# A Phase II Trial of Antibody-Drug Conjugate (IHX-01) in Patients with Locally Advanced/ Recurrent or Metastatic, P-Glycoprotein Over-Expressing, Triple-Negative Breast Cancer (The HOPE Study)

**Protocol Number: IH-LK151118**

**National Clinical Trial Identified Number: NCT12345678**

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**IND Sponsor: ImmunoHuman**

**Version Number: v.0.1**

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# STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council for Harmonisation Good Clinical Practice (ICH GCP) and the United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812)

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

# 1 PROTOCOL SUMMARY

## 1.1 SYNOPSIS

**Title:** A Phase II, Randomized, Multicenter, Pivotal Study of IHX-01 in Patients with Metastatic, P-Glycoprotein Over-Expressing, Triple-Negative Breast Cancer (The HOPE Study)

**Study Description:** This is Phase II, randomized, parallel assignment, open-label trial to evaluate the efficacy, safety and tolerability, pharmacokinetics of IHX-01 in patients with an over-expression of the P-glycoprotein (PGP) and triple-negative breast cancer (TNBC). Glengouldamab cagavant, IHX-01, is a fully-human IgG2 monoclonal antibody-drug conjugate designed to target the internalizable transmembrane marker PGP, which is highly expressed in many breast cancer patients. IHX-01 is linked to the potent antineoplastic agent, diprimanib. The effect of IHX-01 will be compared to treatment with paclitaxel chemotherapy. Eligible patients who enroll in the study will be randomly assigned to receive treatment with IHX-01 or with paclitaxel. For every 3 patients enrolled, 2 will receive IHX-01 and one will receive treatment with paclitaxel.

**Objectives:** *Primary Objective:* To compare Progression-Free Survival (PFS) of IHX-01 compared to paclitaxel in participants with TNBC who are treatment-naïve to paclitaxel and IHX-01 or other monomethyl auristatin E (MMAE) agents.

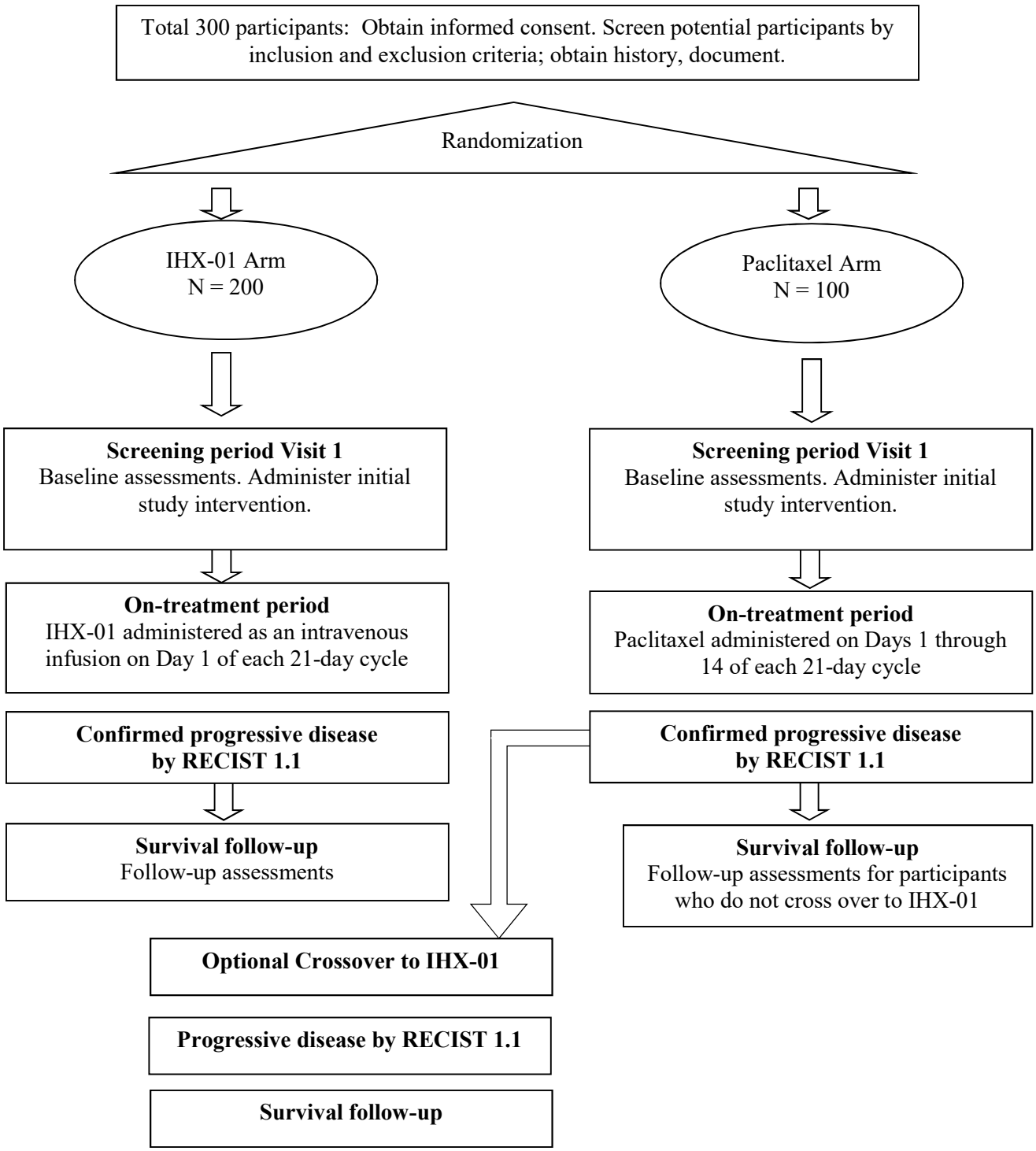
*Secondary Objectives:*

- To evaluate the Objective Response Rate (ORR), the proportion of patients who achieve best overall response of complete or partial response according to RECIST 1.1

