OPEN-LABEL PHASE 1B/2/3 TRIAL OF SACITUZUMAB GOVITECAN-HZIY PLUS CHEMOIMMUNOTHERAPY FOR THE TREATMENT OF SUBJECTS WITH ADVANCED TRIPLE-NEGATIVE BREAST CANCER AFTER PRIOR THERAPY

Study Number:	QUILT-3.058
IND Sponsor:	ImmunityBio, Inc. 9920 Jefferson Blvd Culver City, CA 90232
Sponsor Contact: **(For medical questions/emergencies)**	Sandeep Bobby Reddy, MD Chief Medical Officer, ImmunityBio, Inc. 9920 Jefferson Blvd Culver City, CA 90232 Email: Bobby.Reddy@ImmunityBio.com Cell Phone: +1-562-631-4945

Protocol Version	**Date**
Version 1	15 March 2021

STATEMENT OF COMPLIANCE

This trial will be conducted in accordance with Good Clinical Practice (GCP) as described in the International Conference on Harmonization (ICH) Guideline for GCP E6(R2) and in accordance with United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and 21 CFR Part 312) and the general ethical principles outlined in the Declaration of Helsinki. The study will receive approval from an Institutional Review Board (IRB) prior to commencement. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the IRB, except where necessary to eliminate an immediate hazard(s) to the trial participants.

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitments.

Signed: _____ Date: _____

PROTOCOL SYNOPSIS

Name of Sponsor/Company:
ImmunityBio, Inc.

Name of Investigational Products:

1. N-803 (also known as ALT-803; recombinant human superagonist interleukin [IL]-15 complex)
2. PD-L1 t-haNK Suspension for Infusion (PD-L1 t-haNK for Infusion)

Name of Approved Products:

3. Cyclophosphamide (Cyclophosphamide Capsules, for oral use; or Cyclophosphamide Tablets, USP)
4. Sacituzumab govitecan-hziy (TRODELVY™, for injection)

Name of Active Ingredients
Investigational Products:

1. N-803, recombinant human superagonist IL-15 complex (also known as IL-15N72D:IL-15RαSu/IgG1 Fc complex)
2. PD-L1 t-haNK

Approved Products:

3. Cyclophosphamide (anhydrous)
4. Sacituzumab govitecan-hziy

Title of Study:
Open-Label Phase 1b/2/3 Study of Sacituzumab Govitecan-Hziy Plus Chemoimmunotherapy for the Treatment of Subjects With Advanced Triple-Negative Breast Cancer After Prior Therapy.

Study Number:
QUILT-3.058

Study Phase:
Phase 1b/2/3

Study Objectives:

Phase 1b

Primary Objectives:

- Determine the maximum tolerated dose (MTD) or highest tested dose (HTD) and designate a recommended phase 2 dose (RP2D).
- Evaluate the overall safety profile of sacituzumab govitecan-hziy plus chemoimmunotherapy (cyclophosphamide, PD-L1 t-haNK, and N-803) in subjects with advanced triple-negative breast cancer (TNBC) after prior therapy.

Secondary Objectives:

- Obtain preliminary estimates of efficacy by objective response rate (ORR), duration of response (DOR), disease control rate (DCR), and progression free survival (PFS) per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 and modified RECIST guidelines for immunotherapy trials (iRECIST), overall survival (OS), and quality of life (QoL) by patient-reported outcomes (PROs).

Exploratory Objectives:

- Assess tumor molecular profiles and their correlations with subject outcomes.

Phase 2 and Phase 3

Primary Objectives:

- Phase 2: Evaluate the efficacy of sacituzumab govitecan-hziy, cyclophosphamide, PD-L1 t-haNK, and N-803 as assessed by ORR per RECIST Version 1.1.
- Phase 3: Compare the efficacy of sacituzumab govitecan-hziy vs sacituzumab govitecan-hziy, cyclophosphamide, PD-L1 t-haNK, and N-803 as assessed by ORR per RECIST Version 1.1.

Secondary Objectives:

- Evaluate safety and obtain additional measures of efficacy by PFS, DOR, and DCR per RECIST Version 1.1 and iRECIST, ORR per iRECIST, OS, and QoL by PROs.

Exploratory Objectives:

- Assess tumor molecular profiles and their correlations with subject outcomes.

Study Design:

This is a phase 1b/2/3 open-label study to evaluate the safety and efficacy of sacituzumab govitecan-hziy in combination with chemoimmunotherapy (cyclophosphamide, N-803, and PD-L1 t-haNK) in subjects with TNBC after at least 2 prior treatments for metastatic disease.

The phase 1b portion of the study will be conducted in 2 parts: part 1 will involve dose escalation using a 3 + 3 design, and part 2 will involve the expansion of the RP2D to further evaluate the safety and efficacy of sacituzumab govitecan-hziy plus chemoimmunotherapy. The phase 2 portion of the study will be based on Simon's two-stage optimal design.

In phases 1b and 2, all subjects will receive sacituzumab govitecan-hziy plus chemoimmunotherapy (cyclophosphamide, N-803, and PD-L1 t-haNK) as per the experimental treatment regimen outlined below. The dose of sacituzumab govitecan-hziy will be dependent on dose level cohort for phase 1b

and will be set at the RP2D for phase 2. The doses of cyclophosphamide, N-803, and PD-L1 t haNK will remain the same in all dose level cohorts and phases.

In part 1 of phase 1b, 3 to 6 subjects will be sequentially enrolled starting at dose level 1 and will be assessed for dose-limiting toxicities (DLTs). Dose level cohorts for sacituzumab govitecan-hziy are as follows:

- Dose level 1: Sacituzumab govitecan-hziy (7.5 mg/kg IV)
- Dose level 2: Sacituzumab govitecan-hziy (10 mg/kg IV)
- Dose level -1 (if needed): Sacituzumab govitecan-hziy (5.0 mg/kg IV)

In part 2 of phase 1b, dose expansion will occur when the RP2D has been determined. An additional 4 subjects may be enrolled, for a total of up to 10 subjects at the RP2D. Following part 2 of the phase 1b portion of the study, the Safety Review Committee (SRC) will meet to determine if enrollment into phase 2 should proceed.

In the phase 2 portion of the study, 22 subjects will be enrolled at the RP2D in the first stage of Simon's two-stage optimal design. If ≥ 9 of 22 subjects exhibit a confirmed response, the study will proceed to the second stage. If the study proceeds to the second stage, an additional 41 subjects will be enrolled for a total of 63 subjects in the phase 2. If ≥ 27 of the 63 subjects exhibit a confirmed response, the trial will proceed to phase 3.

In the phase 3 portion of the study, subjects will be randomly assigned 1:1 to either the control arm or the experimental arm. Randomization will be stratified by baseline PD-L1 expression (tumor infiltrating immune cells 0% vs ≥ 1%) and by time from last line of therapy (< 6 months vs ≥ 6 months). Subjects randomized to the experimental arm will receive sacituzumab govitecan-hziy in combination with cyclophosphamide, N-803, and PD-L1 t-haNK per the experimental treatment regimen outlined below. Subjects randomized to the control arm will receive sacituzumab govitecan-hziy monotherapy per the control treatment regimen outlined below.

All subjects may receive up to 17 cycles (ie, 51 weeks) of treatment administered in 3-week cycles as follows:

Experimental Treatment Regimen (All Phases):

Days 1–5 and 15–19, every 3 weeks:

- Cyclophosphamide (25 mg by mouth [PO] twice per day [BID])

Days 1 and 8, every 3 weeks:

- PD-L1 t-haNK (~2×10^9 cells IV)
- Sacituzumab govitecan-hziy (5.0, 7.5, or 10 mg/kg IV)
  per dose level cohort in phase 1b/at RP2D in phases 2 and 3

Day 8, every 3 weeks:

- N-803 (15 µg/kg subcutaneously [SC])

Control Treatment Regimen (Phase 3 Only):

Days 1 and 8, every 3 weeks:

- Sacituzumab govitecan-hziy (10 mg/kg intravenously [IV])

Treatment will be discontinued if the subject experiences disease progression or symptomatic deterioration indicating treatment failure, unacceptable toxicity, or a treatment delay > 3 weeks for any reason. (Treatment delays of up to 3 weeks will be allowed at the Investigator's discretion.) The subject

may withdraw from the study at any time for any reason or may be withdrawn if the Investigator feels it is no longer in the subject's best interest to continue treatment.

Safety will be assessed for all subjects and will include vital signs, physical examinations, and the incidence and severity of adverse events (AEs), graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. Blood samples will be collected for safety laboratory tests.

Tumors will be assessed at screening, and tumor response will be assessed by the Investigator every 8 weeks by computed tomography (CT) or magnetic resonance imaging (MRI) of target and non-target lesions in accordance with RECIST Version 1.1 and iRECIST. Imaging should continue until progressive disease (PD) is confirmed or the subject completes study follow-up and the same mode of assessment (ie, CT/MRI) used to identify/evaluate lesions at baseline should be used throughout the course of the study unless subject safety necessitates a change (eg, allergic reaction to contrast media).

Study Endpoints:

Phase 1b

Primary Endpoints:

- MTD or HTD and RP2D.
- Incidence of DLTs, treatment-emergent AEs, and serious AEs (SAEs), graded using the NCI CTCAE Version 5.0.

Secondary Endpoints:

- ORR per RECIST Version 1.1 and iRECIST.
- PFS per RECIST Version 1.1 and iRECIST.
- OS.
- DOR per RECIST Version 1.1 and iRECIST.
- DCR (confirmed CR, PR, or stable disease [SD] lasting for ≥ 8 weeks) per RECIST Version 1.1 and iRECIST.
- QoL by PROs.
- Laboratory tests.
- Vital signs.

Exploratory Endpoints:

- Tumor molecular profiles and correlations with subject outcomes.

Phase 2 and Phase 3

Primary Efficacy Endpoint:

- ORR per RECIST Version 1.1 (based on investigator assessment for phase 2 and using blinded independent central review [BICR] for phase 3).

Key Secondary Efficacy Endpoints:

- PFS per RECIST Version 1.1 (based on investigator assessment for phase 2 and using BICR for phase 3).

- OS.

Additional Secondary Endpoints:

- DOR per RECIST Version 1.1.
- DCR, defined as percentage of subjects who have achieved confirmed complete response (CR), partial response (PR), or stable disease (SD) lasting for at least 2 months per RECIST Version 1.1.
- ORR, PFS, DOR, and DCR evaluated by iRECIST.
- QoL by PROs.

Safety Endpoints:

- Incidence of treatment-emergent AEs and SAEs, graded using the NCI CTCAE Version 5.0.
- Safety laboratory tests.
- Vital signs.

Exploratory Endpoints:

- Tumor molecular profiles and correlations with subject outcomes.

Enrollment (planned):

In the phase 1b portion of the study, up to 16 subjects may be enrolled with up to 12 subjects in part 1 (dose escalation) and up to 4 subjects in part 2 (dose expansion).

In the phase 2 portion of the study, 22 subjects will be enrolled in the first stage of Simon's two-stage optimal design. If the study proceeds to the second stage, an additional 41 subjects will be enrolled for a total of 63 subjects in the phase 2.

In the phase 3 portion of the study, a total of 374 subjects will be randomized (1:1) to either the control or experimental arm initially. Based on the interim ORR analysis, the phase 3 sample size may be increased to a maximum of 748 subjects using "Promising Zone" methodology for an adaptive sample size increase.

The maximum total enrollment for this study is 827 subjects.

Inclusion and Exclusion Criteria:

Inclusion Criteria:

1. Age ≥ 18 years.
2. Able to understand and provide a signed informed consent that fulfills the relevant Institutional Review Board (IRB) or Independent Ethics Committee (IEC) guidelines.
3. Histologically confirmed stage IV TNBC. Subjects must have had at least 2 prior treatments for TNBC. TNBC is defined as breast cancer that lacks estrogen receptor (ER) and progesterone receptor (PgR) expression (both ≤ 1% of tumor cell nuclei), and human epidermal growth factor receptor 2 (*HER2*) overexpression and/or amplification (IHC 0 or 1+, or IHC 2+ and fluorescence in situ hybridization [FISH]-), according to American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guideline criteria, as evaluated by local institutions.

4. Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 to 2.
5. Have at least 1 measurable lesion of ≥ 1.0 cm and/or non-measurable disease evaluable in accordance with RECIST V1.1.
6. Ability to attend required study visits and return for adequate follow-up, as required by this protocol.
7. Agreement to practice effective contraception for female subjects of child-bearing potential and non-sterile males. Female subjects of child-bearing potential must agree to use effective contraception while on study and for at least 5 months after the last dose of study therapy. Non-sterile male subjects must agree to use a condom while on study and for up to 5 months after the last dose of study therapy. Effective contraception includes surgical sterilization (eg, vasectomy, tubal ligation), two forms of barrier methods (eg, condom, diaphragm) used with spermicide, intrauterine devices (IUDs), oral contraceptives, and abstinence.

