Patient Information Sheet and Informed Consent Form

PATIENT INFORMATION SHEET

Name of the Study: An Open-Label, Randomized, Multicenter Phase 3 Clinical Trial of SHR-A1811 Versus Investigator-selected Chemotherapy for Platinum-Resistant Relapsed Epithelial Ovarian, Fallopian Tube, Or Primary Peritoneal Cancer

Study No.: GSP 402-301 (SHR-A1811-315_Extension)

Introduction

We are inviting you to take part in the above-mentioned clinical study that is being carried out by this clinic/centre. The Sponsor of the study is a pharmaceutical company called Glenmark Specialty SA. (Glenmark Specialty SA. has authorized Glenmark Pharmaceuticals Ltd. to conduct the study on its behalf in India). The **INSTITUTIONAL REVIEW BOARD** has reviewed the study protocol and has granted approval for the conduct of the study at this center.

In this study this informed consent form will help you to decide whether you should take part. This document is intended to explain the study purposes, procedures, possible risks and benefits, possible discomforts from participation in the study, and the precautions. In addition, this document is also intended to explain other alternative treatment regimens (if you choose not to take part in this study) and your right to withdraw from the study at any time.

Before you decide on whether to take part in this study, it is important for you to understand why the research is being done and what it involves. Kindly take time to read the below mentioned information carefully and discuss it with friends, relatives and your family doctor if you wish. Ask us if anything is not clear or if you would like more information. Whether or not you wish to take part, take adequate time to decide. Thank you for reading this.

What is the purpose of this study?

The purpose of this study is to help answer the below mentioned research question(s):

- To evaluate if trastuzumab rezetecan injection (Code name: SHR-A1811) can help patients with human epidermal growth factor receptor 2 (HER2)-expressing platinum resistant recurrent ovarian cancer (including epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer) in comparison to investigator's choice of chemotherapy.
- To evaluate safety (adverse event profile) of trastuzumab rezetecan in the treatment of patients with HER2-expressing platinum resistant ovarian cancer.
- To assess concentration of the study drug and anti-drug antibody (ADA/Nab – these are proteins that the body makes against the study drug trastuzumab rezetecan) in the patients who are administered with trastuzumab rezetecan.

About 70 patients, who have HER2-expressing platinum resistant advanced/recurrent ovarian cancer, will take part in this study GSP 402-301 (SHR-A1811-315_Extension). This study will be conducted in multiple countries including India, Australia and/or other countries. About 35-50

patients from India will take part in the study. In the main cohort (SHR-A1811-315), about 350 patients are planned to take part in China.

The study requires that you complete the scheduled visits to the study site/clinic during your participation in the study. Your participation in this study could last for about a maximum 16 months (about 1.5 years).

Your study doctor will be running the study at this site. The Sponsor will pay the study doctor and/or the institution a fee for his/her help in running this study.

Why have I been chosen?

You have been approached for the below mentioned reasons:

- You have been diagnosed with ovarian cancer (including epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer).
- Your cancer is not responding to platinum chemotherapy.
- Your study doctor will confirm if you qualify for participation in the study after assessment of all eligible criteria according to the approved study protocol.

Do I have to take part?

It is up to you whether or not you take part; it's entirely voluntary. Only when you feel satisfied that you have been given enough information about the study and would like to take part will you be asked to sign the consent form attached. You will be given a copy of the patient information sheet and the signed informed consent form to keep. Even if you take part, you are still free to withdraw at any time and without giving a reason. If you withdraw from the study you may be requested to undergo an end-of-study examination, below mentioned which no new information will be collected from you and you have the right to request that any of your previously retained samples be destroyed to prevent future analyses. Data that have already been collected on safety and efficacy will not be deleted and cannot be withdrawn due to legislation on the use of data from clinical studies. Withdrawing from the study will not affect the standard of care you receive.

How long will the study last?

The study will run for a maximum of about 16 months (~1.5 years) for each patient and will involve multiple visits (up to about 20 visits) to the study doctor/clinic.

What will happen to me if I take part?

This study participation includes three parts: Screening period, Treatment period, and Follow-up period. Each part of the study is described below.

Screening Period:

If you agree to take part in this study and have signed this informed consent form, you will undergo the below mentioned assessments at the hospital before enrolment:

- Medical history, including your tumor history and other past medical history (clinical/pathological diagnosis, time of diagnosis, clinical/pathological stage, HER2 expression/mutation status, and main oncogenic gene mutation; whether you have

undergone surgery, neoadjuvant therapy, adjuvant therapy, radiotherapy, local therapy, or palliative systemic therapy, time of progression, basis for diagnosis progression), smoking and drinking history, drug allergy history (drug name, allergy symptoms), concomitant diseases and treatments (disease name, concomitant medication name, dose, and method of administration).