| | |
|---|---|
| | • To evaluate the Duration of Response (DOR)<br>• To evaluate Overall Survival (OS)<br>• To evaluate the safety and tolerability profiles, the percentage of patients experiencing one or more Adverse Events (AE) by treatment arm, relationship to study drug, and severity<br>• To determine the concentration of IHX-01 expression |
| **Endpoints:** | *Primary Efficacy Endpoint*: PFS<br>*Secondary Efficacy Endpoints:* ORR, DOR, and OS<br>*Safety Endpoint:* AEs<br>*Pharmacokinetic (PK) Endpoint:* IHX-01 concentration, both total antibody and free MMAE |
| **Study Population:** | The trial will enroll approximately 300 adults of both sexes, 18 years of age and older with TNBC tumor confirmed to express PGP who have received no more than 2 prior chemotherapy treatments. |
| **Phase:** | II |
| **Description of Sites Enrolling Participants:** | Approximately 140 investigational sites will participate in North America and the rest of world. |
| **Description of Study Intervention:** | The investigational drug IHX-01 will be administered intravenously on Day 1 of each 21-day cycle for up to 18 courses in the absence of disease progression or unacceptable toxicity. The active comparator paclitaxel will be administered intravenously on Days 1 through 14 of each 21-day cycle for up to 12 courses in the absence of disease progression or unacceptable toxicity. |
| **Study Duration:** | The trial will require approximately 5 years from the time the first participant signs the informed consent until the last participant's last study-related phone call or visit. |
| **Participant Duration:** | Participants should begin study treatment within 3 days of randomization and will continue on study treatment until progression, unacceptable toxicity, withdrawal of consent, or the study ends, whichever comes first. |

## 1.2 SCHEMA

***Figure 1: Randomized Control Trial Flow Diagram***



## 1.3 SCHEDULE OF ACTIVITIES

Refer to the Study Assessments and Procedures (Section 8) for additional details regarding each assessment

### 1.3.1 SCHEDULE OF ASSESSMENTS FOR IHX-01 ARM

| Time Period/Cycle | Screening [a] | Study Treatment Period | | | | | | EOT | LTFU [b] | SFU [c] |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Cycle 1 | Cycle 2 | Cycle 3 | Cycle 4 | Cycle 5 | Cycle 6 and beyond | | | |
| Window (Days) | Day -7 to -1 | ±3 | ±3 | ±3 | ±3 | ±3 | ±3 | ±7 | ±7 | ±14 |
| **Assessments** | | | | | | | | | | |
| Informed consent | X | | | | | | | | | |
| Demographics | X | | | | | | | | | |
| Medical history | X | | | | | | | | | |
| Randomization | X | | | | | | | | | |
| IHX-011 [d] | | X | X | X | X | X | X | | | |
| Concomitant medication review | X | X | X | X | X | X | X | X | X | |
| Physical exam [e] | X | X | X | X | X | X | X | X | X | |
| Hematology | X | | | | | | | | | |
| Serum chemistry [f] | X | | | | | | | | | |
| Tissue sampling | X | | | | | | | | | |
| Pregnancy test [g] | X | | | | | | | | | |
| PK/Immunogenicity | X | X | X | X | X | X | X | X | X | |
| 12-lead electrocardiogram | X | | | | | | | | | |
| Anatomical imaging (CT and/or MRI) [h] | X [i] | | X | | X | | X [h] | X [j] | X | |
| AE review and evaluation | X | X | X | X | X | X | X | X | X | |
| Survival status | | | | | | | | | | X |

*Abbreviations:* EOT, end of treatment; LTFU, long-term follow-up; SFU, safety follow-up; IHX-011, investigational agent; PK, pharmacokinetic; CT, computed tomography; MRI, magnetic resonance imaging; AE, adverse event.

a Participants on the paclitaxel arm who experience progressive disease per RECIST 1.1 (per central verification) and who meet all the criteria for crossover will have the option to receive IHX-01 in the Crossover Phase. Assessments acquired from the EOT visit will served as the screening data for the Crossover Phase participants.

b Long-term follow-up: Participants must be followed for at least 100 days after last dose of study treatment. Follow-up visit #1 should occur 30 days from the last dose (±7 days) or can be performed on the date of discontinuation if that date is greater than 42 days from the last dose. Follow-up visit #2 should occur approximately 100 days (±7 days) from last dose of study treatment. Both follow-up visits should be conducted in person.

c Survival follow-up, after the start of new anti-cancer therapy contacts will be made by telephone Q8W

d Administered as an intravenous infusion on Day 1 of each 21-day cycle at 2.5 mg/kg with a maximum dose of 200 mg

e Includes height, weight, vital signs, and ECOG performance status. (Height will be measured only at screening.)

f Albumin, alkaline phosphatase, total bilirubin, bicarbonate, BUN, calcium, chloride, creatinine, glucose, LDH, phosphorus, potassium, total protein, AST, ALT, sodium.