Exclusion Criteria:

1. Serious uncontrolled concomitant disease that would contraindicate the use of the investigational drug used in this study or that would put the subject at high risk for treatment-related complications.
2. Systemic autoimmune disease (eg, lupus erythematosus, rheumatoid arthritis, Addison's disease, autoimmune disease associated with lymphoma).
3. Documented Gilbert's syndrome.
4. History of organ transplant requiring immunosuppression.
5. History of or active inflammatory bowel disease (eg, Crohn's disease, ulcerative colitis).
6. Inadequate organ function, evidenced by the following laboratory results:
   a. Absolute neutrophil count (ANC) < 1000 cells/mm^3.
   b. Platelet count < 75,000 cells/mm^3.
   c. Hemoglobin < 9 g/dL.
   d. Total bilirubin greater than the upper limit of normal (ULN; unless the subject has documented Gilbert's syndrome).
   e. Aspartate aminotransferase (AST [SGOT]) or alanine aminotransferase (ALT [SGPT]) > 2.5 × ULN (> 5 × ULN in subjects with liver metastases).
   f. Alkaline phosphatase (ALP) levels > 2.5 × ULN (> 5 × ULN in subjects with liver metastases, or > 10 × ULN in subjects with bone metastases).
   g. Serum creatinine > 2.0 mg/dL or 177 μmol/L.

   Each site should use its own institution's ULN to determine eligibility.
7. Uncontrolled hypertension (systolic > 160 mm Hg and/or diastolic > 110 mm Hg) or clinically significant (ie, active) cardiovascular disease, cerebrovascular accident/stroke, or myocardial infarction within 6 months prior to first study medication; unstable angina; congestive heart failure of New York Heart Association grade 2 or higher; or serious cardiac arrhythmia requiring medication.
8. Current chronic daily treatment (continuous for > 3 months) with systemic corticosteroids (dose equivalent to or greater than 10 mg/day methylprednisolone), excluding inhaled steroids.

Short-term steroid use to prevent IV contrast allergic reaction or anaphylaxis in subjects who have known contrast allergies is allowed.

9. Known hypersensitivity to any component of the study medication(s).
10. Subjects taking any medication(s) (herbal or prescribed) known to have an adverse drug reaction with any of the study medications.
11. Known uridine diphosphate-glucuronosyl transferase 1A1 (*UGT1A1*) gene polymorphism resulting in reduced function.
12. Assessed by the Investigator to be unable or unwilling to comply with the requirements of the protocol.
13. Concurrent participation in any interventional clinical trial.
14. Pregnant and nursing women. A negative serum pregnancy test during screening and a negative pregnancy test within 72 hours prior to the first dose must be documented before study therapy is administered to a female subject of child-bearing potential.

Investigational Product, Dosage, and Mode of Administration:

Experimental treatment regimen

Investigational Products	**Dosage**	**Mode of Administration**
N-803	15 µg/kg on day 8	SC
PD-L1 t-haNK	~2×10^9 cells/dose on days 1 and 8	IV
Approved Products	**Dosage**	**Mode of Administration**
Cyclophosphamide	25 mg BID on days 1–5 and 15–19	PO
Sacituzumab govitecan-hziy	5.0, 7.5, or 10 mg/kg on days 1 and 8	IV

Duration of Treatment:

The length of the treatment is 51 weeks or until unacceptable toxicity, disease progression, symptomatic deterioration indicating treatment failure, or treatment delay greater than 3 weeks for any reason.

Duration of Follow-up:

Subjects who discontinue study treatment should remain in the study and continue to be followed for:

- CT or MRI imaging and response assessment
- Collection of vital status every 12 weeks (± 2 weeks)

Subjects should be followed until either death (any cause) or for a minimum of 48 months past administration of the first dose of study drug.

After a subject has confirmed disease progression, he/she will continue to be followed for survival status via phone call until either death (any cause) or for a minimum of 48 months past administration of the first dose of study drug.

Reference Therapy, Dosage, and Mode of Administration:

Control treatment regimen (phase 3 only)

Approved Products	Dosage	Mode of Administration
Sacituzumab govitecan-hziy	10 mg/kg on days 1 and 8	IV

Evaluation of Endpoints:

Safety

Safety endpoints include assessments of DLTs, MTD or HTD, treatment-emergent AEs, SAEs, clinically significant changes in safety laboratory tests, and vital signs. All subjects will be evaluable for toxicity from the time of their first study treatment. Toxicities will be graded using the NCI CTCAE Version 5.0. or in the case of cytokine release syndrome (CRS) and CAR T-cell–related encephalopathy syndrome (CRES) using the specified grading system defined in the protocol.

Efficacy

Tumor response will be assessed by CT or MRI every 8 weeks and will be evaluated per RECIST Version 1.1 and iRECIST. In order to document PD, unscheduled tumor assessments may be done if the Investigator observes any signs and symptoms of PD. Efficacy endpoints include ORR, DOR, DCR, PFS, and OS. In phases 1b and 2, tumor response will be based on investigator assessment; in phase 3, tumor response will be based on BICR.

Exploratory Analyses

Tumor Molecular Profiling: Exploratory analyses will be conducted on tissue and blood to evaluate a potential biomarker signature to identify appropriate patients for the treatments tested in the trial.

Statistical Methods:

The phase 1b portion of the study will use a standard 3 + 3 design to determine the MTD or HTD and designate the RP2D. The phase 2 portion of the study will be based on Simon's two-stage optimal design to evaluate the null hypothesis that the ORR is ≤ 33% tested against the one-sided alternative that the ORR is > 33%.

Phase 3 Sample Size, Randomization, and Interim Analyses: The primary efficacy endpoint for the phase 3 portion of the study is ORR per RECIST Version 1.1 based on BICR.

Initially 374 subjects will be randomly assigned (1:1) to either the control arm or the experimental arm (187 subjects per arm). The randomization will be stratified by baseline PD-L1 expression (tumor infiltrating immune cells 0% vs ≥ 1% and by time from last line of therapy (< 6 months vs ≥ 6 months). Sample size of 187 subjects per arm provides 90% power to detect an improvement in ORR from 33% to 50% based on a two-sided 5% type 1 error rate.

An interim ORR analysis is planned when 50% of subjects (94 subjects per arm) are randomized and have been followed for at least 2 response assessments. The Lan DeMets/O'Brien Fleming spending function will be used for the interim and final ORR analyses which allocates $\alpha = 0.003$ to the interim analysis and $\alpha = 0.049$ to the final analysis. Positive efficacy may be claimed early if the interim ORR analysis shows superiority (ie, p-value < 0.003). Enrollment may be stopped early for futility if the interim ORR analysis displays a conditional power < 10%. Based on the interim ORR analysis, the phase 3 sample size may be increased to a maximum of 748 subjects using "Promising Zone" methodology for an adaptive sample size increase.

All interim analyses will be performed by an independent statistician separate from the study team. The interim analyses results will not be shared with the study team during the conduct of the study. The interim analysis results will be presented to the Independent Data Monitoring Committee (IDMC) who may make recommendations to the Sponsor regarding safety and efficacy.

Analysis Populations

In phases 1b and 2, all subjects receiving at least 1 dose of any study drug (ie, the safety population) will be included in the analysis of safety and efficacy.

In phase 3, all randomized subjects (ie, intent-to-treat [ITT] population), regardless of whether subjects received any study drug or had any efficacy assessments collected, will be included in the efficacy analyses and analyzed according to the randomized treatment arm assigned. In phase 3, all subjects receiving at least 1 dose of study drug (ie, the safety population) will be included in the safety analyses and analyzed according to the actual treatment received.

In phase 1b, endpoints will be summarized for each dose level and all phase 1b subjects; in phase 3 endpoints will be summarized by each treatment arm.

Safety Analyses

The rate of DLTs and the MTD (or HTD) will be assessed in phase 1b. Overall safety will be assessed by descriptive analyses using tabulated frequencies of AEs by grade in terms of treatment-emergent AEs, SAEs, and clinically significant changes in safety laboratory tests and vital signs.

Efficacy Analyses

The ORR and DCR will be summarized along with the 95% confidence intervals (CIs) using Clopper-Pearson methods. DOR, PFS, and OS will be analyzed using Kaplan-Meier methods.

In phase 3, comparison of ORR and DCR between the control and experimental arms will be based on the Cochran-Mantel-Haenszel (CMH) test stratified by the randomization strata.

The key secondary efficacy endpoints (PFS and OS) in phase 3 will be tested only if the primary efficacy endpoint, ORR, is statistically significant in favor of the experimental arm. In order to control the type 1 error rate for multiple key secondary efficacy endpoints, a hierarchical/gate-keeping approach will be used. Each key secondary efficacy endpoint will be tested at $\alpha = 0.05$ according to the following hierarchy:

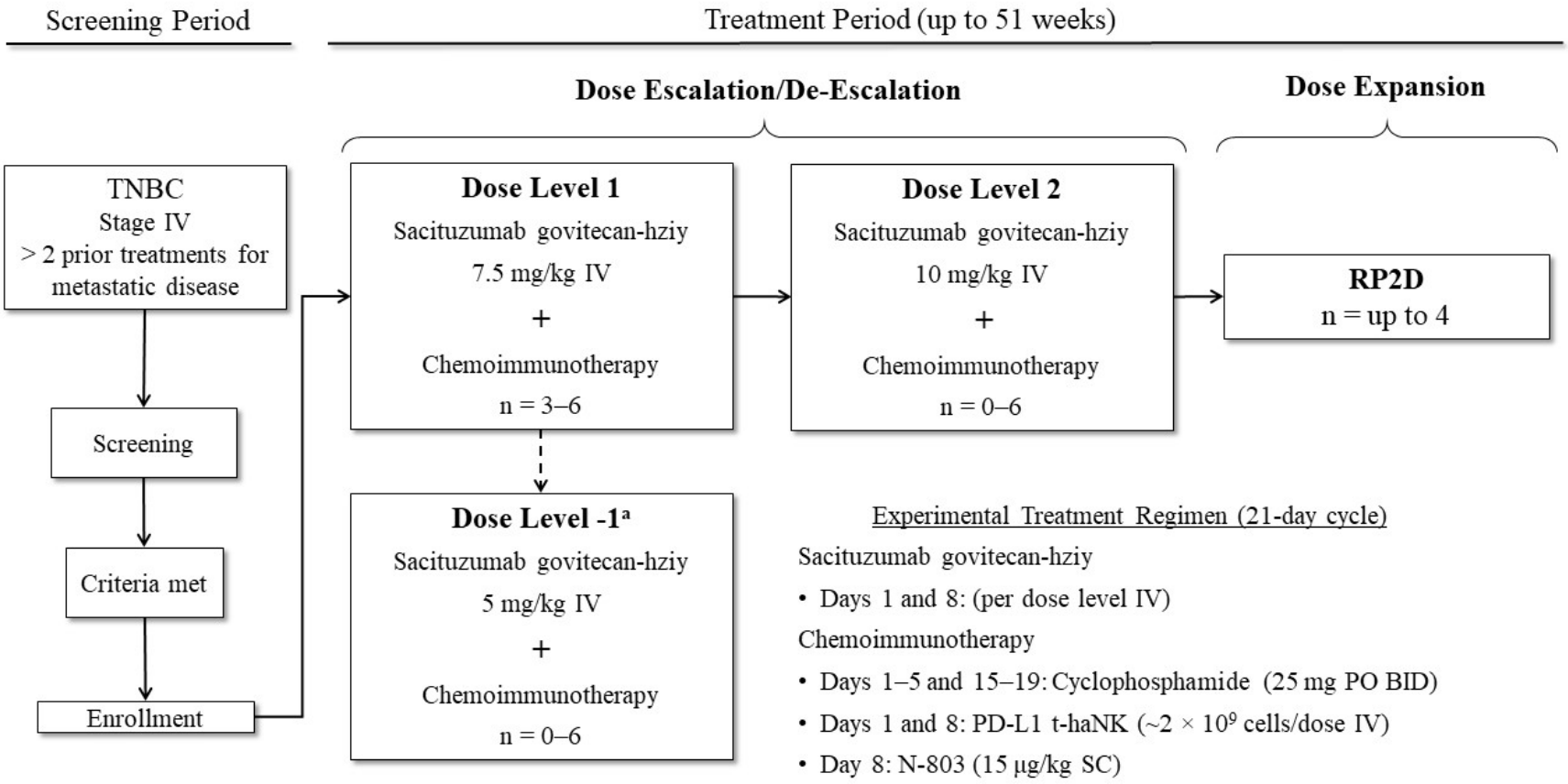
- PFS
- OS

Comparison of PFS and OS between the control and experimental arms in phase 3 will be based on the stratified log-rank test stratified by the randomization strata.

