Affix Participant Label Here

Masonic Cancer Center, University of Minnesota

CONSENT TO PARTICIPATE IN RESEARCH

A Phase I Study of HCW9218, a Bifunctional TGF-β Antagonist/IL-15 Protein Complex, in Select Advanced Solid Tumors After Failing at Least Two Prior Therapies

Investigator Team Contact Information:

For questions about research appointments, the research study, research results, or other concerns, call the study team at:

Investigator Name: Melissa A Geller, MD Division of Gynecologic Oncology, Department of Obstetrics, Gynecology and Women's Health **Phone Number:** 612 626-3111 **Email Address:** gelle005@umn.edu	**Study Coordinator:** Shannon Lunn, RN **Phone Number:** 612-626-2569 **Email Address:** lunnx020@umn.edu

Outside of business hours or if immediate assistance is needed please call the Hospital's main switchboard at 612-273-3000 and ask for the oncologist on call. For an emergency call 911.

If your doctor is also the person responsible for this research study, please note that she is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Supported By: This research is partially supported by HCW Biologics who is providing the study drug, HCW9218 and performing most of the research related testing.

Financial Interest Disclosure: None

Affix Participant Label Here

Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is provided later on in this form.

What is research?

The doctors and investigators are committed to your care and safety. There are important differences between research and standard treatment plans:

- The goal of research is to answer one or more questions about a new treatment approach to learn if it is safe and effective in the treatment of cancer. Researchers learn by following the same treatment plan with a set number of participants. You, as an individual, may or may not benefit by volunteering for a research study; however, your participation helps answer the research question(s). Often one or more of the drugs offered on a research study are only available on a research study.
- The goal of routine (standard) treatment is to control your cancer or to improve your quality of life using drugs and other methods that have been proven (often through previous research studies). Standard treatments are available from any cancer doctor.

Why am I being asked to take part in this research study?

You are invited to take part in this research study because you have cancer that has failed to be controlled by previous treatment.

This study is testing a new drug, HCW9218, made by the company HCW Biologics. It is investigational, which means that it has not been approved by the FDA, but the FDA has given permission for HCW9218 to be tested in this research study. This is considered an early in human study.

What should I know about a research study?

- The research study will be explained to you.
- You will receive a copy of this consent form to review.
- You can ask all the questions you want before you decide.
- It is up to you whether or not you take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.

Affix Participant Label Here

Why is this research being done?

The study drug HCW9218 contains substances normally found in our cells, called interleukin-15 (IL-15) and transforming growth factor beta receptor type 2 (TGFβRII).

- IL-15 is made by certain white blood cells that help to fight infection and to kill cancer cells.
- TGFβRII is made by many types of cells and binds to a substance called TGF-β that helps cancer cells to grow and spread. The form of TGFβRII in HCW9218 blocks this activity of TGF-β.

The study drug HCW9218 has been tested in animals; however, is early in use for people. This is one of the two initial studies using HCW9218.

This study enrolls patients with any solid tumor cancer except pancreatic and brain tumors. HCW Biologics, Inc. is conducting a large, multi-site study for pancreatic cancer. Brain tumors are not permitted as their treatment is different because many therapies do not cross the blood-brain barrier.

The goal of this study is to find a safe dose of HCW9218 by testing up to 4 dose levels of the drug (plus a -1 dose level which most likely won't be used). The dose level you are assigned depends on when you enter the study. Enrollment starts with 1 person per dose level until the 1st "unacceptable" side effect occurs or Dose Level 4 is reached without side effects.

At the 1st "unacceptable" side effect, the enrollment plan changes and 2 additional participants are added to the current dose level and future enrollment is in groups of 3.

For safety, each enrollment is separated by at least 21 days so there is sometimes a wait for a treatment slot. You will be told of this.

Enrollment continues until 9 patients in a row are treated at the same dose level without unacceptable side effects or a maximum of 24 patients are treated, whichever occurs earlier.

This study is only being done at the University of Minnesota, but is uses the same dose levels of HCW9218 as in the pancreatic study. HCW9218 is investigational (experimental) and only available on a research trial like this study.