g Serum pregnancy test (women of childbearing potential)

h Anatomical imaging (computed tomography [CT] and/or magnetic resonance imaging [MRI]) of the chest, abdomen, and pelvis will be conducted every 6 weeks to 8 weeks (or earlier if clinically indicated), scheduling should not be contingent upon the timing of study therapy administration. Participants with a history of brain metastasis should undergo neuroimaging (MRI without and with gadolinium contrast) every 12 weeks (±7 days) or sooner if clinically indicated.

i Anatomical imaging of adequate diagnostic quality acquired within 28 days prior to randomization will be considered acceptable

| Time Period/Cycle | Screening [a] | Study Treatment Period | | | | | | EOT | LTFU [b] | SFU [c] |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Cycle 1 | Cycle 2 | Cycle 3 | Cycle 4 | Cycle 5 | Cycle 6 and beyond | | | |

j For participants who discontinue study therapy without confirmed progression by site RECIST 1.1, confirmatory tumor imaging should be performed at the time of treatment discontinuation unless previous imaging was obtained within 4 weeks prior to discontinuation

## 1.3.2 SCHEDULE OF ASSESSMENTS FOR PACLITAXEL ARM

| Time Period/Cycle | Screening [a] | Study Treatment Period | | | | | | EOT [a] | LTFU [b] | SFU [c] |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Cycle 1 | Cycle 2 | Cycle 3 | Cycle 4 | Cycle 5 | Cycle 6 and beyond | | | |
| Window (Days) | Day -7 to -1 | ±3 | ±3 | ±3 | ±3 | ±3 | ±3 | ±7 | ±7 | |
| **Assessments** | | | | | | | | | | |
| Informed consent | X | | | | | | | | | |
| Demographics | X | | | | | | | | | |
| Medical history | X | | | | | | | | | |
| Randomization | X | | | | | | | | | |
| Paclitaxel [d] | | X | X | X | X | X | X | | | |
| Concomitant medication review | X | X | X | X | X | X | X | X | X | |
| Physical exam [e] | X | X | X | X | X | X | X | X | X | |
| Hematology | X | | | | | | | | | |
| Serum chemistry [f] | X | | | | | | | | | |
| Tissue sampling | X | | | | | | | | | |
| Pregnancy test [g] | X | | | | | | | | | |
| PK/Immunogenicity | X | X | X | X | X | X | X | X | X | |
| 12-lead electrocardiogram | X | | | | | | | | | |
| Anatomical imaging (CT/MRI) [h] | X [i] | | X | | X | | X [h] | X [j] | X | |
| AE review and evaluation | X | X | X | X | X | X | X | X | X | |
| Survival status | | | | | | | | | | X |

*Abbreviations:* EOT, end of treatment; LTFU, long-term follow-up; SFU, safety follow-up; PK, pharmacokinetic; CT, computed tomography; MRI, magnetic resonance imaging; AE, adverse event.

a Participants on the paclitaxel arm who experience progressive disease per RECIST 1.1 (per central verification) and who meet all the criteria for crossover will have the option to receive IHX-01 in the Crossover Phase.

b Long-term follow-up: Participants must be followed for at least 100 days after last dose of study treatment. Follow-up visit #1 should occur 30 days from the last dose (±7 days) or can be performed on the date of discontinuation if that date is greater than 42 days from the last dose. Follow-up visit #2 should occur approximately 100 days (±7 days) from last dose of study treatment. Both follow-up visits should be conducted in person.

c Survival follow-up, after the start of new anti-cancer therapy contacts will be made by telephone Q8W

d Administered as an intravenous infusion on Day 1 of each 21-day cycle at a dose of 175 mg/m$^2$ administered intravenously over 3 hours

e Includes height, weight, vital signs, and ECOG performance status. (Height will be measured only at screening.)

f Albumin, alkaline phosphatase, total bilirubin, bicarbonate, BUN, calcium, chloride, creatinine, glucose, LDH, phosphorus, potassium, total protein, AST, ALT, sodium.

g Serum pregnancy test (women of childbearing potential)

| Time Period/Cycle | Screening | Study Treatment Period | | | | | | EOT [a] | LTFU [b] | SFU [c] |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Cycle 1 | Cycle 2 | Cycle 3 | Cycle 4 | Cycle 5 | Cycle 6 and beyond | | | |

h Anatomical imaging (computed tomography [CT] and/or magnetic resonance imaging [MRI]) of the chest, abdomen, and pelvis will be conducted every 6 weeks to 8 weeks (or earlier if clinically indicated), scheduling should not be contingent upon the timing of study therapy administration. Participants with a history of brain metastasis should undergo neuroimaging (MRI without and with gadolinium contrast) every 12 weeks (±7 days) or sooner if clinically indicated.

i Anatomical imaging of adequate diagnostic quality acquired within 28 days prior to randomization will be considered acceptable

j For participants who discontinue study therapy without confirmed progression by site RECIST 1.1, confirmatory tumor imaging should be performed at the time of treatment discontinuation unless previous imaging was obtained within 4 weeks prior to discontinuation

# 2 INTRODUCTION

## 2.1 STUDY RATIONALE

Breast cancer is categorized as having a triple-negative phenotype when the tumor is lacking in genes that express estrogen-, progesterone-, and human epidermal growth factor-receptors). TNBC contributes to approximately 12% to 20% of breast cancer occurrences.[1] TNBC presents unique challenges to patients and oncologists with its characteristic resistance to effective treatment by the targeted therapies. Anticipated survival rates for patients with this aggressive diagnosis tend to be lower than for other types of breast cancer. The treatment options available to patients with TNBC are typically limited to surgical intervention and chemotherapy. Aside from the often drastic and routine toxicities associated with chemotherapy, its use is associated with only moderate efficacy in TNBC.[2] Meanwhile, incidents of the disease are increasing worldwide.[3] The need for new options with reduced toxicities and increased efficacy is urgent.