Exploratory Analyses

Correlations of tumor molecular profiles with subject outcomes will be explored.

Figure 1: Phase 1b Treatment Schema



[a] If needed, subjects will be enrolled into a de-escalation cohort at dose level -1 (dashed line).
[b] Safety Review Committee will meet to determine if enrollment into phase 3 can proceed.

Figure 2: Phase 2 Treatment Schema

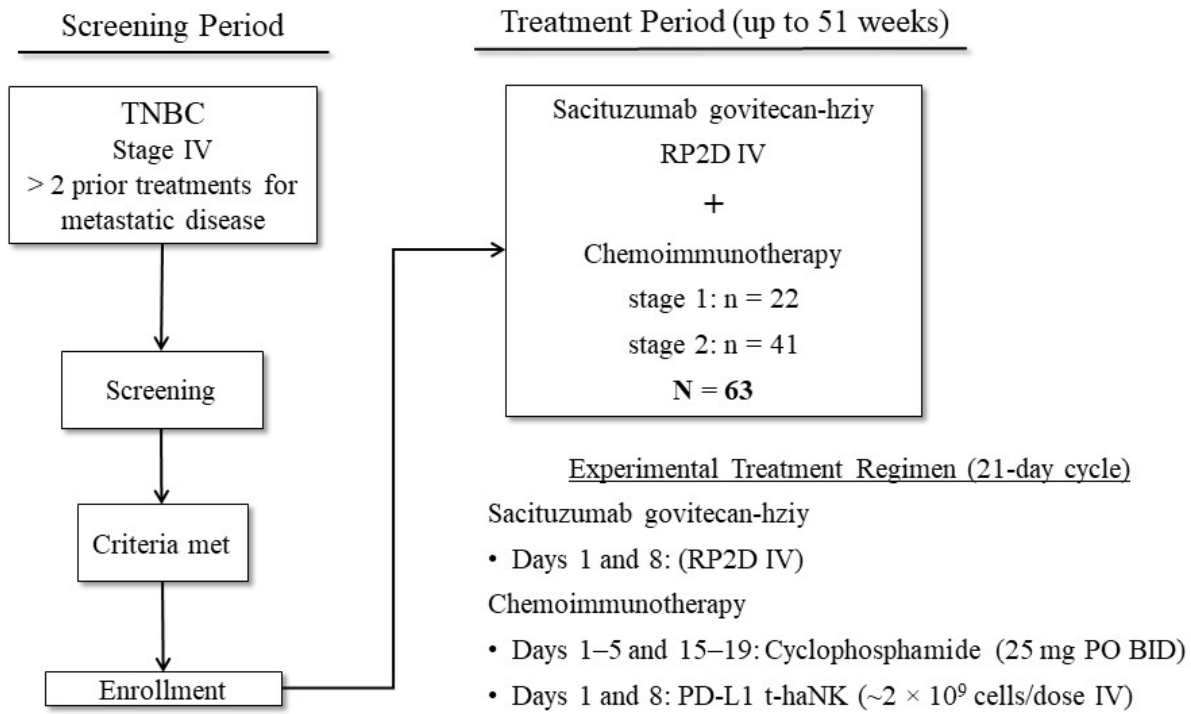
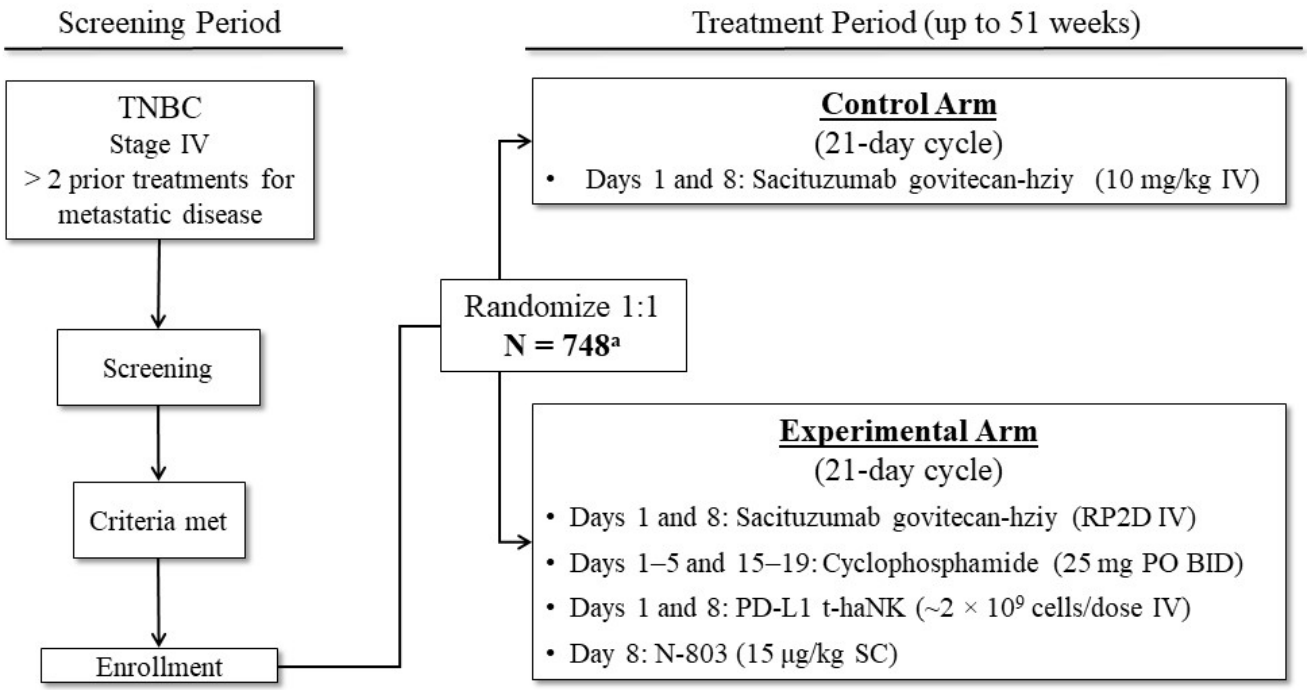


Figure 3: Phase 3 Treatment Schema



[a] The phase 3 sample may be increased up to a maximum of 748 subjects using "Promising Zone" methodology for an adaptive sample size increase.

APPENDIX 1. SPONSOR SIGNATURE

Study Title:	Open-Label Phase 1b/2/3 Study of Sacituzumab Govitecan-Hziy Plus Chemoimmunotherapy for the Treatment of Subjects With Advanced Triple-Negative Breast Cancer After Prior Therapy.
Study Number:	QUILT-3.058
Version Number	1
Date:	15 March 2021

This clinical study protocol was subject to critical review and has been approved by ImmunityBio.

Signed: _____ Date: MARCH 16, 2021

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OPEN-LABEL PHASE 1B/2 STUDY OF SACITUZUMAB GOVITECAN-HZIY PLUS CHEMOIMMUNOTHERAPY FOR THE TREATMENT OF SUBJECTS WITH ADVANCED TRIPLE-NEGATIVE BREAST CANCER AFTER PRIOR THERAPY

Study Number:	QUILT-3.058
IND Sponsor:	ImmunityBio, Inc. 9920 Jefferson Blvd Culver City, CA 90232
Sponsor Contact: **(For medical questions/emergencies)**	Sandeep Bobby Reddy, MD Chief Medical Officer, ImmunityBio, Inc. 9920 Jefferson Blvd Culver City, CA 90232 Email: Bobby.Reddy@ImmunityBio.com Cell Phone: +1-562-631-4945

Protocol Version	**Date**
Version 1	15 March 2021
Version 2	27 April 2021

STATEMENT OF COMPLIANCE

This trial will be conducted in accordance with Good Clinical Practice (GCP) as described in the International Conference on Harmonization (ICH) Guideline for GCP E6(R2) and in accordance with United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and 21 CFR Part 312) and the general ethical principles outlined in the Declaration of Helsinki. The study will receive approval from an Institutional Review Board (IRB) prior to commencement. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the IRB, except where necessary to eliminate an immediate hazard(s) to the trial participants.

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitments.

Signed: _____ Date: _____

PROTOCOL SYNOPSIS

Name of Sponsor/Company:
ImmunityBio, Inc.

Name of Investigational Products:

1. N-803 (also known as ALT-803; recombinant human superagonist interleukin [IL]-15 complex)
2. PD-L1 t-haNK Suspension for Infusion (PD-L1 t-haNK for Infusion)

Name of Approved Products:

3. Cyclophosphamide (Cyclophosphamide Capsules, for oral use; or Cyclophosphamide Tablets, USP)
4. Sacituzumab govitecan-hziy (TRODELVY™, for injection)

Name of Active Ingredients
Investigational Products:

1. N-803, recombinant human superagonist IL-15 complex (also known as IL-15N72D:IL-15RαSu/IgG1 Fc complex)
2. PD-L1 t-haNK

Approved Products:

3. Cyclophosphamide (anhydrous)
4. Sacituzumab govitecan-hziy

Title of Study:
Open-Label Phase 1b/2 Study of Sacituzumab Govitecan-Hziy Plus Chemoimmunotherapy for the Treatment of Subjects With Advanced Triple-Negative Breast Cancer After Prior Therapy.

Study Number:
QUILT-3.058

Investigational New Drug (IND) Number:
027223

Study Phase:
Phase 1b/2

Study Objectives:

Phase 1b

Primary Objectives:

- Determine the maximum tolerated dose (MTD) or highest tested dose (HTD) and designate a recommended phase 2 dose (RP2D).
- Evaluate the overall safety profile of sacituzumab govitecan-hziy plus chemoimmunotherapy (cyclophosphamide, PD-L1 t-haNK, and N-803) in subjects with advanced triple-negative breast cancer (TNBC) after prior therapy.

Secondary Objectives:

- Obtain preliminary estimates of efficacy by objective response rate (ORR), duration of response (DOR), disease control rate (DCR), and progression free survival (PFS) per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 and modified RECIST guidelines for immunotherapy trials (iRECIST), overall survival (OS), and quality of life (QoL) by patient-reported outcomes (PROs).

Exploratory Objectives:

- Assess tumor molecular profiles and their correlations with subject outcomes.

Phase 2

Primary Objectives:

- Evaluate the efficacy of sacituzumab govitecan-hziy, cyclophosphamide, PD-L1 t-haNK, and N-803 as assessed by ORR per RECIST Version 1.1.

Secondary Objectives:

- Evaluate safety and obtain additional measures of efficacy by PFS, DOR, and DCR per RECIST Version 1.1 and iRECIST, ORR per iRECIST, OS, and QoL by PROs.

Exploratory Objectives:

- Characterize the pharmacokinetic (PK) profiles of N-803 and PD-L1 t-haNK.
- Characterize the immunogenicity of N-803, PD-L1 t-haNK, and sacituzumab govitecan-hziy and their correlations with subject outcomes and impact on PK.
- Assess tumor molecular profiles and their correlations with subject outcomes.

Study Design:

This is a phase 1b/2 open-label study to evaluate the safety and efficacy of sacituzumab govitecan-hziy in combination with chemoimmunotherapy (cyclophosphamide, N-803, and PD-L1 t-haNK) in subjects with TNBC after at least 2 prior treatments for metastatic disease.

The phase 1b portion of the study will be conducted in 2 parts: part 1 will involve dose escalation using a 3 + 3 design, and part 2 will involve the expansion of the RP2D to further evaluate the safety and efficacy of sacituzumab govitecan-hziy plus chemoimmunotherapy. The phase 2 portion of the study will be based on Simon's two-stage optimal design.

In phases 1b and 2, all subjects will receive sacituzumab govitecan-hziy plus chemoimmunotherapy (cyclophosphamide, N-803, and PD-L1 t-haNK) as per the treatment regimen outlined below. The dose

of sacituzumab govitecan-hziy will be dependent on dose level cohort for phase 1b and will be set at the RP2D for phase 2. The doses of cyclophosphamide, N-803, and PD-L1 t haNK will remain the same in all dose level cohorts and phases.