- Physical examination, including your general condition such as height and weight, vital signs such as blood pressure and pulse, and other routine physical examinations.
- Physical condition (ECOG performance status), which will be evaluated by your doctor.
- Your urine sample (urinalysis test), stool sample (routine stool test), and blood sample will be collected to check your cell count (routine blood test), organ function (blood biochemistry test), coagulation test, virological test (hepatitis B, hepatitis C, and HIV tests), tumor marker (CA-125) test, cardiac enzyme profile test, and thyroid function test. The blood samples of this study will be collected by venipuncture in the arm.
- An electrocardiogram (ECG) and an echocardiogram will be performed, which record the electrical activity and function of your heart. B-mode ultrasound of deep veins in both lower limbs will be performed to check for presence of blood clot in the lower limb veins.
- If you are a woman of childbearing age, blood will be drawn for a pregnancy test. Your pregnancy test must be negative, OR the investigator must judge that an HCG positive result is clinically insignificant and pregnancy is ruled out, in order to take part in this study.
- Imaging examinations include chest, abdominal, and pelvic examinations, and neck examinations, cranial examinations, bone scans, etc. may be added based on clinical needs. A contrast-enhanced CT (computed tomography) or contrast-enhanced MRI (magnetic resonance imaging) scan will be preferred, as determined by your study doctor based on your physical condition. A contrast agent will be injected into your vein before the CT/MRI scan to make the lesions more visible, unless you are allergic to the contrast agent.
    - CT scan: a scan in which the X-ray penetrates your body to generate a series of images when you lie on a narrow bed inside a machine (an imaging examination that locates and measures the size of your tumor).
    - MRI scan: a scan in which a series of images are obtained when you lie on a narrow bed inside a machine that produces magnetic force (an imaging examination that locates and measures the size of your tumor).
- Your tumor tissue pathology specimens (6 unstained FFPE sections) will be collected during the screening period, and they will be analyzed, stored, and processed for HER2 expression testing in this study only.
- Kindly consult your study doctor at any time if you require more details on the inclusion criteria or have any questions about the inclusion criteria.

After evaluating all the above test results, you may fail to meet any one or multiple inclusion criteria and thus will not be able to take part in this study. Although, there are other alternative treatments

available to treat your disease, including other drugs or symptomatic treatments. Your study doctor will discuss the best other treatment options with you.

Treatment Period:

If you are found eligible for enrolment after all the screening examinations, and you agree to continue to take part in this study, your doctor will treat you according to the study protocol and perform various clinical examinations on you regularly.

- **Cycle 1**

  - ✓ Cycle 1 Day 1 (C1D1): Pre-dose physical examination, vital signs, body weight measurement, ECOG PS score, EQ-5D-5L and FOSI scale, 12-lead ECG, dosing, and PK and immunogenicity sample collection (only for subjects receiving trastuzumab rezetecan). A PK blood sample of approximately 5 mL and an immunogenicity blood sample of approximately 4 mL will be collected before dosing, and a PK blood sample of approximately 2 mL will be collected within 5 minutes after the completion of dosing (the completion of line flushing).
  - ✓ C1D8: Vital signs, routine blood test, blood biochemistry test (applicable to subjects receiving trastuzumab rezetecan, paclitaxel, topotecan, or gemcitabine therapy).
  - ✓ C1D15: Vital signs, routine blood test, blood biochemistry test (applicable to subjects receiving trastuzumab rezetecan, paclitaxel, topotecan, or gemcitabine therapy).
  - ✓ C1D22: Vital signs, routine blood test, blood biochemistry test (applicable to subjects receiving paclitaxel therapy).

  At the same time, your other recent treatments and medications will also be collected. You will be asked some questions about your physical condition. If you have any physical discomfort, kindly inform the study doctor about the relevant information, including the time of occurrence, duration, symptoms, etc.

- **Cycle 2 and beyond**

  - ✓ C2D1 (C3D1...end of treatment): Routine blood test, blood biochemistry test, routine urine test, coagulation test, pregnancy test, pre-dose physical examination, vital signs, weight measurement, ECOG PS score, 12-lead ECG, and dosing.
  - ✓ C2D8 (C3D8...and so on): Vital signs, routine blood test, blood biochemistry test (applicable to subjects receiving trastuzumab rezetecan, paclitaxel, topotecan, or gemcitabine therapy).
  - ✓ C2D15 (C3D15...and so on): Vital signs, routine blood test, blood biochemistry test (applicable to subjects receiving trastuzumab rezetecan, paclitaxel, topotecan, or gemcitabine therapy).
  - ✓ C2D22 (C3D22...and so on): Vital signs, routine blood test, blood biochemistry test (applicable to subjects receiving paclitaxel therapy).