Antibody-drug conjugates (ADCs) use an antibody that selectively delivers a cytotoxic agent “payload” to tumor cell surface receptors. The development of ADCs has established a new method for the delivery of targeted therapies. Although these immune-conjugate methods are still in the early stage, ADCs offer a promising approach that may enhance survival rates.[4] Preliminary data from studies evaluating IHX-01 have achieved efficacy comparable to paclitaxel with potentially less toxicity in patients with advanced and metastatic breast cancer.[5]

The targeted antigen, PGP, has been selected for its expression on target tissue and homogenous expression. The fully-human PGP-specific monoclonal antibody has been selected for its high specificity and affinity to PGP expression in a setting that is lacking in adequate expression of hormone related receptors. The cytoxic payload MMAE was selected for its potency while possessing acceptable metabolic and pharmacokinetic effects when delivered via ADC.

This trial aims to determine the effect of treatment with IHX-01 in participants with metastatic TNBC who have over-expressing PGP and were not previously treated with paclitaxel. The goal is based upon

the hypothesis that treatment with IHX-01 will improve PFS when compared with paclitaxel for the trial participants. The trial's objectives also include the measurement of safety and pharmacokinetics, as well as changes in patient-reported outcomes for quality of life assessments.

## 2.2 BACKGROUND

This section will summarize findings from nonclinical in vivo studies that have potential clinical significance. It will include a summary of relevant clinical research and all history of human use of IHX-01. We will discuss important literature and data, relevant to the trial and which provide background.

## 2.3 RISK/BENEFIT ASSESSMENT

### 2.3.1 KNOWN POTENTIAL RISKS

This section will discuss the known potential risks from previous clinical and nonclinical studies. The IB provide risk information for IHX-01. The respective package insert will provide the risk information paclitaxel.

We will describe here any physical, psychological, social, legal, economic, or any other risks to participants by participating in the study that the Principal Investigator (PI) foresees. The text will address intermediate as well as long-term risks and alternative procedures that have been considered in the trial design.

### 2.3.2 KNOWN POTENTIAL BENEFITS

This section will discuss known potential benefits from either clinical or nonclinical studies. The IB will be the primary source of the benefit information for the investigational therapy. The package insert from paclitaxel will provide benefit information. Relevant published literature will also provide relevant benefit information.

### 2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

This section will include the rationale for the necessity of exposing participants to risks and a summary of the ways that the study is designed to minimize risks to participants.

# 3 OBJECTIVES AND ENDPOINTS

| OBJECTIVES | ENDPOINTS | JUSTIFICATION FOR ENDPOINTS |
|---|---|---|
| *Primary* | | |

| OBJECTIVES | ENDPOINTS | JUSTIFICATION FOR ENDPOINTS |
|---|---|---|
| To compare Progression-Free Survival (PFS) of antibody-drug conjugate glengouldamab cagavant (IHX-01) compared to paclitaxel in participants with triple-negative breast cancer (TNBC) who are treatment-naïve to paclitaxel and IHX-01 or other monomethyl auristatin E (MMAE) agents. | PFS defined as the time from randomization to the earlier of disease progression according to the revised Response Criteria in Solid Tumor (RECIST 1.1) as determined by central review or death due to any cause. | PFS has been justified as a suitable surrogate endpoint for overall survival (OS) to estimate anti-tumor efficacy due to the risk that second- or third-line treatment may confound accurate measurement. Furthermore, PFS will be supported by OS as a secondary endpoint.[6] |
| *Secondary* | | |
| *Efficacy Objectives:*<br>• To evaluate the Objective Response Rate (ORR), the proportion of patients who achieve best overall response of complete or partial response according to RECIST 1.1.<br>• To evaluate the Duration of Response (DOR)<br>• To evaluate OS<br>*Safety Objective:* To evaluate the safety and tolerability profiles, the percentage of patients experiencing one or more adverse events (AEs) by treatment arm, relationship to study drug, and severity<br>*Pharmacokinetic Objective:* To determine the concentration of IHX-01 expression | *Efficacy Endpoints:*<br>• ORR<br>• DOR<br>• OS<br>*Safety Endpoint:* AEs, measuring the percentage of participants who experience 1 or more AEs, to be summarized by treatment arm, relationship to study drug, and severity.<br>*PK Endpoint:* Measurement of IHX-01 concentration for both total antibody and free MMAE | The efficacy endpoints have been chosen as justifiable measures of efficacy to support the primary endpoint and provide further analysis of efficacy in comparison with the selected control for this trial. ORR in previous studies of IHX-01 for various PGP-overexpressing breast cancers was increased for those patients with TNBC.<br>The measurement of AEs will provide meaningful pharmacovigilance data for establishing accurate safety profile and risk management analysis. |

# 4 STUDY DESIGN

## 4.1 OVERALL DESIGN

This is a two-arm, multicenter, international, randomized, open-label, controlled Phase 2 trial of antibody-drug conjugate IHX-01 versus paclitaxel for disease treatment in participants who have advanced/recurrent or metastatic TNBC with an over-expression of PGP. Participants will have at least 1 lesion that is measurable according to RECIST 1.1. From a tissue sample, tumor will have been confirmed to express PGP by a central laboratory. The trial will test the hypothesis that IHX-01 will induce treatment response in TNBC tumors that reflect an immune phenotype based on gene expression

signatures of PGP while having a superior effect as compared with the standard chemotherapy regimen of paclitaxel. Participants will be randomly assigned in a 2:1 ratio to receive the experimental ADC IHX-01 or paclitaxel (control chemotherapy). No interim analysis has been planned. Those participants enrolled in the paclitaxel arm who experience disease progression as confirmed by the central imaging vendor will have the option of participating in a Crossover Phase to receive treatment with IHX-01.