In part 1 of phase 1b, 3 to 6 subjects will be sequentially enrolled starting at dose level 1 and will be assessed for dose-limiting toxicities (DLTs). Dose level cohorts for sacituzumab govitecan-hziy are as follows:

- Dose level 1: Sacituzumab govitecan-hziy (7.5 mg/kg IV)
- Dose level 2: Sacituzumab govitecan-hziy (10 mg/kg IV)
- Dose level -1 (if needed): Sacituzumab govitecan-hziy (5.0 mg/kg IV)

In part 2 of phase 1b, dose expansion will occur when the RP2D has been determined. An additional 4 subjects may be enrolled, for a total of up to 10 subjects at the RP2D. Following part 2 of the phase 1b portion of the study, the Safety Review Committee (SRC) will meet to determine if enrollment into phase 2 should proceed.

In the phase 2 portion of the study, 22 subjects will be enrolled at the RP2D in the first stage of Simon's two-stage optimal design. If ≥ 9 of 22 subjects exhibit a confirmed response, the study will proceed to the second stage. If the study proceeds to the second stage, an additional 41 subjects will be enrolled for a total of 63 subjects in the phase 2. If ≥ 27 of the 63 subjects exhibit a confirmed response, the combination therapy will be considered for further development.

All subjects may receive up to 17 cycles (ie, 51 weeks) of treatment administered in 3-week cycles as follows:

Days 1 and 8, every 3 weeks:

- Sacituzumab govitecan-hziy (5.0, 7.5, or 10 mg/kg IV)
  per dose level cohort in phase 1b/at RP2D in phase 2
- PD-L1 t-haNK (~2×10^9 cells IV)

Day 8, every 3 weeks:

- N-803 (15 µg/kg subcutaneously [SC])

Days 1–5 and 15–19, every 3 weeks:

- Cyclophosphamide (25 mg by mouth [PO] twice per day [BID])

Treatment will be discontinued if the subject experiences disease progression or symptomatic deterioration indicating treatment failure, unacceptable toxicity, or a treatment delay > 3 weeks for any reason. (Treatment delays of up to 3 weeks will be allowed at the Investigator's discretion.) The subject may withdraw from the study at any time for any reason or may be withdrawn if the Investigator feels it is no longer in the subject's best interest to continue treatment.

Safety will be assessed for all subjects and will include vital signs, physical examinations, and the incidence and severity of adverse events (AEs), graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. Blood samples will be collected for safety laboratory tests.

Tumors will be assessed at screening, and tumor response will be assessed by the Investigator every 8 weeks by computed tomography (CT) or magnetic resonance imaging (MRI) of target and non-target lesions in accordance with RECIST Version 1.1 and iRECIST. Imaging should continue until progressive disease (PD) is confirmed or the subject completes study follow-up and the same mode of

assessment (ie, CT/MRI) used to identify/evaluate lesions at baseline should be used throughout the course of the study unless subject safety necessitates a change (eg, allergic reaction to contrast media).

Study Endpoints:

Phase 1b

Primary Endpoints:

- MTD or HTD and RP2D.
- Incidence of DLTs, treatment-emergent AEs, and serious AEs (SAEs), graded using the NCI CTCAE Version 5.0.

Secondary Endpoints:

- ORR per RECIST Version 1.1 and iRECIST.
- PFS per RECIST Version 1.1 and iRECIST.
- OS.
- DOR per RECIST Version 1.1 and iRECIST.
- DCR (confirmed CR, PR, or stable disease [SD] lasting for ≥ 8 weeks) per RECIST Version 1.1 and iRECIST.
- QoL by PROs.
- Laboratory tests.
- Vital signs.

Exploratory Endpoints:

- Tumor molecular profiles and correlations with subject outcomes.

Phase 2

Primary Efficacy Endpoint:

- ORR per RECIST Version 1.1.

Key Secondary Efficacy Endpoints:

- PFS per RECIST Version 1.1.
- OS.

Additional Secondary Endpoints:

- DOR per RECIST Version 1.1.
- DCR, defined as percentage of subjects who have achieved confirmed complete response (CR), partial response (PR), or stable disease (SD) lasting for at least 2 months per RECIST Version 1.1.
- ORR, PFS, DOR, and DCR evaluated by iRECIST.
- QoL by PROs.

Safety Endpoints:

- Incidence of treatment-emergent AEs and SAEs, graded using the NCI CTCAE Version 5.0.
- Safety laboratory tests.
- Vital signs.

Exploratory Endpoints:

- PK profiles of N-803 and PD-L1 t-haNK.
- Immunogenicity of N-803 PD-L1 t-haNK, and sacituzumab govitecan-hziy; their correlations with subject outcomes and impact on PK.
- Tumor molecular profiles and correlations with subject outcomes.

Enrollment (planned):

In the phase 1b portion of the study, up to 16 subjects may be enrolled with up to 12 subjects in part 1 (dose escalation) and up to 4 subjects in part 2 (dose expansion).

In the phase 2 portion of the study, 22 subjects will be enrolled in the first stage of Simon's two-stage optimal design. If the study proceeds to the second stage, an additional 41 subjects will be enrolled for a total of 63 subjects in the phase 2.

The maximum total enrollment for this study is 79 subjects.

Inclusion and Exclusion Criteria:

Inclusion Criteria:

1. Age ≥ 18 years.
2. Able to understand and provide a signed informed consent that fulfills the relevant Institutional Review Board (IRB) or Independent Ethics Committee (IEC) guidelines.
3. Histologically confirmed stage IV TNBC. Subjects must have had at least 2 prior treatments for TNBC. TNBC is defined as breast cancer that lacks estrogen receptor (ER) and progesterone receptor (PgR) expression (both ≤ 1% of tumor cell nuclei), and human epidermal growth factor receptor 2 (*HER2*) overexpression and/or amplification (IHC 0 or 1+, or IHC 2+ and fluorescence in situ hybridization [FISH]-), according to American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guideline criteria, as evaluated by local institutions.
4. Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 to 2.
5. Have at least 1 measurable lesion of ≥ 1.0 cm and/or non-measurable disease evaluable in accordance with RECIST V1.1.
6. Ability to attend required study visits and return for adequate follow-up, as required by this protocol.
7. Agreement to practice effective contraception for female subjects of child-bearing potential and non-sterile males. Female subjects of child-bearing potential must agree to use effective contraception while on study and for at least 5 months after the last dose of study therapy. Non-sterile male subjects must agree to use a condom while on study and for up to 5 months

after the last dose of study therapy. Effective contraception includes surgical sterilization (eg, vasectomy, tubal ligation), two forms of barrier methods (eg, condom, diaphragm) used with spermicide, intrauterine devices (IUDs), oral contraceptives, and abstinence.

Exclusion Criteria:

1. Have previously received or are currently receiving treatment with sacituzumab govitecan-hziy.
2. Serious uncontrolled concomitant disease that would contraindicate the use of the investigational drug used in this study or that would put the subject at high risk for treatment-related complications.
3. Systemic autoimmune disease (eg, lupus erythematosus, rheumatoid arthritis, Addison's disease, autoimmune disease associated with lymphoma).
4. Documented Gilbert's syndrome.
5. History of organ transplant requiring immunosuppression.
6. History of or active inflammatory bowel disease (eg, Crohn's disease, ulcerative colitis).
7. Inadequate organ function, evidenced by the following laboratory results:
   a. Absolute neutrophil count (ANC) < 1500 cells/mm^3.
   b. Platelet count < 75,000 cells/mm^3.
   c. Hemoglobin < 9 g/dL.
   d. Total bilirubin greater than the upper limit of normal (ULN; unless the subject has documented Gilbert's syndrome).
   e. Aspartate aminotransferase (AST [SGOT]) or alanine aminotransferase (ALT [SGPT]) > 2.5 × ULN (> 5 × ULN in subjects with liver metastases).
   f. Alkaline phosphatase (ALP) levels > 2.5 × ULN (> 5 × ULN in subjects with liver metastases, or > 10 × ULN in subjects with bone metastases).
   g. Serum creatinine > 2.0 mg/dL or 177 μmol/L.

   Each site should use its own institution's ULN to determine eligibility.
8. Uncontrolled hypertension (systolic > 160 mm Hg and/or diastolic > 110 mm Hg) or clinically significant (ie, active) cardiovascular disease, cerebrovascular accident/stroke, or myocardial infarction within 6 months prior to first study medication; unstable angina; congestive heart failure of New York Heart Association grade 2 or higher; or serious cardiac arrhythmia requiring medication.
9. Current chronic daily treatment (continuous for > 3 months) with systemic corticosteroids (dose equivalent to or greater than 10 mg/day methylprednisolone), excluding inhaled steroids. Short-term steroid use to prevent IV contrast allergic reaction or anaphylaxis in subjects who have known contrast allergies is allowed.
10. Known hypersensitivity to any component of the study medication(s).
11. Subjects taking any medication(s) (herbal or prescribed) known to have an adverse drug reaction with any of the study medications.

12. Known uridine diphosphate-glucuronosyl transferase 1A1 (*UGT1A1*) gene polymorphism resulting in reduced function.
13. Assessed by the Investigator to be unable or unwilling to comply with the requirements of the protocol.
14. Concurrent participation in any interventional clinical trial.
15. Pregnant and nursing women. A negative serum pregnancy test during screening and a negative pregnancy test within 72 hours prior to the first dose must be documented before study therapy is administered to a female subject of child-bearing potential.

Investigational Product, Dosage, and Mode of Administration:

Investigational Products	**Dosage**	**Mode of Administration**
N-803	15 µg/kg on day 8	SC
PD-L1 t-haNK	~2×10^9 cells/dose on days 1 and 8	IV
Approved Products	**Dosage**	**Mode of Administration**
Cyclophosphamide	25 mg BID on days 1–5 and 15–19	PO
Sacituzumab govitecan-hziy	5.0, 7.5, or 10 mg/kg on days 1 and 8	IV

Duration of Treatment:

The length of the treatment is 51 weeks or until unacceptable toxicity, disease progression, symptomatic deterioration indicating treatment failure, or treatment delay greater than 3 weeks for any reason.

Duration of Follow-up:

Subjects who discontinue study treatment should remain in the study and continue to be followed for:

- CT or MRI imaging and response assessment every 8 weeks (± 1 week)
- Collection of vital status every 12 weeks (± 2 weeks)

Subjects should be followed until either death (any cause) or for a minimum of 48 months past administration of the first dose of study drug.

After a subject has confirmed disease progression, he/she will continue to be followed for survival status via phone call until either death (any cause) or for a minimum of 48 months past administration of the first dose of study drug.

Reference Therapy, Dosage, and Mode of Administration:

Not applicable.

Evaluation of Endpoints:

Safety

Safety endpoints include assessments of DLTs, MTD or HTD, treatment-emergent AEs, SAEs, clinically significant changes in safety laboratory tests, and vital signs. All subjects will be evaluable for toxicity from the time of their first study treatment. Toxicities will be graded using the NCI CTCAE Version 5.0. or in the case of cytokine release syndrome (CRS) and CAR T-cell–related encephalopathy syndrome (CRES) using the specified grading system defined in the protocol.

Efficacy

Tumor response will be assessed by CT or MRI every 8 weeks and will be evaluated per RECIST Version 1.1 and iRECIST. In order to document PD, unscheduled tumor assessments may be done if the Investigator observes any signs and symptoms of PD. Efficacy endpoints include ORR, DOR, DCR, PFS, and OS. Tumor response will be based on investigator assessment.

Exploratory Analyses

Pharmacokinetics(phase 2 only): The PK profile of N-803 will be evaluated using validated enzyme-linked immunosorbent assay (ELISA) methods. The PK profile of PD-L1 t-haNK will be evaluated using quantitative polymerase chain reaction (qPCR).

Immunogenicity (phase 2 only): Immunogenicity (antidrug antibodies [ADA], neutralizing antibodies [NAb], cross-reactivity) to N-803, PD-L1 t-haNK, and sacituzumab govitecan-hziy will be evaluated by standard immune assays. For PD-L1 t-haNK, cellular immunogenicity will also be characterized.

Tumor Molecular Profiling: Exploratory analyses will be conducted on tissue and blood to evaluate a potential biomarker signature to identify appropriate patients for the treatments tested in the trial.

Statistical Methods:

The phase 1b portion of the study will use a standard 3 + 3 design to determine the MTD or HTD and designate the RP2D. The phase 2 portion of the study will be based on Simon's two-stage optimal design to evaluate the null hypothesis that the ORR is ≤ 33% tested against the one-sided alternative that the ORR is > 33%.

Analysis Populations

All subjects receiving at least 1 dose of any study drug (ie, the safety population) will be included in the analysis of safety and efficacy.

In phase 1b, endpoints will be summarized for each dose level and all phase 1b subjects.

Safety Analyses

The rate of DLTs and the MTD (or HTD) will be assessed in phase 1b. Overall safety will be assessed by descriptive analyses using tabulated frequencies of AEs by grade in terms of treatment-emergent AEs, SAEs, and clinically significant changes in safety laboratory tests and vital signs.