- ✓ Thyroid function, cardiac enzyme profile test, and echocardiogram will be performed once every 4 cycles starting from Cycle 5 (e.g. C5D1, C9D1, C13D1...and so on).
- ✓ Routine stool examination will be performed as clinically indicated.
- ✓ EQ-5D-5L and FOSI scales (once every 2 cycles such as C3D1, C5D1... and so on).
- ✓ PK and immunogenicity sample collection (applicable for subjects receiving trastuzumab rezetecan):
  - About 3 mL of blood will be collected each time to test the PK concentration of trastuzumab rezetecan within 2 h before dosing on C2D1 and C6D1; within 2 h before dosing every 9 cycles thereafter; and at the end of treatment or withdrawal.
  - About 2 mL of blood will be collected each time to test the PK concentration of SHR169265 (free toxin) within 2 h before dosing on C2D1 and C6D1; within 2 h before dosing every 9 cycles thereafter; and at the end treatment or withdrawal.
  - About 4 mL of blood will be collected each time for anti-drug antibody (ADA) and NAb analysis within 2 h before dosing on C6D1 and every 9 cycles thereafter; at the end of treatment or withdrawal; and at 40 days (+7 d) after the last dose of study drug.
- ✓ Tumor marker (CA-125) testing: It will be performed simultaneously with each imaging examination, and unscheduled tests may be performed when deemed necessary by the investigator.
- ✓ Imaging examinations: During the treatment period, imaging examinations should be performed under the same conditions as the baseline examination (slice thickness of the scan, use of contrast agent, etc.). Tumor imaging evaluation will be performed once every 6 weeks ± 7 days during the first 36 weeks after the first dose, and then once every 12 weeks ± 7 days. The imaging evaluation cycle will be determined after the start of the study treatment and is not affected by drug suspension. The investigator may add examination sites and unscheduled examinations as appropriate according to the actual situation of the patient. The allowable time window for tumor imaging examination is ± 7 days. Subjects initially assessed as CR or PR must be reassessed 4 weeks later (may be at the next scheduled efficacy assessment according to the protocol) to confirm the response; this confirmed tumor assessment should not change the previously established fixed assessment time points.

PK blood samples will be used to detect the plasma concentration of trastuzumab rezetecan and the free payload (i.e., the free toxin SHR169265) in the trastuzumab rezetecan. Immunogenicity blood samples will be used for ADA and neutralizing antibody (NAb) testing. The blood samples will not be used in studies other than this study.

At the same time, your other recent treatments and medication details will also be collected. You will be asked some questions about your physical condition. If you have any physical discomfort,

kindly inform the study doctor about the relevant information, including the time of occurrence, duration, symptoms, etc.

Allocation to study treatment group:

You will be randomly allocated into one of the below mentioned two groups in a 1:1 ratio if you are eligible for participation in the study.

- Experimental group: Trastuzumab rezetecan (4.8 mg/kg)
- Control group: Investigator's choice of chemotherapy (paclitaxel or doxorubicin liposome or topotecan or gemcitabine)

Dosing in experimental group:

Trastuzumab rezetecan will be administered via intravenous infusion on Day 1 of each treatment cycle at a dose of 4.8 mg/kg once, with every 3 weeks as one treatment cycle. For treatment discontinuation, treatment will continue until the occurrence of any event that meets the protocol-defined criteria.

Dosing in control group:

The investigator may administer conditioning drugs prior to dosing based on the package insert or the standard of care at the study site. The investigator will select one of the below mentioned treatment regimens (to be determined prior to enrolment) and continue treatment until the occurrence of any event that meets the protocol-defined criteria for treatment discontinuation:

- Doxorubicin liposome: Administered via intravenous infusion on D1 of each cycle at a dose of 40 mg/m^2, with every 4 weeks as one treatment cycle.
- Paclitaxel: Administered via intravenous infusion on D1, D8, D15, and D22 of each cycle at a dose of 80 mg/m^2, with every 4 weeks as one treatment cycle.
- Topotecan: Administered via intravenous infusion on D1, D8, and D15 of each cycle at a dose of 4 mg/m^2 per day, with every 4 weeks as one treatment cycle.
- Gemcitabine: Administered via intravenous infusion on D1 and D8 of each cycle at a dose of 1,000 mg/m^2 per day, with every 3 weeks as one treatment cycle.

After completion of the entire study treatment or discontinuation of treatment, we need your cooperation in continuing follow-up visits to monitor the side effects or benefits you may experience after receiving the study treatment.

Follow-up Period:

Safety follow-up

After you finish treatment, you will enter the safety follow-up period. The safety follow-up period is 40 days (+7 days) after the last dose. Assessments include physical examination, vital signs, ECOG PS score, EQ 5D-5L, FOSI, routine blood test, blood biochemistry test, urinalysis, 12-lead ECG, and adverse event follow-up. Concomitant medications/treatments of subjects will also be recorded. The study doctor will continue to assess changes in your health and medications,

including any side effect(s) you may experience, and also record your new anti-tumor therapy and survival status.

Survival follow-up

After the safety follow-up is completed, the study doctor will initiate survival follow-up for you. During this period you do not need to visit the study site. The study doctor will contact you by telephone until the survival follow-up endpoint. The study doctor will contact you every 60 days ± 7 days. Kindly inform the study doctor of the treatment(s) you are receiving. Kindly give the study site with as many contact details for you and your family as possible to ensure that the study doctor can reach you. If you receive medical treatment at a healthcare institution other than the study site, the study doctor may also contact the doctors there to gather information about your survival follow-up and treatment.