To minimize bias, data that are crucial to efficacy endpoints will be assessed by a central imaging vendor, which will independently determine the dates of progression (a method accepted by regulatory authorities). Since the trial is open-label, images read by central imaging vendor will be blinded to treatment assignment to minimize bias in the assessment of response. Furthermore, the central imaging vendor will confirm radiologic progression.

An external data monitoring committee (eDMC) will serve as the primary reviewer of the treatment-level results and will make recommendations to ImmunoHuman for discontinuation of the study or modification to an executive oversight committee. A separate eDMC charter will detail the eDMC responsibilities and review schedules.

### 4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

The following content will be included in this section: 1) Rationale for the use of paclitaxel as a control. Rationale for the superiority study design. 2) Known or potential problems associated with participants with advanced/recurrent and metastatic TNBC and paclitaxel and IHX-01.

### 4.3 JUSTIFICATION FOR DOSE

This section will provide the justification for the selections for route of administration, planned maximum dosage, and dosing regimen. It will include the starting dose for IHX-01 and paclitaxel.

### 4.4 END OF STUDY DEFINITION

The trial will be considered completed when participants are no longer being examined or the last participant's last study visit has occurred.

## 5 STUDY POPULATION

### 5.1 INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Diagnosed with locally advanced/recurrent or metastatic TNBC
    a. Minimal or no expression of estrogen and progesterone receptors (ER/PR) <10% of cells positive by immunohistochemistry (IHC)

b. ERBB2 staining 0 or 1+ by IHC or copy number <4.0 signals per cell

2. Documented progression of disease based on radiographic, clinical, or pathologic assessment during or subsequent to the last anti-cancer regimen received
3. The presence of 1 or more lesions measurable according to RECIST 1.1
4. Breast cancer tumor confirmed to express PGP. This will be determined by submitting a tissue sample from the advanced (locally advanced/recurrent or metastatic) disease setting to a central laboratory for analysis
5. Received no more than 2 prior chemotherapy treatments for advanced (locally advanced/recurrent or metastatic) breast cancer
6. Prior chemotherapy treatment must have contained an anthracycline (eg, doxorubicin or Doxil) if clinically indicated and a taxane (eg: Taxol)
7. ECOG performance status of 0 to 1
8. Adequate bone marrow and adequate liver and renal function

## 5.2 EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Progression or recurrence of breast cancer during or within 3 months of completion of neoadjuvant or adjuvant chemotherapy
2. Ongoing neuropathy or other conditions due to other chemotherapy or radiation treatment that are moderate (Grade 2) or worse in severity
3. Known brain metastases, unless previously treated and asymptomatic for 2 months and not progressive in size or number for 2 months (participant must be off corticosteroid therapy)
4. Significant cardiovascular disease
5. Previously received capecitabine and discontinued due to progression or intolerance; previously received CDX-OII or other
6. MMAE containing agents
7. Active systemic infection requiring treatment; infection controlled by oral therapy will not be exclusionary
8. Chronic use of systemic corticosteroids

## 5.3 LIFESTYLE CONSIDERATIONS

Restrictions during the study that pertain to lifestyle and/or diet (eg, food and drink restrictions, timing of meals relative to dosing, intake of caffeine, alcohol, or tobacco, or limits on activity) will be described here. ~~There are p~~Prohibited medications and treatments ~~that~~ will also be described here.

## 5.4 SCREENING EXCLUSIONS

Participants who have consented to participate in the clinical trial and who, however, do not meet one or more eligibility criteria required for participation in the trial during the screening procedures, will not be enrolled and randomly assigned to treatment. Re-screening will not be acceptable for this trial.

## 5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

A recruitment and retention plan is detailed within the Manual of Procedures (MOP).

# 6 STUDY INTERVENTION

## 6.1 STUDY INTERVENTION(S) ADMINISTRATION

### 6.1.1 STUDY INTERVENTION DESCRIPTION

#### 6.1.1.1 IHX-01 DESCRIPTION

Glengouldamab cagavant (HDX-01) is an immunoglobulin 2 human antibody targeting transmembrane glycoprotein gene (PGP) conjugated to monomethyl auristatin E (MMAE), a cytotoxic drug that, when released in cancer cells, may lead to tumor cell death. High expression of PGP has been reported in TNBC and correlates with a poor prognosis and increased risk for recurrence.

#### 6.1.1.2 PACLITAXEL DESCRIPTION

Paclitaxel injection is a clear, colorless to slightly yellow viscous solution. It is supplied as a nonaqueous solution intended for dilution with a suitable parenteral fluid prior to intravenous infusion. Paclitaxel is a commercially available therapy and is being used in accordance with the approved labeling.

### 6.1.2 DOSING AND ADMINISTRATION

All study treatments will begin on Day 1 of each cycle after all pre-dose study procedures and assessments have been completed as detailed on the Schedule of Assessment Section 1.3. All study treatments will be administered on an outpatient basis.

#### 6.1.2.1 IHX-01 ADMINISTRATION

IHX-01 will be administered intravenously on Day 1 of each 21-day cycle at a dose of 2.5 milligrams per kilogram (mg/kg), with a maximum dose of 200 mg per cycle.