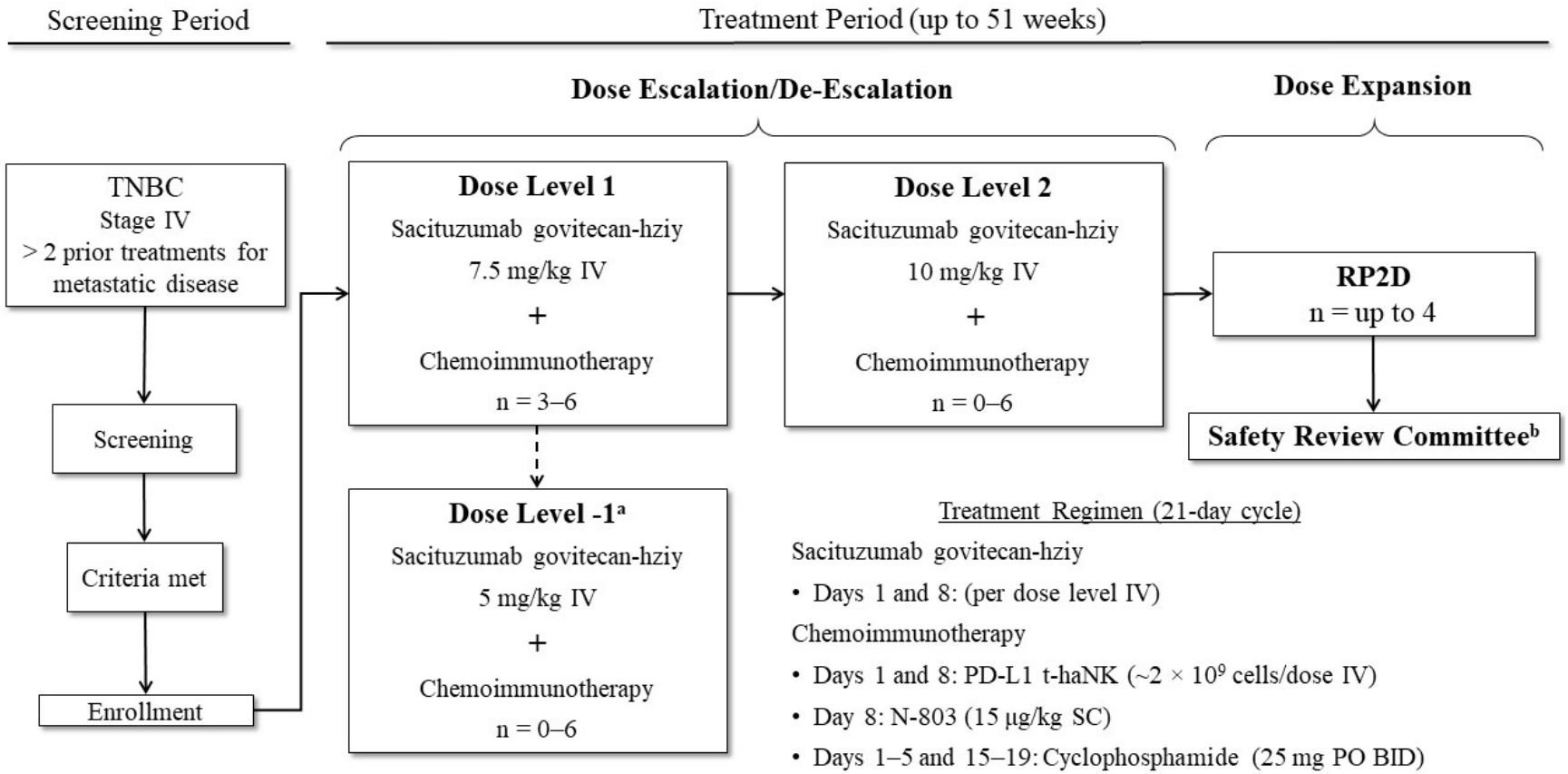
Efficacy Analyses

The ORR and DCR will be summarized along with the 95% confidence intervals (CIs) using Clopper-Pearson methods. DOR, PFS, and OS will be analyzed using Kaplan-Meier methods.

Exploratory Analyses

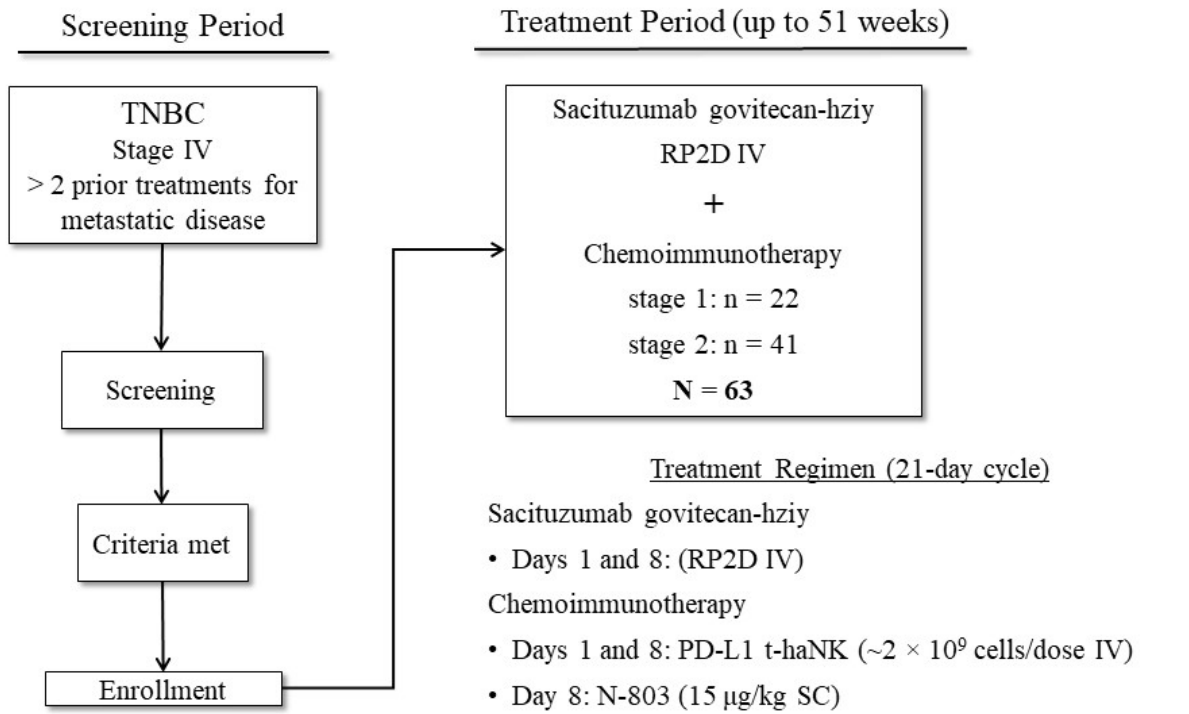
Correlations of tumor molecular profiles with subject outcomes will be explored. Correlations of PK and immunogenicity with subject outcomes and the impact of immunogenicity on PK will be explored in phase 2.

Figure 1: Phase 1b Treatment Schema



[a] If needed, subjects will be enrolled into a de-escalation cohort at dose level -1 (dashed line).
[b] Safety Review Committee will meet to determine if enrollment into phase 2 can proceed.

Figure 2: Phase 2 Treatment Schema



APPENDIX 1. SPONSOR SIGNATURE

Study Title:	Open-Label Phase 1b/2 Study of Sacituzumab Govitecan-Hziy Plus Chemoimmunotherapy for the Treatment of Subjects With Advanced Triple-Negative Breast Cancer After Prior Therapy.
Study Number:	QUILT-3.058
Version Number	2
Date:	27 April 2021

This clinical study protocol was subject to critical review and has been approved by ImmunityBio.

Signed: _____ Date: April 27, 2021

Sandeep Bobby Reddy, MD
Chief Medical Officer
ImmunityBio, Inc.
9920 Jefferson Blvd
Culver City, CA 90232
Email: Bobby.Reddy@ImmunityBio.com
Cell Phone: +1-562-631-4945

OPEN-LABEL PHASE 1B/2 STUDY OF SACITUZUMAB GOVITECAN-HZIY PLUS CHEMOIMMUNOTHERAPY FOR THE TREATMENT OF SUBJECTS WITH ADVANCED TRIPLE-NEGATIVE BREAST CANCER AFTER PRIOR THERAPY

Study Number:	QUILT-3.058
IND Sponsor:	ImmunityBio, Inc. 9920 Jefferson Blvd Culver City, CA 90232
Sponsor Contact: **(For medical questions/emergencies)**	Sandeep Bobby Reddy, MD Chief Medical Officer, ImmunityBio, Inc. 9920 Jefferson Blvd Culver City, CA 90232 Email: Bobby.Reddy@ImmunityBio.com Cell Phone: +1-562-631-4945

Protocol Version	**Date**
Version 1	15 March 2021
Version 2	27 April 2021
Version 3	03 June 2021

STATEMENT OF COMPLIANCE

This trial will be conducted in accordance with Good Clinical Practice (GCP) as described in the International Conference on Harmonization (ICH) Guideline for GCP E6(R2) and in accordance with United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and 21 CFR Part 312) and the general ethical principles outlined in the Declaration of Helsinki. The study will receive approval from an Institutional Review Board (IRB) prior to commencement. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the IRB, except where necessary to eliminate an immediate hazard(s) to the trial participants.

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitments.

Signed: _____ Date: _____

PROTOCOL SYNOPSIS

Name of Sponsor/Company:
ImmunityBio, Inc.

Name of Investigational Products:

1. N-803 (also known as ALT-803; recombinant human superagonist interleukin [IL]-15 complex)
2. PD-L1 t-haNK Suspension for Infusion (PD-L1 t-haNK for Infusion)

Name of Approved Products:

3. Cyclophosphamide (Cyclophosphamide Capsules, for oral use; or Cyclophosphamide Tablets, USP)
4. Sacituzumab govitecan-hziy (TRODELVY™, for injection)

Name of Active Ingredients
Investigational Products:

1. N-803, recombinant human superagonist IL-15 complex (also known as IL-15N72D:IL-15RαSu/IgG1 Fc complex)
2. PD-L1 t-haNK

Approved Products:

3. Cyclophosphamide (anhydrous)
4. Sacituzumab govitecan-hziy

Title of Study:
Open-Label Phase 1b/2 Study of Sacituzumab Govitecan-Hziy Plus Chemoimmunotherapy for the Treatment of Subjects With Advanced Triple-Negative Breast Cancer After Prior Therapy.

Study Number:
QUILT-3.058

Investigational New Drug (IND) Number:
027223

Study Phase:
Phase 1b/2

Study Objectives:

Phase 1b

Primary Objectives:

- Determine the maximum tolerated dose (MTD) or highest tested dose (HTD) and designate a recommended phase 2 dose (RP2D).
- Evaluate the overall safety profile of sacituzumab govitecan-hziy plus chemoimmunotherapy (cyclophosphamide, PD-L1 t-haNK, and N-803) in subjects with advanced triple-negative breast cancer (TNBC) after prior therapy.

Secondary Objectives:

- Obtain preliminary estimates of efficacy by objective response rate (ORR), duration of response (DOR), disease control rate (DCR), and progression free survival (PFS) per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 and modified RECIST guidelines for immunotherapy trials (iRECIST), overall survival (OS), and quality of life (QoL) by patient-reported outcomes (PROs).

Exploratory Objectives:

- Assess tumor molecular profiles and their correlations with subject outcomes.

Phase 2

Primary Objectives:

- Evaluate the efficacy of sacituzumab govitecan-hziy, cyclophosphamide, PD-L1 t-haNK, and N-803 as assessed by ORR per RECIST Version 1.1.

Secondary Objectives:

- Evaluate safety and obtain additional measures of efficacy by PFS, DOR, and DCR per RECIST Version 1.1 and iRECIST, ORR per iRECIST, OS, and QoL by PROs.

Exploratory Objectives:

- Characterize the pharmacokinetic (PK) profiles of N-803 and PD-L1 t-haNK.
- Characterize the immunogenicity of N-803, PD-L1 t-haNK, and sacituzumab govitecan-hziy and their correlations with subject outcomes and impact on PK.
- Assess tumor molecular profiles and their correlations with subject outcomes.

Study Design:

This is a phase 1b/2 open-label study to evaluate the safety and efficacy of sacituzumab govitecan-hziy in combination with chemoimmunotherapy (cyclophosphamide, N-803, and PD-L1 t-haNK) in subjects with TNBC after at least 2 prior treatments for metastatic disease.

