, broadly dispersed nodules and/or abscesses; large amount of spontaneous drainage occurring over broad area(s); severe pain and/or tenderness with palpation, subject may wince and attempt to withdraw with palpation

APPENDIX 10: INTERNATIONAL HIDRADENITIS SUPPURATIVA SEVERITY SCORE SYSTEM

IHS4 (points) =

Number of nodules	× 1 +
Number of abscesses	× 2 +
Number of draining tunnels (fistulae/sinuses)	× 4
	Total IHS4 score

Mild HS:	≤ 3 points
Moderate HS:	4-10 points
Severe HS:	≥ 11 points

APPENDIX 11: CLINICAL LABORATORY TESTS

The tests detailed in Table 8 will be performed by the central laboratory. The time points are specified in the SoA (Section 1.3).

Local laboratory tests will be allowed in the event that the central laboratory results will not be available immediately, and the Investigator needs to take an immediate decision for any safety concerns. If a local sample is required, it is important that the sample for central analysis is obtained at the same time. Urine pregnancy dipstick will be performed at the study site prior to study treatment administration.

Protocol-specific requirements for inclusion or exclusion of subjects are detailed in Section 5 of the protocol.

Additional tests may be performed at any time during the study as determined necessary by the Investigator or required by local regulations.

Investigators must document their review of each laboratory safety report.

Table 8: Protocol-required Safety Laboratory Assessments by Central Laboratory

Laboratory Assessments	**Parameters**	
Hematology	Hemoglobin Hematocrit Packed cell volume (PCV) Mean cell hemoglobin (MCH) Mean cell volume (MCV) Mean cell hemoglobin concentration (MCHC) Platelet count Red blood cell (RBC) count	White Blood Cell (WBC) count with Differential: Neutrophils Lymphocytes Monocytes Eosinophils Basophils
Biochemistry	Alanine aminotransferase (ALT) Albumin Alkaline phosphatase (ALP) Aspartate aminotransferase (AST) Bicarbonate Bilirubin (Total) Bilirubin (Direct-only if total is elevated) Calcium Chloride Uric acid Lactate dehydrogenase	Creatinine Gamma glutamyl transferase Glucose Potassium Phosphate (Inorganic) Protein (Total) Sodium Blood urea nitrogen (urea) Creatine kinase (CK) Triglycerides human C-reactive protein
Serum pregnancy	Human chorionic gonadotropin pregnancy test (as needed for women of childbearing potential)	
Follicle stimulating hormone (FSH)	In women of nonchildbearing potential only (postmenopausal woman with at least 12 months of amenorrhea without an alternative medical cause)	

Laboratory Assessments	**Parameters**	
Urinalysis	Bilirubin Blood Glucose Ketones Leukocytes Nitrites	pH Protein Specific gravity Urobilinogen Microscopy (At discretion of Investigator based on urinalysis results)
Viral serology and testing	Antibodies to hepatitis B core antigen Hepatitis B surface antigen Hepatitis C antibody and reflex RNA Human immunodeficiency virus antibodies	
Tuberculosis (TB) screening	QuantiFERON-TB Gold® In-Tube, the third-generation test (If the test indeterminate it can be retested only once)	
NOTES: Please see SoA for laboratory tests time points. All blood samples must be drawn prior to administration of the study treatment, unless otherwise specified. The date and exact time of sample collection must be recorded.		

APPENDIX 12: FITZPATRICK SKIN TYPE CLASSIFICATION

Fitzpatrick Classification of Skin Types					
Skin Type	**Hair**	**Complexion**	**Freckles**	**Sun Reaction**	**Tanning**
I	Red or Blond	Very fair	+++	Always burns	Never tans
II	Blond	Fair	++	Often burns	Tans lightly
III	Blond or Light Brown	Fair to medium	+ to 0	Sometimes burns	Tans progressively
IV	Brown	Olive	0	Rarely burns	Tans easily
V	Brown to Black	Dark	0	Rarely burns	Tans deeply
VI	Black	Very dark	0	Never burns	Tans deeply

Source: Attwa 2016; Fitzpatrick 1988; Wallace 2017; Zalaudek 2007