What do I have to do? (Responsibilities)

- You must visit the hospital at the follow-up time points as scheduled with your study doctor. Your prompt attendance at follow-up visits is very important, because your doctor will determine whether the treatment you receive is truly effective.
- By your study doctor you must take and store the drugs as directed.
- If you go to other hospitals for treatment or the pharmacy to purchase other therapeutic drugs during the trial, you must truthfully explain it to the investigator, and give a photocopy of the medical records from other hospitals to the investigator. Otherwise, your continued participation in this clinical trial will be affected.
- If you need to visit other departments during the trial, kindly explain it to the study doctor and make necessary records according to the actual situation.
- During the study, the doctor will ask about the drugs and treatments you are currently receiving. Kindly describe your health experiences and the doctor will discuss the possible side effects with you.
- During your participation in this study, you are not allowed to take part in other clinical trials.
- If you are going to take part in another clinical study, you must inform the doctor in charge of that study that you are currently participating in this study. To discuss other necessary treatment measures, you should ask that doctor to contact your study doctor.
- If you have other concomitant diseases and need to continue taking the corresponding drugs, kindly inform your study doctor in a timely manner. If you are using any “non-prescription drugs,” herbal medicines or natural therapies, it is very important that you inform your doctor.
- You need to inform your study doctor of all medical treatments you receive during this study (e.g., elective surgery or radiotherapy).

- Other than yourself, we hope that at least one of your family members is aware of the nature of the clinical study in which you will be participating and is able to understand your condition, and also be able to give feedback on your health status to the doctor at subsequent follow-up visits. Your family members should notify your study doctor promptly when you experience severe discomfort (including discomfort that requires hospitalization and treatment).
- If there are changes to your address, telephone number or other contact information, kindly inform your study doctor promptly.
- During the survival follow-up period after the end of the study treatment, you or your family needs to inform the study doctor of the treatments you receive during the survival follow-up period and the survival status and give corresponding supporting documents (including the death certificate, etc.).

What is the drug being tested?

The name of the study drug is trastuzumab rezetecan – this is an antibody-drug conjugate and consists of recombinant humanized antibody (known as anti-HER2 IgG1 monoclonal antibody) conjugated to anti-cancer small molecule (toxin SHR169265 that kills tumor cells by inhibiting DNA topoisomerase I). Trastuzumab rezetecan can specifically bind to HER2 on the surface of tumor cells. Subsequently, the conjugate is internalized into the cells and releases the free toxin SHR169265, which can inhibit the activity of DNA topoisomerase I and induce killing of tumor cells. After being released within tumor cells, the toxin can permeate surrounding cells and exert killing effect on HER2-negative tumor cells (this is known known as bystander effect).

Trastuzumab rezetecan is being developed for the treatment of advanced solid tumors with HER2 expression or mutation. It is not currently approved for use in patients with HER2-expressing recurrent platinum-resistant ovarian cancer; therefore, it is still in the research stage for treatment of this type of ovarian cancer.

What are the benefits of the study?

You may not benefit from taking part in this study, and you may experience side effects from the drug, but you may also benefit by experiencing disease remission from taking the study drug. If the disease progresses or the side effects of the drug are unbearable, or if new scientific developments indicate that this study is no longer the best option for you, the study doctor will discuss other alternative treatment regimens with you. Your treatment outcome may serve as a reference for other patients with similar diseases, so that they have the opportunity to obtain new treatment options. Thank you for your contribution to the treatment options that other patients may obtain.

What are the alternatives for treatment?

Your participation or non-participation in this clinical study is entirely up to you. Participation in the study is not the only option for treatment. If you do not take part in this clinical study, your doctor will recommend appropriate treatment methods based on your tumor type and actual physical condition. The possible treatment options include:

- Chemotherapy

- Radiotherapy
- Targeted therapy
- Best supportive care to help relieve your pain, fatigue, or other symptoms
- Other clinical studies in advanced gynecological malignancies or other treatments as deemed appropriate by the doctor.

What are the side effects of the treatment received during the study?

Any clinical study poses a certain risk. You may receive a treatment that does not work for you or has limited efficacy, and your condition may worsen or not improve.

The possible side effects and risks that may occur throughout the study (including the screening period, treatment period, and follow-up period) include but are not limited to the below mentioned items. Any study drug may also cause other unforeseen and even serious side effects.

Observed adverse reactions of trastuzumab rezetecan:

In cancer patients receiving trastuzumab rezetean monotherapy, commonly reported (incidence ≥ 10%) drug-related adverse reactions, some of which may also be severe, included the below mentioned:

- Hematological system: Blood cell count decrease (e.g., neutrophil, white blood cell, platelet, lymphocyte), anemia;
- Gastrointestinal system: Nausea, vomiting, diarrhea, stomatitis, constipation;
- Liver function: Elevated liver enzymes in blood, elevated blood bilirubin;
- Metabolism and nutrition: Decreased appetite, hypoalbuminemia, weight loss hypertriglyceridemia, hyperglycemia, hyponatremia, hyperuricemia, hypokalemia, hypocalcemia;
- Others: Alopecia (hair loss), proteinuria (protein in urine), fatigue, elevated blood lactate dehydrogenase, urinary tract infection, general weakness.