The phase 1b portion of the study will be conducted in 2 parts: part 1 will involve dose escalation using a 3 + 3 design, and part 2 will involve the expansion of the RP2D to further evaluate the safety and efficacy of sacituzumab govitecan-hziy plus chemoimmunotherapy. The phase 2 portion of the study will be based on Simon's two-stage optimal design.

In phases 1b and 2, all subjects will receive sacituzumab govitecan-hziy plus chemoimmunotherapy (cyclophosphamide, N-803, and PD-L1 t-haNK) as per the treatment regimen outlined below. The dose

of sacituzumab govitecan-hziy will be dependent on dose level cohort for phase 1b and will be set at the RP2D for phase 2. The doses of cyclophosphamide, N-803, and PD-L1 t haNK will remain the same in all dose level cohorts and phases.

In part 1 of phase 1b, 3 to 6 subjects will be sequentially enrolled starting at dose level 1 and will be assessed for dose-limiting toxicities (DLTs). Dose level cohorts for sacituzumab govitecan-hziy are as follows:

- Dose level 1: Sacituzumab govitecan-hziy (7.5 mg/kg IV)
- Dose level 2: Sacituzumab govitecan-hziy (10 mg/kg IV)
- Dose level -1 (if needed): Sacituzumab govitecan-hziy (5.0 mg/kg IV)

In part 2 of phase 1b, dose expansion will occur when the RP2D has been determined. An additional 4 subjects may be enrolled, for a total of up to 10 subjects at the RP2D. Following part 2 of the phase 1b portion of the study, the Safety Review Committee (SRC) will meet to determine if enrollment into phase 2 should proceed.

In the phase 2 portion of the study, 22 subjects will be enrolled at the RP2D in the first stage of Simon's two-stage optimal design. If ≥ 9 of 22 subjects exhibit a confirmed response, the study will proceed to the second stage. If the study proceeds to the second stage, an additional 41 subjects will be enrolled for a total of 63 subjects in the phase 2. If ≥ 27 of the 63 subjects exhibit a confirmed response, the combination therapy will be considered for further development.

All subjects may receive up to 17 cycles (ie, 51 weeks) of treatment administered in 3-week cycles as follows:

Days 1 and 8, every 3 weeks:

- Sacituzumab govitecan-hziy (5.0, 7.5, or 10 mg/kg IV)
  per dose level cohort in phase 1b/at RP2D in phase 2
- PD-L1 t-haNK (~2×10^9 cells IV)

Day 8, every 3 weeks:

- N-803 (15 µg/kg subcutaneously [SC])

Days 1–5 and 15–19, every 3 weeks:

- Cyclophosphamide (25 mg by mouth [PO] twice per day [BID])

Treatment will be discontinued if the subject experiences disease progression or symptomatic deterioration indicating treatment failure, unacceptable toxicity, or a treatment delay > 3 weeks for any reason. (Treatment delays of up to 3 weeks will be allowed at the Investigator's discretion.) The subject may withdraw from the study at any time for any reason or may be withdrawn if the Investigator feels it is no longer in the subject's best interest to continue treatment.

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Study Endpoints:

Phase 1b

Primary Endpoints:

- MTD or HTD and RP2D.
- Incidence of DLTs, treatment-emergent AEs, and serious AEs (SAEs), graded using the NCI CTCAE Version 5.0.

Secondary Endpoints:

- ORR per RECIST Version 1.1 and iRECIST.
- PFS per RECIST Version 1.1 and iRECIST.
- OS.
- DOR per RECIST Version 1.1 and iRECIST.
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- QoL by PROs.
- Laboratory tests.
- Vital signs.

Exploratory Endpoints:

- Tumor molecular profiles and correlations with subject outcomes.

Phase 2

Primary Efficacy Endpoint:

- ORR per RECIST Version 1.1.

Key Secondary Efficacy Endpoints:

- PFS per RECIST Version 1.1.
- OS.

Additional Secondary Endpoints:

- DOR per RECIST Version 1.1.
- DCR, defined as percentage of subjects who have achieved confirmed complete response (CR), partial response (PR), or stable disease (SD) lasting for at least 2 months per RECIST Version 1.1.
- ORR, PFS, DOR, and DCR evaluated by iRECIST.
- QoL by PROs.

Safety Endpoints:

- Incidence of treatment-emergent AEs and SAEs, graded using the NCI CTCAE Version 5.0.
- Safety laboratory tests.
- Vital signs.

Exploratory Endpoints:

- PK profiles of N-803 and PD-L1 t-haNK.
- Immunogenicity of N-803 PD-L1 t-haNK, and sacituzumab govitecan-hziy; their correlations with subject outcomes and impact on PK.
- Tumor molecular profiles and correlations with subject outcomes.

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In the phase 2 portion of the study, 22 subjects will be enrolled in the first stage of Simon's two-stage optimal design. If the study proceeds to the second stage, an additional 41 subjects will be enrolled for a total of 63 subjects in the phase 2.

The maximum total enrollment for this study is 79 subjects.

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2. Able to understand and provide a signed informed consent that fulfills the relevant Institutional Review Board (IRB) or Independent Ethics Committee (IEC) guidelines.
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4. Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 to 2.
5. Have at least 1 measurable lesion of ≥ 1.0 cm and/or non-measurable disease evaluable in accordance with RECIST V1.1.
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4. History of organ transplant requiring immunosuppression.
5. History of or active inflammatory bowel disease (eg, Crohn's disease, ulcerative colitis).
6. Inadequate organ function, evidenced by the following laboratory results:
   a. Absolute neutrophil count (ANC) < 1500 cells/mm^3.
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   e. Aspartate aminotransferase (AST [SGOT]) or alanine aminotransferase (ALT [SGPT]) > 2.5 × ULN (> 5 × ULN in subjects with liver metastases).
   f. Alkaline phosphatase (ALP) levels > 2.5 × ULN (> 5 × ULN in subjects with liver metastases, or > 10 × ULN in subjects with bone metastases).
   g. Serum creatinine > 2.0 mg/dL or 177 µmol/L.

   Each site should use its own institution's ULN to determine eligibility.
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Subjects should be followed until either death (any cause) or for a minimum of 48 months past administration of the first dose of study drug.

After a subject has confirmed disease progression, he/she will continue to be followed for survival status via phone call until either death (any cause) or for a minimum of 48 months past administration of the first dose of study drug.

Reference Therapy, Dosage, and Mode of Administration:

Not applicable.

Evaluation of Endpoints:

Safety

Safety endpoints include assessments of DLTs, MTD or HTD, treatment-emergent AEs, SAEs, clinically significant changes in safety laboratory tests, and vital signs. All subjects will be evaluable for toxicity from the time of their first study treatment. Toxicities will be graded using the NCI CTCAE Version 5.0. or in the case of cytokine release syndrome (CRS) and CAR T-cell–related encephalopathy syndrome (CRES) using the specified grading system defined in the protocol.

Efficacy

Tumor response will be assessed by CT or MRI every 8 weeks and will be evaluated per RECIST Version 1.1 and iRECIST. In order to document PD, unscheduled tumor assessments may be done if the Investigator observes any signs and symptoms of PD. Efficacy endpoints include ORR, DOR, DCR, PFS, and OS. Tumor response will be based on investigator assessment.

Exploratory Analyses

Pharmacokinetics(phase 2 only): The PK profile of N-803 will be evaluated using validated enzyme-linked immunosorbent assay (ELISA) methods. The PK profile of PD-L1 t-haNK will be evaluated using quantitative polymerase chain reaction (qPCR).

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The phase 1b portion of the study will use a standard 3 + 3 design to determine the MTD or HTD and designate the RP2D. The phase 2 portion of the study will be based on Simon's two-stage optimal design to evaluate the null hypothesis that the ORR is ≤ 33% tested against the one-sided alternative that the ORR is > 33%.

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All subjects receiving at least 1 dose of any study drug (ie, the safety population) will be included in the analysis of safety and efficacy.

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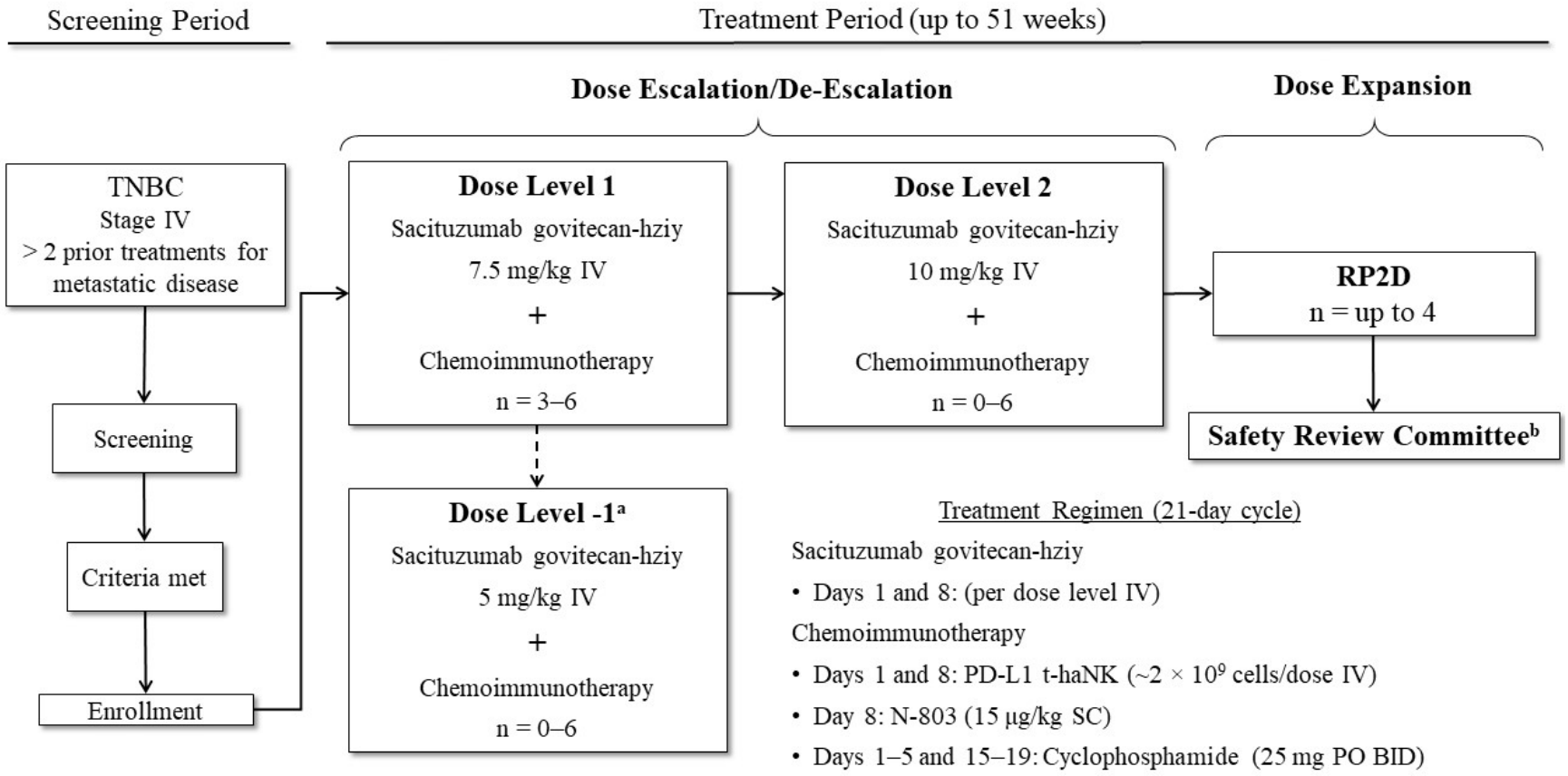
The ORR and DCR will be summarized along with the 95% confidence intervals (CIs) using Clopper-Pearson methods. DOR, PFS, and OS will be analyzed using Kaplan-Meier methods.