Sites should make every effort to target infusion timing to be as close to 30 minutes as possible. However, given the variability of infusion pumps from site to site, a window of ±10 minutes is permitted. The Pharmacy Manual contains specific instructions for preparation of the IHX-01 infusion fluid and administration. Every effort should be made to begin the first dose of study treatment on the day of randomization, but if this is not achieved, trial therapy should be initiated no later than 3 days from the date of randomization.

All subsequent cycles of study treatment may be administered up to 3 days before or 3 days after the scheduled Day 1 of each cycle due to administrative reasons guided by the PI's judgment.

#### 6.1.2.2 PACLITAXEL ADMINISTRATION

Paclitaxel will be administered intravenously on Day 1 of each 21-day cycle at a dose of 175 mg/m$^2$ over 3 hours.

Sites should make every effort to target infusion timing to approximate a 3-hour infusion. Variations in infusion schedule per tolerability may be followed per institutional practice. Every effort should be made to begin the first dose of study treatment on the day of randomization, but if this is not achieved, trial therapy should be initiated no later than 3 days from the date of randomization.

All subsequent cycles of study treatment may be administered up to 3 days before or 3 days after the scheduled Day 1 of each cycle due to administrative reasons guided by the PI's judgment.

### 6.2 PREPARATION/HANDLING/STORAGE/ACCOUNTABILITY

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### 6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

### 6.4 STUDY INTERVENTION COMPLIANCE

### 6.5 CONCOMITANT THERAPY

## 7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

## 8 STUDY ASSESSMENTS AND PROCEDURES

## 8.1 EFFICACY ASSESSMENTS

Study evaluations will take place in accordance with the Schedules of Assessments in Section 1.3. Evaluations for efficacy are based on the assessment of diagnostic quality anatomical imaging (contrast enhanced computed tomography [CT] and/or magnetic resonance imaging [MRI]) of the chest, abdomen, and pelvis according to RECIST 1.1. will be acquired by the investigational site and submitted for blinded independent central review conducted by the designated central imaging vendor. Tumor assessment for ongoing study treatment decisions will be conducted by the site radiologist(s) using RECIST 1.1. Treatment decisions will be based upon the investigator's medical assessment and in collaboration with the trial participant; such decisions are not based upon central image review.

### 8.1.1 TUMOR ASSESSMENT SCHEDULE

Baseline (screening) images should be acquired within 28 days prior to randomization and every 6 weeks to 8 weeks, not contingent upon the scheduling of study therapy administration. Additional imaging may also be acquired at unscheduled time points and/or covering additional anatomy if it is intended to may demonstrate tumor response or progression. Images that the investigator believes to be evidence of radiologic progression must be submitted to the imaging vendor for an expedited central review to verify disease progression. Participants with a history of brain metastasis should undergo neuroimaging (MRI without and with gadolinium contrast) every 12 weeks (±7 days) or sooner if clinically indicated.

Tumor assessments should continue until 1) radiologic disease progression per RECIST 1.1 has been verified by the central image vendor, 2) the start of new anti-cancer treatment, 3) withdrawal of consent, 4) treatment discontinuation, or 5) death, whichever occurs first.

### 8.1.2 METHODS OF MEASUREMENT

CT acquired with intravenous and oral iodine-based contrast is the preferred modality to obtain imaging of the participant's chest, abdomen, and pelvis. If the participant has a condition that is contraindicated for iodine-based enhancement, an unenhanced chest scan and MRI acquired using intravenous gadolinium-based enhancement of the abdomen and pelvis. If the participant has a clinical contraindication for both contrast enhanced CT and MRI the investigational site may obtain unenhanced CT for chest, abdomen, and pelvis (and unenhanced brain MRI, if necessary).

*Note:* The same scanner and the same techniques should be across trial duration for each participant.

A technical manual will be provided to the investigational sites that details the required and recommended image acquisition techniques for this trial.

## 8.2 SAFETY AND OTHER ASSESSMENTS

This section will list and describe all study procedures and evaluations to be done as part of the study to monitor safety and support the understanding of the study intervention's safety or that are done for other purposes (eg, screening, eligibility, enrollment).

## 8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

### 8.3.1 DEFINITION OF ADVERSE EVENTS

An adverse event (AE) is defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug-related. An AE (also referred to as an adverse experience) can be any unfavorable and unintended sign (eg, an abnormal laboratory finding), symptom, or disease temporally associated with the use of a drug and does not imply any judgment about causality. An AE can arise with any use of the drug (eg, off-label use, use in combination with another drug) and with any route of administration, formulation, or dose, including an overdose.

### 8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

An adverse event or suspected adverse reaction is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes: Death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical 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 patient or participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include 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.

### 8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

#### 8.3.3.1 SEVERITY OF EVENT

The following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant'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.
- **Severe** – Events interrupt a participant'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."

#### 8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION

All AEs must have their relationship to study intervention assessed by the clinician who examines and evaluates the participant based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

- **Definitely Related** – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to study intervention administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the study intervention (dechallenge) should be clinically plausible. The event must be pharmacologically or phenomenologically definitive, with use of a satisfactory rechallenge procedure if necessary.
- **Probably Related** – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time after administration of the study intervention, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfill this definition.
- **Potentially Related** – There is some evidence to suggest a causal relationship (eg, the event occurred within a reasonable time after administration of the trial medication). However, other factors may have contributed to the event (eg, the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related", as appropriate.
- **Unlikely to be related** – A clinical event, including an abnormal laboratory test result, whose temporal relationship to study intervention administration makes a causal relationship improbable (eg, the event did not occur within a reasonable time after administration of the study intervention) and in which other drugs or chemicals or underlying disease provides plausible explanations (eg, the participant's clinical condition, other concomitant treatments).
- **Not Related** – The AE is completely independent of study intervention administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.