Among the above adverse reactions, common (incidence ≥10%) Grade 3 or higher adverse reactions include: Decreased neutrophil count, decreased white blood cell count, anemia, and decreased platelet, and most of the remaining cases were Grade 1 – 2. Most adverse reactions could be controlled with or without medical intervention.

In subjects who receive trastuzumab rezetecan therapy in the clinical studies, in addition to the above adverse reactions, other serious events with a lower incidence may occur. Suspected serious adverse reactions that occurred in ≥ 2 subjects also include: interstitial lung disease, pneumonitis, myelosuppression (bone marrow suppression), febrile neutropenia (low counts of white blood cells with fever), pneumonia, gastroenteritis, functional gastrointestinal disorders, epistaxis (nose bleed), infusion-related reactions, and allergic reactions.

During treatment with trastuzumab rezetecan, vigilance should be exercised against the occurrence of hematological toxicities (especially neutropenia [low count of white blood cells], because there have been reports of severe cases of infection caused by neutropenia), gastrointestinal toxicity,

interstitial lung disease/non-infectious pneumonitis (which may manifest as dry cough, shortness of breath, dyspnea, or asthenia and fever, and severe case reports of interstitial lung disease have been made), and left ventricular dysfunction (mainly decreased left ventricular ejection fraction). These adverse reactions can typically be detected in time through regular follow-up and examination. If you experience any discomfort during the treatment period, kindly be sure to inform your study doctor in a timely manner, and he/she will make a judgment and give medical treatment.

Based on the mode of action of trastuzumab rezetecan, itself and the adverse reactions of same-class drugs, attention also should be paid to the below mentioned adverse reactions during participation in the study: abdominal pain, abdominal distension, organizing pneumonia, QT prolongation in electrocardiogram, pain in joints, musculoskeletal pain, hot flashes, headache, numbness, dry eyes, dry skin, etc.

Trastuzumab rezetecan is still under clinical study, and currently there are relatively limited data on the safety of it in human body. The above adverse reactions may not necessarily occur to you, but other unknown side effects that have not been reported previously may also occur. Therefore, if you experience any discomfort or new symptoms, even if you are not sure if they are drug-induced or not, kindly notify your study doctor in a timely manner so that he/she may make a judgment and give medical treatment.

Adverse reactions of doxorubicin hydrochloride liposome injection:

According to the package insert for doxorubicin hydrochloride liposome injection, commonly reported adverse reactions include myelosuppression (most common), decreased white blood cell count, (most common), anemia, decreased platelet count, elevated alkaline phosphatase, elevated aspartate aminotransferase, elevated blood bilirubin, nausea, asthenia, alopecia, pyrexia, diarrhea, acute infusion-related reactions (the primary manifestations of infusion reactions include flushing, dyspnea, facial edema, headache, chills, back pain, tightness in the chest and throat, and hypotension), stomatitis, and respiratory disorders. Other less common adverse reactions (< 5%) include palmar-plantar erythrodysesthesia syndrome, oral candidiasis, nausea, vomiting, weight loss, rash, mouth ulceration, dyspnea, abdominal pain, and allergic reactions including hypersensitivity, vasodilation, dizziness, anorexia, glossitis, constipation, paresthesia, retinitis, and confusion. Congestive heart failure has been reported at a high incidence with conventional doxorubicin formulations. In rare cases, radiation recall reactions have been observed in patients previously treated with radiotherapy during treatment with doxorubicin hydrochloride liposome.

Adverse reactions of paclitaxel injection:

According to the package insert for paclitaxel injection, the common adverse reactions in 812 patients with solid tumors who received monotherapy with this product include bone marrow reactions (decreased neutrophils, decreased white blood cell count, decreased platelets, anemia, infection, bleeding), allergic reactions, cardiovascular reactions (vital sign changes, hypotension, bradycardia, significant cardiovascular events), abnormal ECGs, peripheral neuropathy, muscle pain/arthralgia, gastrointestinal reactions (nausea, vomiting, diarrhea, mucositis), alopecia, liver reactions (elevated bilirubin, elevated alkaline phosphatase , elevated aspartate aminotransferase), and injection site reactions.

Adverse reactions of topotecan hydrochloride injection:

According to the package insert for topotecan hydrochloride for injection, the common adverse reactions include hematological system reactions (decreased white blood cell count, decreased platelets, anemia, and other reactions; myelosuppression (primarily neutropenia) is the dose-limiting toxicity of this drug); digestive system disorders (nausea, vomiting, diarrhea, constipation, intestinal obstruction, abdominal pain, stomatitis, anorexia), skin and appendage disorders (alopecia, occasional severe dermatitis and pruritus), neuromuscular disorders (headache, joint pain, muscle pain, systemic pain paresthesia), respiratory system disorders (dyspnea), liver disorders (hepatic function abnormal, transaminases increased), general disorders (asthenia, fever, discomfort), local disorders (drug leakage outside the blood vessels may lead to local irritation, redness and swelling), and allergic reaction (rare anaphylaxis and angioedema).