Exploratory Analyses

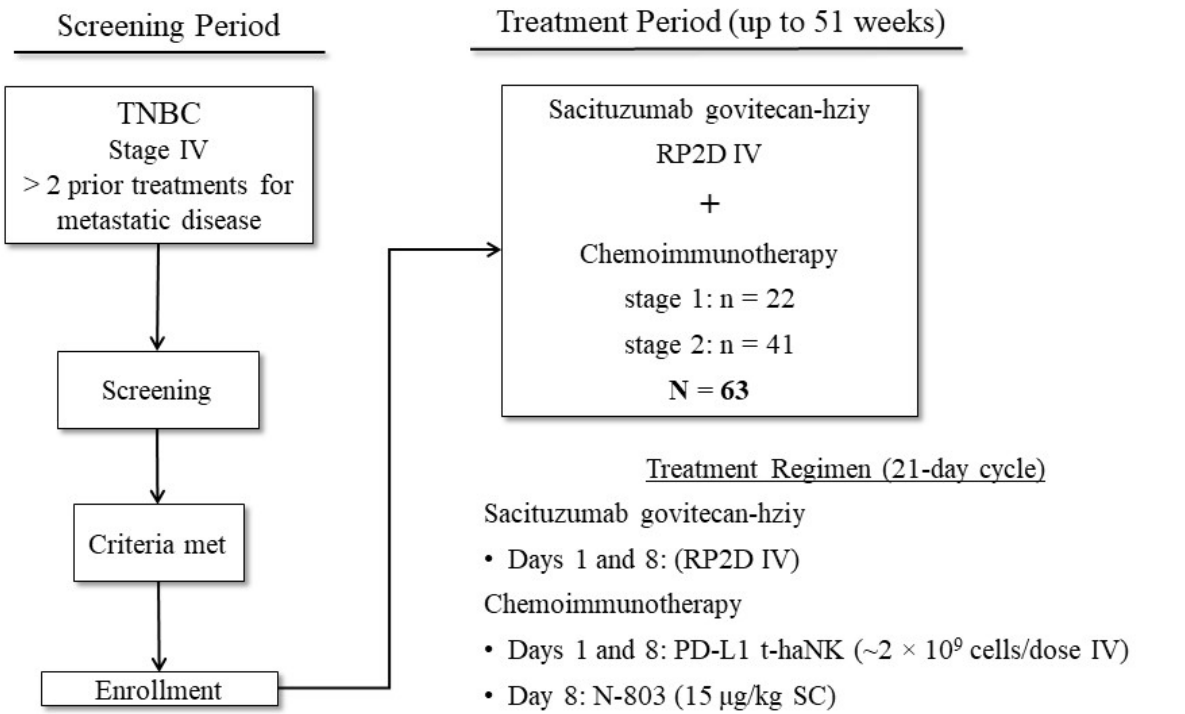
Correlations of tumor molecular profiles with subject outcomes will be explored. Correlations of PK and immunogenicity with subject outcomes and the impact of immunogenicity on PK will be explored in phase 2.

Figure 1: Phase 1b Treatment Schema



[a] If needed, subjects will be enrolled into a de-escalation cohort at dose level -1 (dashed line).
[b] Safety Review Committee will meet to determine if enrollment into phase 2 can proceed.

Figure 2: Phase 2 Treatment Schema



APPENDIX 1. SPONSOR SIGNATURE

Study Title:	Open-Label Phase 1b/2 Study of Sacituzumab Govitecan-Hziy Plus Chemoimmunotherapy for the Treatment of Subjects With Advanced Triple-Negative Breast Cancer After Prior Therapy.
Study Number:	QUILT-3.058
Version Number	3
Date:	03 June 2021

This clinical study protocol was subject to critical review and has been approved by ImmunityBio.

Signed: _____ Date: MAY JUNE 4, 2021

Sandeep Bobby Reddy, MD
Chief Medical Officer
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OPEN-LABEL PHASE 1B/2 STUDY OF SACITUZUMAB GOVITECAN-HZIY PLUS CHEMOIMMUNOTHERAPY FOR THE TREATMENT OF SUBJECTS WITH ADVANCED TRIPLE-NEGATIVE BREAST CANCER AFTER PRIOR THERAPY

Study Number:	QUILT-3.058
IND Sponsor:	ImmunityBio, Inc. 9920 Jefferson Blvd Culver City, CA 90232
Sponsor Contact: **(For medical questions/emergencies)**	Sandeep Bobby Reddy, MD Chief Medical Officer, ImmunityBio, Inc. 9920 Jefferson Blvd Culver City, CA 90232 Email: Bobby.Reddy@ImmunityBio.com Cell Phone: +1-562-631-4945

Protocol Version	**Date**
Version 1	15 March 2021
Version 2	27 April 2021
Version 3	03 June 2021
Version 4	06 September 2022

STATEMENT OF COMPLIANCE

This trial will be conducted in accordance with Good Clinical Practice (GCP) as described in the International Conference on Harmonization (ICH) Guideline for GCP E6(R2) and in accordance with United States (US) Code of Federal Regulations (CFR) applicable to clinical studies and the general ethical principles outlined in the Declaration of Helsinki. The study will receive approval from an Institutional Review Board (IRB) or Independent Ethics Committee (IEC) prior to commencement. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the IRB, except where necessary to eliminate an immediate hazard(s) to the trial participants.

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitments.

Signed: _____ Date: _____

PROTOCOL SYNOPSIS

Name of Sponsor/Company: ImmunityBio, Inc.
Name of Investigational Products: 1. N-803 (also known as ALT-803; recombinant human superagonist interleukin [IL]-15 complex) 2. PD-L1 t-haNK Suspension for Infusion (PD-L1 t-haNK for Infusion) **Name of Approved Products:** 3. Cyclophosphamide (Cyclophosphamide Capsules, for oral use; or Cyclophosphamide Tablets, USP) 4. Sacituzumab govitecan-hziy (TRODELVY™, for injection)
Name of Active Ingredients **Investigational Products:** 1. N-803, recombinant human superagonist IL-15 complex (also known as IL-15N72D:IL-15RαSu/IgG1 Fc complex) 2. PD-L1 t-haNK **Approved Products:** 3. Cyclophosphamide (anhydrous) 4. Sacituzumab govitecan-hziy
Title of Study: Open-Label Phase 1b/2 Study of Sacituzumab Govitecan-Hziy Plus Chemoimmunotherapy for the Treatment of Subjects With Advanced Triple-Negative Breast Cancer After Prior Therapy.
Study Number: QUILT-3.058
Investigational New Drug (IND) Number: 027223
Study Phase: Phase 1b/2

Study Objectives:

Phase 1b

Primary Objectives:

- Determine the maximum tolerated dose (MTD) or highest tested dose (HTD) and designate a recommended phase 2 dose (RP2D).
- Evaluate the overall safety profile of sacituzumab govitecan-hziy plus chemoimmunotherapy (cyclophosphamide, PD-L1 t-haNK, and N-803) in subjects with advanced triple-negative breast cancer (TNBC) after prior therapy.

Secondary Objectives:

- Obtain preliminary estimates of efficacy by objective response rate (ORR), duration of response (DOR), disease control rate (DCR), and progression free survival (PFS) per Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 and modified RECIST guidelines for immunotherapy trials (iRECIST), overall survival (OS), and quality of life (QoL) by patient-reported outcomes (PROs).

Exploratory Objectives:

- Assess tumor molecular profiles and their correlations with subject outcomes.

Phase 2

Primary Objectives:

- Evaluate the efficacy of sacituzumab govitecan-hziy, cyclophosphamide, PD-L1 t-haNK, and N-803 as assessed by ORR per RECIST Version 1.1.

Secondary Objectives:

- Evaluate safety and obtain additional measures of efficacy by PFS, DOR, and DCR per RECIST Version 1.1 and iRECIST, ORR per iRECIST, OS, and QoL by PROs.

Exploratory Objectives:

- Characterize the pharmacokinetic (PK) profiles of N-803 and PD-L1 t-haNK.
- Characterize the immunogenicity of N-803, PD-L1 t-haNK, and sacituzumab govitecan-hziy and their correlations with subject outcomes and impact on PK.
- Assess tumor molecular profiles and their correlations with subject outcomes.

Study Design:

This is a phase 1b/2 open-label study to evaluate the safety and efficacy of sacituzumab govitecan-hziy in combination with chemoimmunotherapy (cyclophosphamide, N-803, and PD-L1 t-haNK) in subjects with TNBC after at least 2 prior treatments for metastatic disease.

The phase 1b portion of the study will be conducted in 2 parts: part 1 will involve dose escalation using a 3 + 3 design, and part 2 will involve the expansion of the RP2D to further evaluate the safety and efficacy of sacituzumab govitecan-hziy plus chemoimmunotherapy. The phase 2 portion of the study will be based on Simon's two-stage optimal design.

In phases 1b and 2, all subjects will receive sacituzumab govitecan-hziy plus chemoimmunotherapy (cyclophosphamide, N-803, and PD-L1 t-haNK) as per the treatment regimen outlined below. The dose

of sacituzumab govitecan-hziy will be dependent on dose level cohort for phase 1b and will be set at the RP2D for phase 2. The doses of cyclophosphamide, N-803, and PD-L1 t haNK will remain the same in all dose level cohorts and phases.

In part 1 of phase 1b, 3 to 6 subjects will be sequentially enrolled starting at dose level 1 and will be assessed for dose-limiting toxicities (DLTs). Dose level cohorts for sacituzumab govitecan-hziy are as follows:

- Dose level 1: Sacituzumab govitecan-hziy (7.5 mg/kg IV)
- Dose level 2: Sacituzumab govitecan-hziy (10 mg/kg IV)
- Dose level -1 (if needed): Sacituzumab govitecan-hziy (5.0 mg/kg IV)

In part 2 of phase 1b, dose expansion will occur when the RP2D has been determined. An additional 4 subjects may be enrolled, for a total of up to 10 subjects at the RP2D. Following part 2 of the phase 1b portion of the study, the Safety Review Committee (SRC) will meet to determine if enrollment into phase 2 should proceed.

In the phase 2 portion of the study, 22 subjects will be enrolled at the RP2D in the first stage of Simon's two-stage optimal design. If ≥ 9 of 22 subjects exhibit a confirmed response, the study will proceed to the second stage. If the study proceeds to the second stage, an additional 41 subjects will be enrolled for a total of 63 subjects in the phase 2. If ≥ 27 of the 63 subjects exhibit a confirmed response, the combination therapy will be considered for further development.

All subjects may receive up to 41 cycles (ie, 123 weeks) of treatment administered in 3-week cycles as follows:

Days 1 and 8, every 3 weeks:

- Sacituzumab govitecan-hziy (5.0, 7.5, or 10 mg/kg IV)
  per dose level cohort in phase 1b/at RP2D in phase 2
- PD-L1 t-haNK (~2×10^9 cells IV)

Day 8, every 3 weeks:

- N-803 (15 µg/kg subcutaneously [SC])

Days 1–5 and 15–19, every 3 weeks:

- Cyclophosphamide (25 mg by mouth [PO] twice per day [BID])

Treatment will be discontinued if the subject experiences disease progression or symptomatic deterioration indicating treatment failure, unacceptable toxicity, or a treatment delay > 3 weeks for any reason. (Treatment delays of up to 3 weeks will be allowed at the Investigator's discretion.) The subject may withdraw from the study at any time for any reason or may be withdrawn if the Investigator feels it is no longer in the subject's best interest to continue treatment.

Safety will be assessed for all subjects and will include vital signs, physical examinations, and the incidence and severity of adverse events (AEs), graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. Blood samples will be collected for safety laboratory tests.

Tumors will be assessed at screening, and tumor response will be assessed by the Investigator every 8 weeks by computed tomography (CT) or magnetic resonance imaging (MRI) of target and non-target lesions in accordance with RECIST Version 1.1 and iRECIST. Imaging should continue until progressive disease (PD) is confirmed or the subject completes study follow-up and the same mode of

assessment (ie, CT/MRI) used to identify/evaluate lesions at baseline should be used throughout the course of the study unless subject safety necessitates a change (eg, allergic reaction to contrast media).

Study Endpoints:

Phase 1b

Primary Endpoints:

- MTD or HTD and RP2D.
- Incidence of DLTs, treatment-emergent AEs, and serious AEs (SAEs), graded using the NCI CTCAE Version 5.0.

Secondary Endpoints:

- ORR per RECIST Version 1.1 and iRECIST.
- PFS per RECIST Version 1.1 and iRECIST.
- OS.
- DOR per RECIST Version 1.1 and iRECIST.
- DCR (confirmed CR, PR, or stable disease [SD] lasting for ≥ 8 weeks) per RECIST Version 1.1 and iRECIST.
- QoL by PROs.
- Laboratory tests.
- Vital signs.

Exploratory Endpoints:

- Tumor molecular profiles and correlations with subject outcomes.

Phase 2

Primary Efficacy Endpoint:

- ORR per RECIST Version 1.1.

Key Secondary Efficacy Endpoints:

- PFS per RECIST Version 1.1.
- OS.

Additional Secondary Endpoints:

- DOR per RECIST Version 1.1.
- DCR, defined as percentage of subjects who have achieved confirmed complete response (CR), partial response (PR), or stable disease (SD) lasting for at least 2 months per RECIST Version 1.1.
- ORR, PFS, DOR, and DCR evaluated by iRECIST.
- QoL by PROs.

Safety Endpoints:

- Incidence of treatment-emergent AEs and SAEs, graded using the NCI CTCAE Version 5.0.
- Safety laboratory tests.
- Vital signs.