#### 8.3.3.3 EXPECTEDNESS

The PI or designee will be responsible for determining whether an AE is expected or unexpected. 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 intervention.

### 8.3.4 TIME PERIOD/FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

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

All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring

while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

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

Changes in the severity of an AE 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 PI or designee must record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

### 8.3.5 ADVERSE EVENT REPORTING

All AEs that occur after the consent form is signed but before treatment allocation and/or randomization must be reported by the investigator if they cause the participant to be excluded from the trial or are the result of a protocol-specified intervention, including but not limited to washout or discontinuation of usual therapy, diet, placebo treatment or a procedure. From the time of treatment allocation/randomization through 30 days following cessation of treatment, all AEs must be reported by the investigator. Such events will be recorded at each examination on the AE case report forms/worksheets.

### 8.3.6 SERIOUS ADVERSE EVENT REPORTING

ImmunoHuman will notify the Food and Drug Administration (FDA) and all participating investigators in an IND safety report of potential serious risks, from clinical trials or any other source, as soon as possible, but in no case later than 15 calendar days after the sponsor determines that the information qualifies for reporting. In each IND safety report, ImmunoHuman will identify all IND safety reports previously submitted to FDA concerning a similar suspected adverse reaction and must analyze the significance of the suspected adverse reaction in light of previous, similar reports or any other relevant information. ImmunoHuman will report any suspected adverse reaction that is both serious and unexpected. ImmunoHuman will report an adverse event as a suspected adverse reaction only if there is evidence to suggest a causal relationship between the drug and the adverse event.

ImmunoHuman will also notify FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than 7 calendar days after the sponsor's initial receipt of the information.

The study clinician will immediately report to the sponsor any serious adverse event, whether or not considered study intervention related, including those listed in the protocol or investigator brochure and must include an assessment of whether there is a reasonable possibility that the study intervention caused the event. Study endpoints that are serious adverse events (eg, all-cause mortality) must be reported in accordance with the protocol unless there is evidence suggesting a causal relationship between the study

intervention and the event (eg, death from anaphylaxis). In that case, the investigator must immediately report the event to the sponsor.

All SAEs will be followed until satisfactory resolution or until the site investigator deems the event to be chronic or the participant is stable. Other supporting documentation of the event may be requested by the Data Coordinating Center (DCC)/study sponsor and should be provided as soon as possible.

The study sponsor will be responsible for notifying the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible, but in no case later than 7 calendar days after the sponsor's initial receipt of the information. In addition, ImmunoHuman will notify FDA and all participating investigators in an Investigational New Drug (IND) safety report of potential serious risks, from clinical trials or any other source, as soon as possible, but in no case later than 15 calendar days after the sponsor determines that the information qualifies for reporting.

### 8.3.7 REPORTING EVENTS TO PARTICIPANTS

Participants will be informed about AEs, SAEs, and study-related results on an individual level. Incidental findings associated with study procedures will also be reported to the individuals.

### 8.3.8 REPORTING OF PREGNANCY

The investigator or designee will instruct the participant and/or legal caregiver to call immediately if pregnancy is known or suspected.

## 8.4 UNANTICIPATED PROBLEMS

### 8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets *all* of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research (“possibly related” means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

### 8.4.2 UNANTICIPATED PROBLEM REPORTING

The investigator will report unanticipated problems (UPs) to the reviewing IRB and to the Data Coordinating Center (DCC)/lead PI. The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are SAEs will be reported to the IRB and to the DCC/study sponsor within <insert timeline in accordance with policy> of the investigator becoming aware of the event.
- Any other UP will be reported to the IRB and to the DCC/study sponsor within <insert timeline in accordance with policy> of the investigator becoming aware of the problem.
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and the OHRP within <insert timeline in accordance with policy> of the IRB's receipt of the report of the problem from the investigator.

### 8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

ImmunoHuman will inform participants about UPs on an individual level.

# 9 STATISTICAL CONSIDERATIONS

(Currently being developed by the IH statistical group for the SAP.)

# 10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

## 10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

### 10.1.1 INFORMED CONSENT PROCESS

In obtaining and documenting informed consent, the investigator must comply with applicable regulatory requirements (eg, 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56) and should adhere to ICH GCP. Prior to the beginning of the trial, the investigator should have the IRB's written approval for the protocol

and the written informed consent form(s) and any other written information to be provided to the participants.

#### 10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study intervention. The following consent materials are submitted with this protocol <insert list>.

#### 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. Consent forms will be IRB-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants 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 participants 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 participant undergoes any study-specific procedures. The rights and welfare of the participants 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.

### 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 participants, investigator, funding agency, the IND or Investigational Device Exemption (IDE) sponsor and regulatory authorities>. If the study is prematurely terminated or suspended, the PI will promptly inform study participants, the IRB, and sponsor and will provide the reason(s) for the termination or suspension. Study participants 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 participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable

- Determination that the primary endpoint has been met
- Determination of futility

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the sponsor, IRB and/or FDA.

### 10.1.3 CONFIDENTIALITY AND PRIVACY

This section will describe protections for maintaining confidentiality of participant data, including, but not limited to forms, records and samples and participant privacy.