Adverse reactions of gemcitabine hydrochloride for injection:

According to the package insert of gemcitabine hydrochloride for injection, the most commonly reported treatment-related adverse reactions include: nausea (with or without vomiting) reported by approximately 60% of patients; hepatic transaminases (AST/ALT) increased and alkaline phosphatase increased; proteinuria and hematuria reported by approximately 50% of patients; and dyspnea reported by 10%–40% of patients (with the highest incidence observed in lung cancer patients). Approximately 25% of patients reported allergic rash, and pruritus was present in roughly 10% of these cases. The dose-limiting toxicities include platelet count decreased, white blood cell count decreased, and neutrophil count decreased. In clinical studies, very common and common adverse reactions included: blood and lymphatic system disorders: leukopenia (including neutropenia; grade 3 incidence: 19.3%, grade 4 incidence: 6%. Myelosuppression is generally mild to moderate and most often affects neutrophil counts), platelet count decreased, anemia, febrile neutropenia; metabolism and nutrition disorders: anorexia; nervous system disorders: headache, insomnia, somnolence; respiratory, thoracic and mediastinal disorders: dyspnea (typically mild and self-limiting without treatment), cough, rhinitis; gastrointestinal disorders: nausea, vomiting, diarrhea, stomatitis, mouth ulceration, constipation; hepatobiliary disorders: transaminases increased (ALT/AST), alkaline phosphatase increased, blood bilirubin increased; skin and subcutaneous tissue disorders: allergic rash (often associated with pruritus), alopecia, pruritus, hyperhidrosis; musculoskeletal and connective tissue disorders: back pain, myalgia; renal and urinary disorders: proteinuria (mild), hematuria; general disorders and administration site conditions: flu-like symptoms (most commonly including fever, headache, chills, myalgia, fatigue, and anorexia; other reported symptoms included cough, rhinitis, malaise, hyperhidrosis, and sleep disorder), edema/peripheral edema (including facial edema, which is usually reversible after discontinuation), fever, fatigue, and chills.

Other risks

1) Infusion reactions

The main symptoms are cold, chills, cyanosis of the face and limbs, followed by fever, which may be accompanied by nausea, vomiting, headache, dizziness, irritability, delirium, etc. In severe cases, there may be coma, decreased blood pressure, shock, respiratory failure and other symptoms, which are caused by multiple factors such as pyrogens, drugs, impurities, too low drug solution

temperature, too high drug solution concentration and excessively fast infusion rate during intravenous infusion.

2) Medical examinations/procedures during the study may also put you at risk, for example:

- More frequent blood collection is required during the study phase, and the risks of blood collection may include syncope, pain, and/or ecchymosis. In rare cases, a small blood clot or infection may occur at the needle insertion site, which usually resolves spontaneously.
- The cuff used for blood pressure measurement may also cause discomfort or petechiae to the upper arm, which usually recovers quickly.
- Noise of electromagnetic waves from magnetic resonance imaging (MRI), and low-dose radioactive rays during CT scan and X-ray are also present.
- Allergy to contrast agents: During CT and MRI scans, a contrast agent may be injected into your blood vessels, which may cause allergic reactions. The symptoms of such allergic reaction include pruritus and rash, which may be accompanied by dyspnea and decrease in blood pressure to a dangerous level in severe cases, or other systemic symptoms. If you know you are allergic to the contrast agent, kindly be sure to tell your study doctor and the radiologist.

3) Risks of puncture biopsy

- Hemorrhage or infection may occur at the puncture site and internal hemorrhage may occur in the punctured organ;
- Pneumothorax may occur if the puncture site is at the lungs;
- Puncture may cause new tumor metastasis;
- Puncture may cause significant pain.

During the study period, you need to go to the hospital for follow-up visits and receive some medical examinations which help to understand the efficacy of the drug and discover safety problems in time. At the same time, as you need to return to the hospital for regular follow-up visits, it may cause you trouble or inconvenience.

If you experience any discomfort or new changes in your condition, or encounter any unexpected circumstances during the study, regardless of whether they are associated with the drug, you should inform your study doctor promptly and he/she will make a judgment and give medical treatment.

What if new information becomes available?

Sometimes during the course of a study, new information becomes available about the treatment that is being studied. If there is any new important information during the study, including but not limited to adverse reactions and significant findings that may affect your willingness to continue participating in the study, your doctor will inform you promptly. You will be asked to sign a new informed consent form as a record of the updates you have received.

At any time you can ask any questions about this study. Your doctor will give you his/her phone number so that he/she may answer your questions.

What happens when the study stops?

After the study stops, your study doctor will decide on your future treatment. If your study doctor feels this is appropriate, you may be able to continue on the same treatment as during the study.

Your participation in the study is entirely up to you. You may refuse to take part in this study, or stop taking the drug at any time during the study, or withdraw from this study without affecting your relationship with your doctor and without any loss of medical or other benefits to you. You will still enjoy the same medical benefits.