Affix Participant Label Here

How long will the research treatment last?

Participation in this study is approximately 1 year. HCW9218 is given as an under the skin (subcutaneous) injection in the outpatient clinic once every 3 weeks. Treatment continues until it is no longer of benefit, you have unacceptable side effects, or you decide you want to stop. An End of Treatment visit is done 3-4 weeks after your last dose of HCW9218. This ends your direct study participation.

Follow-up for disease response and general health continues at least once every 3 months through 1 year from the 1st study treatment; however this information can be obtained from your medical record or by contacting your local doctor if you are no longer returning to the University of Minnesota or a MHealth Clinic.

What will I need to do to participate?

If after hearing about this study and reading through this consent form, you are interested in taking part in this study you will be asked to sign this form.

By signing this form you are giving the research staff to permission to review your medical records and order any tests or procedures needed to determine if you are healthy enough to take part in this study. This is called Screening and consist of the following routine evaluations:

- Physical exam and medical history, including previous cancer therapies
- Review of your current medications and supplements – certain herbal and non-herbal supplements such as St. John's wort may potentially interact with HCW9218 – use of such medications and supplements is prohibited for at least 7 days before the 1st dose of the HCW9218 through the End of Treatment visit approximately 3 weeks after the last dose of HCW9218.
- Routine blood tests: Blood tests requiring approximately 1 tablespoon of blood including a complete blood count (WBC, RBC, hemoglobin, hematocrit, platelets), chemistries to check general health including kidney and liver function. If more than 14 days pass between these tests and the 1st day of treatment, you must continue to meet the study eligibility requirements based on blood drawn before your 1st dose of HCW9218.
- Tests to see how well your blood clots requiring approximately 1/2 teaspoon of blood - although this is standard testing, it will be paid for by the study.
- Routine blood tumor markers: Some diagnoses have blood tests such as PSA in

Affix Participant Label Here

prostate cancer and CA-125 in ovarian cancer, requiring about 1/2 teaspoon of blood.

- Imaging studies (CT scan) of your chest, abdomen and pelvis if not done in the previous few weeks
- Electrocardiogram (ECG) and cardiac function monitoring – although this is standard testing, it will be paid for by the study.
- if you have shortness of breath or a history of lung issues, pulmonary function tests (PFT) will be done
- If you had previous spread of the cancer to your brain, a CT or MRI of the brain will be done
- A pregnancy test (urine or blood) will be done if you are a female of child-bearing potential as pregnant or breastfeeding women are not permitted on this study – although this is standard testing, it will be paid for by the study. If more than 14 days pass between this test and the 1st day of treatment, the pregnancy test will be repeated and it must be negative
- Other tests or procedures as ordered by the study doctor as needed.

If you are eligible and still want to take part in this study, you will be scheduled to begin study treatment.

HCW9218 is given once every 3 weeks as an under the skin (subcutaneous or SQ) injection; however, additional visits and blood collections are required during the 1st 6 weeks to monitor for possible side effects.

After the 1st 6 weeks, beginning with the 3rd dose of HCW9218, a clinic visit with bloodwork and the HCW9218 injection is done once every 3 weeks.

Imaging studies (such as CT, MRI, scans) to determine your cancer response are repeated every 8-12 weeks (every 3-4 treatments) depending on your type of cancer.

Treatment continues until it is no longer of benefit, you have unacceptable side effects or you decide you want to stop. During this time you may receive standard of care radiation therapy if you and your doctor decide this is appropriate. An End of Treatment visit is done 3-4 weeks after your last dose of HCW9218. This ends your direct study participation.

Follow-up for disease response and general health continues at least once every 3 months through 1 year from the 1st study treatment; however this information can be

Affix Participant Label Here

obtained from your medical record or by contacting your local doctor if you are no longer returning to the University of Minnesota or a MHealth Clinic.
More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

Is there any way that being in this study could be bad for me?