### 10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

This section will include the provisions for consent and the options that are available for the participant to agree to the future use of his/her specimens, images, audio or video recordings. In addition to the clinical site, specimens and other data will be maintained for 15 years in a secure long-term storage facility adherent with ISOXXOXX. Each site's IRB will review any future studies, and protections of confidentiality for any future studies with the stored specimens or data (eg, specimens will be coded, bar-coded, de-identified, identifying information will be redacted from audio recording transcripts). Genetic testing will be performed.

### 10.1.5 KEY ROLES AND STUDY GOVERNANCE

| **Principal Investigator** | **Medical Monitor** |
|---|---|
| *Name, degree, title* | *Name, degree, title* |
| *Institution Name* | *Institution Name* |
| *Address* | *Address* |
| *Phone Number* | *Phone Number* |
| *Email* | *Email* |

### 10.1.6 SAFETY OVERSIGHT

Safety oversight will be under the direction of a Data and Safety Monitoring Board (DSMB) composed of individuals with the appropriate expertise, including <list expertise>. Members of the DSMB should be independent from the study conduct and free of conflict of interest, or measures should be in place to minimize perceived conflict of interest. The DSMB will meet at least semiannually to assess safety and efficacy data on each arm of the study. The DSMB will operate under the rules of an approved charter that will be written and reviewed at the organizational meeting of the DSMB. At this time, each data element that the DSMB needs to assess will be clearly defined. The DSMB will provide its input to ImmunoHuman.

### 10.1.7 CLINICAL MONITORING

Clinical site monitoring is conducted to ensure that the rights and well-being of trial participants are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with ICH GCP, and with applicable regulatory requirements.

- Monitoring for this study will be performed by <insert text>.
- <Insert brief description of type of monitoring (eg, on-site, centralized), frequency (eg, early, for initial assessment and training versus throughout the study), and extent (eg, comprehensive (100% data verification) versus targeted or random review of certain data (less than 100% data verification or targeted data verification of endpoint, safety and other key data variables)>.
- <Insert text> will be provided copies of monitoring reports within <x> days of visit.
- Details of clinical site monitoring are documented in a Clinical Monitoring Plan (CMP). The CMP describes in detail who will conduct the monitoring, at what frequency monitoring will be done, at what level of detail monitoring will be performed, and the distribution of monitoring reports.
- Independent audits <will/will not> be conducted by <insert text> to ensure monitoring practices are performed consistently across all participating sites and that monitors are following the CMP.

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

Following written Standard Operating Procedures (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, Good Laboratory Practices [GLP], Good Manufacturing Practices [GMP]).

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 the sponsor, and inspection by local and regulatory authorities.

### 10.1.8 DATA HANDLING AND RECORD KEEPING

#### 10.1.8.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

Hardcopies of the study visit worksheets will be provided for use as source document worksheets for recording data for each participant enrolled in the study. Data recorded in the electronic CRF

(eCRF) derived from source documents should be consistent with the data recorded on the source documents.

Clinical data (including AEs, concomitant medications, and expected adverse reactions data) and clinical laboratory data will be entered into IVRS, a 21 CFR Part 11-compliant data capture system provided by the selected contract research organization for data management. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

#### 10.1.8.2 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 intervention. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

### 10.1.9 PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical trial protocol, ICH GCP, or MOP requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

These practices are consistent with ICH GCP according to the following section:

- §4.5 Compliance with Protocol, sub-sections 4.5.1, 4.5.2, and 4.5.3
- §5.1 Quality Assurance and QC, sub-section 5.1.1
- §5.20 Noncompliance, sub-sections 5.20.1, and 5.20.2.

It is the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 2 working days of identification of the protocol deviation, or within 2 working days of the scheduled protocol-required activity. All deviations must be addressed in study source documents, reported to ImmunoHuman. Protocol deviations must be sent to the reviewing IRB per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

### 10.1.10 PUBLICATION AND DATA SHARING POLICY

ImmunoHuman believes that the public has access to the published results its research. ImmunoHuman submits final peer-reviewed journal manuscripts to the digital archive PubMed Central upon acceptance for publication.

ImmunoHuman will register this trial and submits its results to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers 15 years after the completion of the primary endpoint by contacting ImmunoHuman.

### 10.1.11 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, 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 trial.

## 10.2 ABBREVIATIONS

| | |
|---|---|
| ADC | Antibody-drug conjugates |
| AE | Adverse Event |
| CFR | Code of Federal Regulations |
| CMP | Clinical Monitoring Plan |
| CRF | Case report Form |
| CT | Computed tomography |
| CTCAE | Common Terminology Criteria for Adverse Events |
| DSMB | Data Safety Monitoring Board |
| eCRF | Electronic CRF |
| EOT | End of Treatment |
| FDA | Food and Drug Administration |
| IB | Investigator's Brochure |
| ICH | International Conference on Harmonisation |
| IDE | Investigational Device Exemption |
| IND | Investigational New Drug Application |
| MOP | Manual of Procedures |
| MRI | Magnetic resonance imaging |
| NCI | National Cancer Institue |
| OHRP | Office for Human Research Protections |
| ORR | Objective Response Rate |
| OS | Overall Survival |
| PFS | Progression-Free Survival |
| PGP | P-glycoprotein |
| PI | Principal Investigator |
| PK | Pharmacokinetic |

| | |
|---|---|
| QC | Quality Control |
| SAE | Serious Adverse Event |
| SAP | Statistical Analysis Plan |
| SOC | System Organ Class |
| SOP | Standard Operating Procedure |
| UP | Unanticipated Problem |
| US | United States |

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