It is important to inform your doctor in advance if you decide to stop using the study drugs in this study (including trastuzumab rezetecan, doxorubicin liposome, paclitaxel, topotecan, and gemcitabine) because in some cases, sudden discontinuation may have some effects on your body. Your doctor will also explain to you and communicate with you after you have expressed your wish to withdraw from the study.

If you decide to withdraw from this study, the information obtained during the study prior to your withdrawal, including but not limited to data, samples, etc. will still be used and analyzed for scientific purposes, and the results will be shared to ensure the completion of the study and the authenticity of the data. Although, your personal information, such as name, date of birth and identification card number, will not be disclosed.

There are three different situations in which your participation in this study may be terminated. Your study doctor will discuss these three situations with you in detail:

1. ***You may stop using the study drug but still take part in the study, or you are willing to continue to be contacted by your study doctor even if you decline to attend subsequent follow-up visits;***

   If you stop using the study drug but still take part in this study, and agree to receive the follow-up or decline subsequent follow-ups, your study doctor will still communicate with you regularly, approximately once every 60 days until the end of the study, to discuss the state of your health. At the same time, with your consent, your medical information will be collected. This information is crucial for this study and constitutes an important step for scientific research and more effective strategy for subsequent projects. Of course, you may decline to be contacted by your study doctor, and your decision will not affect your future treatment.

2. ***You may stop using the study drug, withdraw your informed consent form and no longer take part in this study, and express your unwillingness to be contacted by your study doctor;***

   If you decide to stop participating in this study, you may be asked about your use of the study drug before withdrawal from the study. You may also be asked to undergo laboratory tests (including imaging examinations) and physical examinations if deemed

necessary by your doctor. This is very important for your safety and benefit. Your information will no longer be collected after the end of this examination.

3. ***Your study doctor may terminate your participation in this study at any time if this is in your best interest.***

   The investigator will notify you to withdraw from the study under the below mentioned circumstances:

   1) Continued participation in the study may cause you harm, including progressive disease and intolerable adverse reactions;
   2) You need other additional treatments that are prohibited in this study;
   3) You fail to comply with the requirements of the study or fail to adhere to the treatment given by your doctor;
   4) During the treatment period you become pregnant;
   5) This study is suspended or terminated by the Regulatory Authority;
   6) The Sponsor, Investigator or Ethics Committee terminates the study out of any safety or other special considerations.

   If your study doctor terminates your participation in this study, he/she will discuss the key reasons with you.

What if something goes wrong?

The Sponsor has taken insurance coverage in accordance with the legal requirements. During the study, any other medical treatment except for emergency situations must always be agreed beforehand with the study doctor. If personal injury is suspected to have occurred as a result of participation in this study, your study doctor must be informed immediately so that he/she can inform the sponsoring company.

The insurance policy taken by the Sponsor covers any claim for medical care or compensation due to injury or death related to the study, wherein such medical care is required or injury or death has resulted from administration of any study drug or any other procedure carried out in accordance with the protocol for the study or due to negligence of the Sponsor.

In the event of an injury occurring to you because of your participation into this clinical study, you shall be given free medical management (as long as required or until such time it is established that the injury is not related to the study, whichever is earlier). You shall be entitled for financial compensation according to the orders of the Licensing Authority.

In case of death caused due to participation into this clinical trial, your nominee would be entitled for financial compensation according to the orders of the Licensing Authority.

Will my taking part and personal information be kept confidential?

No one except you, your study doctor and his team will know that you are taking part in this study. Your personal data, especially medical results, will be collected, stored and evaluated during this clinical study. If there are any updates to the collected data, you have the right to be informed and to correct the said data. In order to verify the study procedures and data, clinical trial-related medical records containing your personal information and the informed consent form that you have signed may be reviewed or copied by the investigator, the Ethics Committee, monitor, auditor, the regulatory authorities of India or other countries, and the Sponsor for study or regulatory purposes. These reviewers will assume the responsibility of keeping your information confidential. The Sponsor includes Glenmark Pharmaceuticals Ltd. and any of its affiliates or subsidiaries related to this study, and any individual or company contracted with the Sponsor and any of its affiliates or subsidiaries related to this study to obtain study information during and after the study. You will not be able to take part in this clinical study if you do not agree with the above data protection clauses.

In this clinical study, your biological samples such as blood, urine, and tumor tissues will be coded, which means they will be labelled with a “code” instead of your name or any other personal information about you. The data collected through sample testing will also be stored and analyzed using codes. Only your study doctor or other personnel authorized by your study doctor can identify your name from a code.

You should understand that if you agree to undergo HER2 expression, PK and immunogenicity testing, you will be agreeing to give tumor tissue for HER2 testing at a laboratory in India and blood samples for PK and immunogenicity testing at central laboratory located in China. After the final report of this study is completed, all your biological samples and any isolates will be returned to the study site or destroyed at the central laboratory.

Your data may be transferred to other countries where it may be subject to a different level of protection and will be subject to restrictions as required by appropriate authorities. If this study is published in academic journals, your name will not be identifiable by others. Your name and other information that can identify you will be deleted and replaced with a number that is linked to your personally identifiable information. Only the personnel mentioned above will have direct access to your original medical records. It is theoretically impossible for an unauthorized individual to identify you.