Exploratory Endpoints:

- PK profiles of N-803 and PD-L1 t-haNK.
- Immunogenicity of N-803 PD-L1 t-haNK, and sacituzumab govitecan-hziy; their correlations with subject outcomes and impact on PK.
- Tumor molecular profiles and correlations with subject outcomes.

Enrollment (planned):

In the phase 1b portion of the study, up to 16 subjects may be enrolled with up to 12 subjects in part 1 (dose escalation) and up to 4 subjects in part 2 (dose expansion).

In the phase 2 portion of the study, 22 subjects will be enrolled in the first stage of Simon's two-stage optimal design. If the study proceeds to the second stage, an additional 41 subjects will be enrolled for a total of 63 subjects in the phase 2.

The maximum total enrollment for this study is 79 subjects.

Inclusion and Exclusion Criteria:

Inclusion Criteria:

1. Age ≥ 18 years.
2. Able to understand and provide a signed informed consent that fulfills the relevant Institutional Review Board (IRB) or Independent Ethics Committee (IEC) guidelines.
3. Histologically confirmed stage IV TNBC. Subjects must have had at least 2 prior treatments for TNBC. TNBC is defined as breast cancer that lacks estrogen receptor (ER) and progesterone receptor (PgR) expression (both ≤ 1% of tumor cell nuclei), and human epidermal growth factor receptor 2 (*HER2*) overexpression and/or amplification (IHC 0 or 1+, or IHC 2+ and fluorescence in situ hybridization [FISH]-), according to American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guideline criteria, as evaluated by local institutions.
4. Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 to 2.
5. Have at least 1 measurable lesion of ≥ 1.0 cm and/or non-measurable disease evaluable in accordance with RECIST V1.1.
6. Ability to attend required study visits and return for adequate follow-up, as required by this protocol.
7. Agreement to practice effective contraception for female subjects of child-bearing potential and non-sterile males. Female subjects of child-bearing potential must agree to use effective contraception while on study and for at least 5 months after the last dose of study therapy. Non-sterile male subjects must agree to use a condom while on study and for up to 5 months

after the last dose of study therapy. Effective contraception includes surgical sterilization (eg, vasectomy, tubal ligation), two forms of barrier methods (eg, condom, diaphragm) used with spermicide, intrauterine devices (IUDs), oral contraceptives, and abstinence.

Exclusion Criteria:

1. Have previously received or are currently receiving treatment with sacituzumab govitecan-hziy.
2. Serious uncontrolled concomitant disease that would contraindicate the use of the investigational drug used in this study or that would put the subject at high risk for treatment-related complications.
3. Systemic autoimmune disease (eg, lupus erythematosus, rheumatoid arthritis, Addison's disease, autoimmune disease associated with lymphoma).
4. History of organ transplant requiring immunosuppression.
5. History of or active inflammatory bowel disease (eg, Crohn's disease, ulcerative colitis).
6. Inadequate organ function, evidenced by the following laboratory results:
   a. Absolute neutrophil count (ANC) < 1500 cells/mm^3.
   b. Platelet count < 75,000 cells/mm^3.
   c. Hemoglobin < 9 g/dL.
   d. Total bilirubin greater than the upper limit of normal (ULN; unless the subject has documented Gilbert's syndrome).
   e. Aspartate aminotransferase (AST [SGOT]) or alanine aminotransferase (ALT [SGPT]) > 2.5 × ULN (> 5 × ULN in subjects with liver metastases).
   f. Alkaline phosphatase (ALP) levels > 2.5 × ULN (> 5 × ULN in subjects with liver metastases, or > 10 × ULN in subjects with bone metastases).
   g. Serum creatinine > 2.0 mg/dL or 177 µmol/L.

   Each site should use its own institution's ULN to determine eligibility.
7. Uncontrolled hypertension (systolic > 160 mm Hg and/or diastolic > 110 mm Hg) or clinically significant (ie, active) cardiovascular disease, cerebrovascular accident/stroke, or myocardial infarction within 6 months prior to first study medication; unstable angina; congestive heart failure of New York Heart Association grade 2 or higher; or serious cardiac arrhythmia requiring medication.
8. Current chronic daily treatment (continuous for > 3 months) with systemic corticosteroids (dose equivalent to or greater than 10 mg/day methylprednisolone), excluding inhaled steroids. Short-term steroid use to prevent IV contrast allergic reaction or anaphylaxis in subjects who have known contrast allergies is allowed.
9. Known hypersensitivity to any component of the study medication(s).
10. Subjects taking any medication(s) (herbal or prescribed) known to have an adverse drug reaction with any of the study medications.
11. Known uridine diphosphate-glucuronosyl transferase 1A1 (*UGT1A1*) gene polymorphism resulting in reduced function.

12. Assessed by the Investigator to be unable or unwilling to comply with the requirements of the protocol.
13. Concurrent participation in any interventional clinical trial.
14. Pregnant and nursing women. A negative serum pregnancy test during screening and a negative pregnancy test within 72 hours prior to the first dose must be documented before study therapy is administered to a female subject of child-bearing potential.

Investigational Product, Dosage, and Mode of Administration:

Investigational Products	**Dosage**	**Mode of Administration**
N-803	15 µg/kg on day 8	SC
PD-L1 t-haNK	~2×10^9 cells/dose on days 1 and 8	IV
Approved Products	**Dosage**	**Mode of Administration**
Cyclophosphamide	25 mg BID on days 1–5 and 15–19	PO
Sacituzumab govitecan-hziy	5.0, 7.5, or 10 mg/kg on days 1 and 8	IV

Duration of Treatment:

The length of the treatment is 123 weeks or until unacceptable toxicity, disease progression, symptomatic deterioration indicating treatment failure, or treatment delay greater than 3 weeks for any reason.

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Subjects who discontinue study treatment should remain in the study and continue to be followed for:

- CT or MRI imaging and response assessment every 8 weeks (± 1 week)
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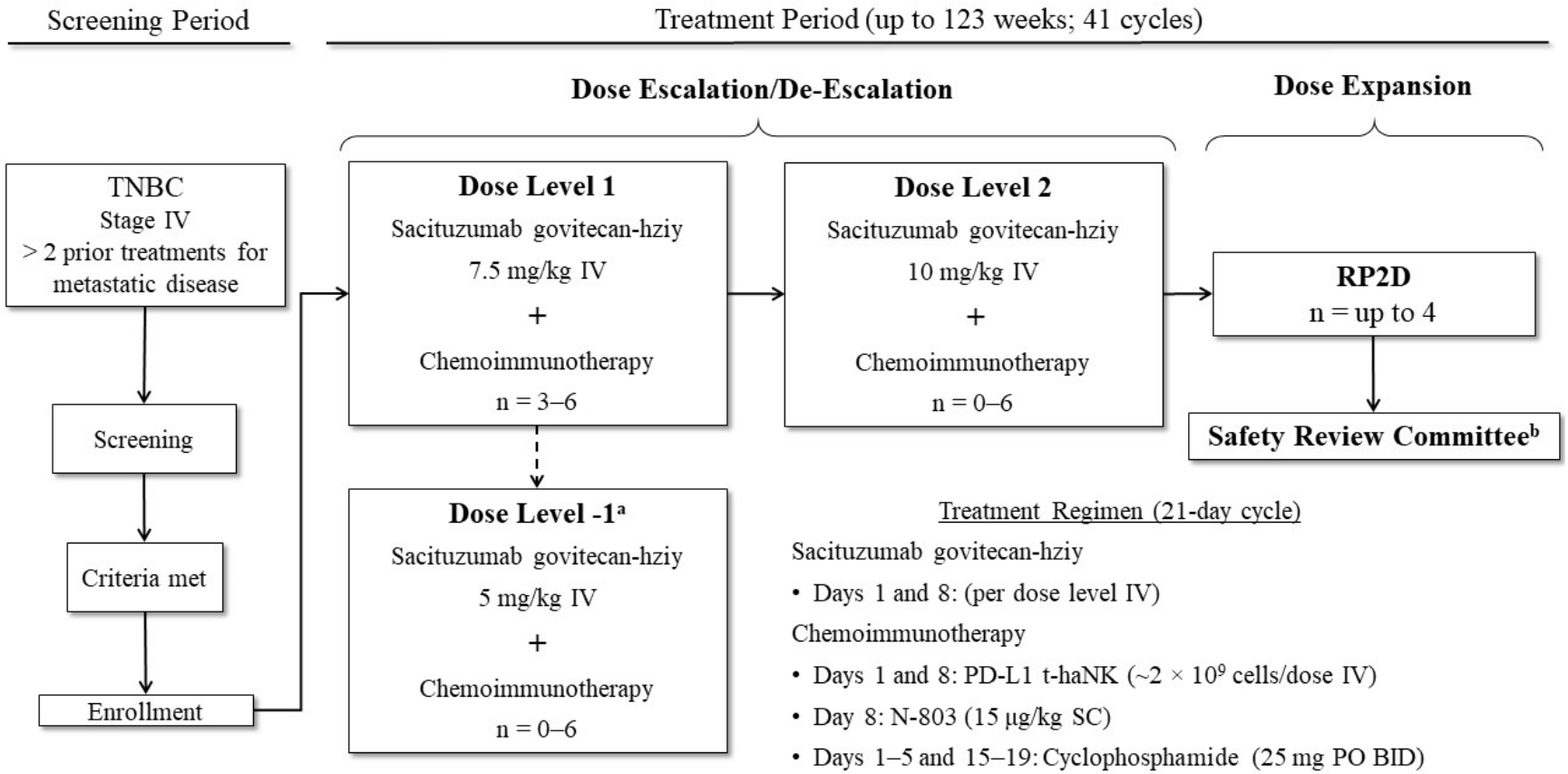

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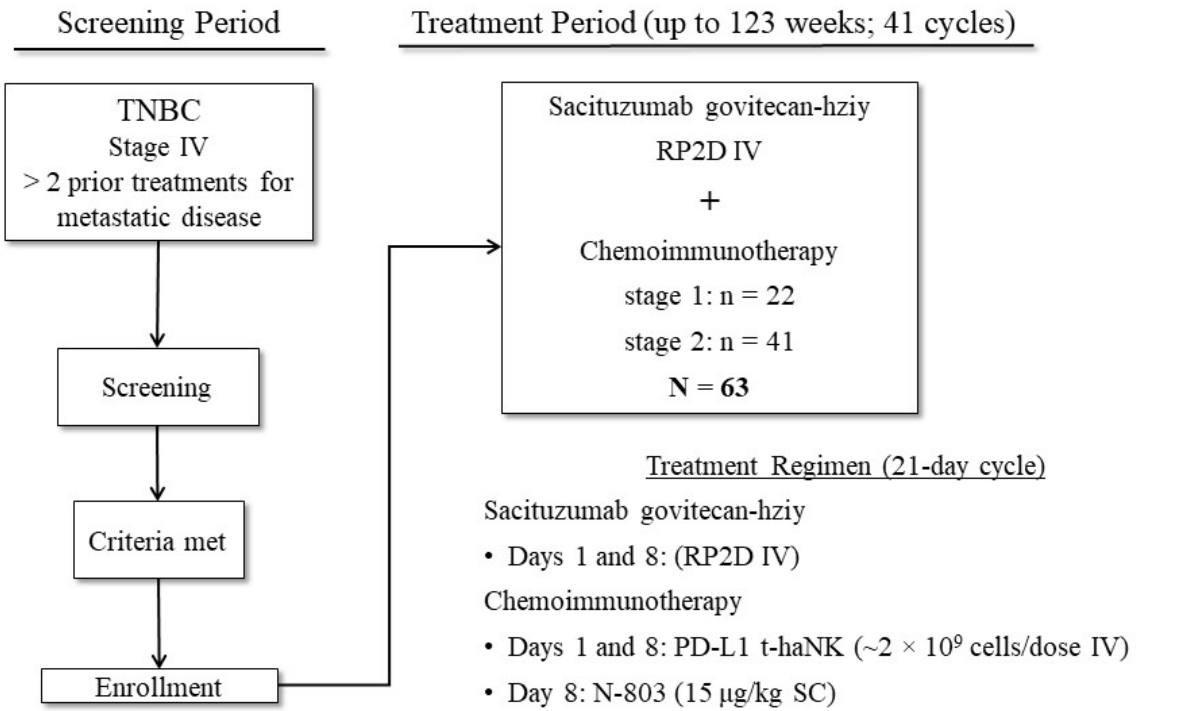
Figure 2: Phase 2 Treatment Schema



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Version Number	4
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This clinical study protocol was subject to critical review and has been approved by ImmunityBio.

Signed: _____ Date: SEPTEMBER 6, 2022

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