This is one of the first in human studies of HCW9218; however, it is similar to other biologic drugs. Some of the most common side effects of these other drugs are localized skin irritation or reaction in your abdomen (belly area) where the HCW9218 is injected, tiredness and flu-like symptoms (fever, chills, muscle aches).

There may be some risks that are not known. You will be told of any new risks associated with HCW9218.

More detailed information about the risks of this study can be found under ***"What are the risks of this study? Is there any way being in this study could be bad for me? (Detailed Risks)" and in the "What happens to the information collected for the research?" section.***

Will being in this study help me in any way?

This study may or may not give you direct medical benefit. However, it may help the study doctors understand how this HCW9218 works. This study may help the study doctors learn things that will help people with cancer in the future.

What happens if I do not want to be in this research (Alternatives)?

You do not have to participate in this research. It is your decision. Instead of being in this research study, your choices may include:

- Other investigational treatments at this institution or at other Cancer Centers.
- Treatment with standard of care therapies without being on a research study – ones that can be given by any cancer doctor.
- No treatment at this time with comfort care only that is focused on symptom control, pain relief, and quality of life.

Your doctor can provide you with specific treatment options based on the type of cancer you have based on your previous treatments and current health status.

Affix Participant Label Here

Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information

Why is this research being done?

The primary purpose of this study is to identify a safe dose of HCW9218 when given by a subcutaneous (under the skin) injection once every 3 weeks. Other goals of this research are to document what side effects occur (including how often and how severe) and early estimates of disease response. Information learned in this study will be used in planning future studies.

How many people will be studied?

At least 12 patients but as many as 24 patients with any solid tumor cancer (except pancreatic and brain cancer) will be treated.

What happens if I say "*Yes, I want to be in this research*"?

If you are eligible and agree to take part in this you will be enrolled into the study and assigned to the currently enrolling dose level of HCW9218.

HCW928 Treatment:
HCW9218 is given in the same manner and on the same schedule regardless of the assigned dose level.

HCW9218, at the assigned dose level, is given as a subcutaneous (under the skin) injection in the abdomen (belly area) once every 3 weeks in the outpatient clinic. Depending on the dose level you are assigned, the drug may be divided into more than one syringe as the volume held by one syringe is very small.

Before each injection, you will have a clinic visit and lab work to ensure there are no ongoing side effects from the previous injection and that you are otherwise feeling well.

If you are having any ongoing side effects or not feeling well, the HCW928 may be delayed for 1 week. If after 1 week delay, if treatment still is not in your best interest, the dose for this cycle would be skipped and you would be scheduled to return in three weeks

Affix Participant Label Here

(the next scheduled cycle start) for an assessment to see if continuing on treatment is in your best interest.

The last page of this Document is a table summarizing the schedule of visits with lab work, disease reassessment, and HCW9218 administration which may be a helpful reference during the consent process and while on study.

First Two HCW9218 Injections:
For the 1st injection, you will be monitored in clinic for a minimum of 6 hours after the injection for any side effects.

For the 2nd injection, the monitoring period may be reduced to 3 hours.

Additional visits for blood work and assessments also are required during the 1st 6 weeks (2 cycles) as detailed below.

Cycle 1 (using an example where Day 1 is a Monday):						
	Day 1	**Day 2**	**Day 3**	**Day 5**	**Day 8**	**Day 15**
Activity	**Monday**	**Tuesday**	**Wednesday**	**Friday**	**Monday**	**Monday**
Clinic visit/physical exam	x					
Provider Assessment	x			x	x	x
Blood work including research related*	x	x	x	x	x	x
HCW9218 followed by monitoring for side effects for a minimum of 6 hours	x					
Assessment for side effects	x	x	x	x	x	x
*research related blood sampling is described in the next section – on Day 1 research samples are collected at 30 minutes and 6 hours after HCW9218 – otherwise research samples are collected at the time of routine blood draws.						

During Cycle 1 Days 1 and 8 bloodwork requires approximately 1 tablespoon of blood. On Days 2, 3, 5, and 15 blood testing is limited to a complete blood count (CBC) and requiring approximately 1 teaspoon plus blood clotting studies paid for by research requiring approximately 1/2 teaspoon. At each timepoint an additional 3 ½ tablespoons are collected for research purposes as described in the next section.