Your family doctor and any other medical practitioners (if not the same as your study doctor) who are treating you for other conditions will be notified of your participation in the study, given that you agree to this. Your study records will be kept on file at the hospital/study site for a period of at least 15 years. All such records will be destroyed at the end of this period.

A description of this clinical study can be found on Clinical Trials Registry-India at https://ctri.nic.in based on the study number. The above websites will not contain any information that can identify you, and will contain an overview of the study results at most. At any time you can visit the above websites. Information about this clinical study may also be disclosed on other registry platforms, which will similarly not contain any information that can identify you.

What will happen to the results of the study?

When the results of this study become available, they will be published in a medical journal but your identity will remain confidential. For this information you can ask your study doctor.

Who is organizing and funding the research?

Glenmark Pharmaceuticals SA. is sponsoring this study and has authorized Glenmark Pharmaceuticals Ltd to conduct the study on its behalf in India. They will pay the study doctor for conducting the study and including you in the study.

You can take part in this study at no cost. The costs required for the study drug, study visits and study-related examinations (routine blood test, blood biochemistry test, infectious disease screening, urinalysis, coagulation test, 12-ECG, routine stool test, thyroid function test, cardiac enzyme profile test, echocardiogram, B-mode ultrasound of deep veins in both lower extremities, blood pregnancy test, CT, MRI, bone scan, and CA-125 test) will not be charged to you or your insurance company, and you may not use medical insurance to pay for it. Although, this study will not cover expenses for the treatments and examinations required for your other concomitant diseases, which are not examinations and drugs required in the clinical study.

You and your carer (if you have one accompanying you) will receive a travel cost of INR **2000** for each visit to the study site due to your participation in the study.

What else should I know?

You may call your study doctor at any time during the course of the study to discuss your treatment and how you are feeling. Your study doctor may decide to call you instead of asking you to perform a visit.

If you are of childbearing potential, you are required to have no plans to become pregnant and take contraceptive measures throughout the study starting from the signing of this Informed Consent Form to 7 months after drug discontinuation. You and your male partner must use a medically acceptable contraceptive method during this period; otherwise, you will not be able to take part in this study. You must discuss contraceptive methods with your doctor.

If you become pregnant during the study, you must inform your study doctor immediately. Your study doctor will tell you about the potential risks to the fetus and the specific measures that can be taken. In consideration of the possible effects and harm to the fetus, treatment must be discontinued. You must undergo medical monitoring during pregnancy and after the baby is born. The medical data about your pregnancy and information on the effects on the fetus will be collected and reported to the Sponsor to help others understand the effects of the drug on pregnancy. The identities of you and your baby will be kept confidential.

Who to call with questions?

If you have any questions about study procedures, adverse effects, or any other aspect of this study, you may contact the doctor in charge of this study (see below).

Name and telephone number of study doctor: **Dr. Arnab Bhattacharjee / 7980672007**

Out-of-hour emergency telephone number: **7980672007**

If you have questions about the rights and interests of the subjects in this study, kindly contact the Ethics Committee as mentioned below.

Name and telephone number of the EC Chairperson/designee: **Prof. Partha Pratim Majumder / 9831004230**

INFORMED CONSENT FORM

Study Title: An Open-Label, Randomized, Multicenter Phase 3 Clinical Trial of SHR-A1811 Versus Investigator-selected Chemotherapy for Platinum-Resistant Relapsed Epithelial Ovarian, Fallopian Tube, Or Primary Peritoneal Cancer

Study Number: GSP 402-301 (SHR-A1811-315_Extension)

Initial of the Subject: _____

Name of the Subject: _____

Date of Birth/ Age: _____

Subject's Address:

_____

_____

_____

Qualification: _____

Occupation: Student/ Self-Employed/ Service/ House-wife/ Others

(Kindly tick as appropriate)

Annual Income of the subject: _____

Details of Nominee (s):

Nominee's Name _____

Nominee's Address:

_____

_____

_____

Relation to the Subject:_____

Kindly initial the boxes (Subject)

(i) I confirm that I have read and understood the information sheet dated DD/MMM/YYYY for the above study and have had the opportunity to ask questions. ☐

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

(iii) I understand that the Sponsor of the clinical study, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my ☐

health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. Although, I understand that my identity will not be revealed in any information released to third parties or published.

(iv) I agree not to restrict the use of any data or results that arise from this study given such a use is only for scientific purpose(s). ☐

(v) I agree to take part in the above study. ☐

Signature (or Thumb impression) of the Subject/ Legally Acceptable

Representative: _____

Date: _____/_____/_____

Name of the Signatory: _____

Investigator's Signature: _____

Date: _____/_____/_____

Name of the Study Investigator: _____

Signature of the Witness _____

Date: _____/_____/_____

Name of the Witness: _____

Copy of the Patient Information Sheet and duly filled Informed Consent Form shall be handed over to the subject or his/her attendant.