Affix Participant Label Here

Cycle 2 begins 1 week after Day 15.

Cycle 2 (using an example where Day 1 is a Monday):					
Activity	**Day 1 Monday**	**Day 2 Tuesday**	**Day 5 Friday**	**Day 8 Monday**	**Day 15 Monday**
Clinic visit	x				
Provider Assessment	x		x	x	x
Blood work including research related*	x	x	x	x	x
HCW9218 followed by monitoring for side effects for a minimum of 3 hours	x				
Assessment for side effects	x	x	x	x	x
Completion of a skin condition questionnaire	x				
*research related blood sampling is described in the next section – on Day 1 research samples are collected at 30 minutes and 3 hours after HCW9218 – otherwise research samples are collected at the time of routine blood draws.					

During Cycle 2 Day 1 bloodwork before HCW9218 requires approximately 1 tablespoon of blood. Days 2, 5, 8, and 15 blood testing is limited to a complete blood count (CBC) and blood clotting studies requiring approximately 1 1/2 teaspoons. At each timepoint an additional 3 ½ tablespoons are collected for research purposes as described in the **Research Related Testing** section.

Beginning with Cycle 3:
You only need to return to clinic once every 3 weeks for bloodwork, a clinic visit and the HCW9218 injection. If you have no issues after the 1st two HCW9218 injections, the wait time after the injection is reduced to 30 minutes.

Cycle 3 and all additional cycles (once every 3 weeks)	
Activity	**Day 1 Monday**
Clinic visit	x
Provider assessment	x
Blood work plus research related samples (requiring 4 ½ tablespoons of blood)	x
HCW9218 followed by monitoring for side effects for a minimum 30 minutes (if no issues with the 1st 2 injections)	x
Assessment for side effects	x
Completion of a skin condition questionnaire	x

Affix Participant Label Here

Additional activities occurring less often than those detailed above:

- If you agreed to the optional tumor biopsy, it is repeated before Cycle 3 treatment.
- Repeat of standard of care imaging studies to assess your disease status every 8 to 12 weeks (3 to 4 cycles).
- Every 12 weeks (every 4 cycles):
  - Repeat of any standard of care cancer specific blood markers (for example, PSA for prostate or CA-125 for ovarian) every 12 weeks – testing done on blood drawn for routine care.
  - Completion of the Quality of Life Form (FACT-G) – the same questionnaire is done at baseline.

Treatment may continue until it is no longer of benefit, you have unacceptable side effects, or you decide you do not want to continue. If at 1 year you are still receiving HCW9218 (the planned end of study participation), it will be set up that you may continue with treatment as long as it is felt to be of benefit.

End of Treatment Visit and Follow-up through 1 Year:

Once treatment is discontinued, you will have a final "End of Treatment" visit to ensure you are not having any ongoing side effects. At this visits the same bloodwork and clinic visit is performed as for Day 1 of any treatment cycle. This may be the final direct study visit.

Follow-up for disease response and general health continues at least once every 3 months through 1 year from the 1st study treatment; however this information can be obtained from your medical record or by contacting your local doctor if you are no longer returning to the University of Minnesota or a MHealth Clinic.

Research Related Testing:

Because this is a research study, you will have research blood samples taken at the time you are having blood collected for your medical care before each dose of HCW9218, at time points described in the tables above during the 1st two cycles of HCW9218 and at the End of Treatment visit. Approximately 3 1/2 tablespoons of blood will be collected at each time point. Research samples are in addition to the standard of care bloodwork described above. Except for small samples (about 1 teaspoonful) collected at 30 minutes and 3 hours after the 1st two doses of HCW9218, research samples are collected when blood is collected for your medical care.

Affix Participant Label Here

These blood samples are for research assessment directly related to this study including pharmacokinetics (a test to see how your body absorbs, metabolizes, distributes, and excretes the study drug) and blood immune cell analyses (these tests check how your immune system reacts to the study drug). Most of the blood collected for research related testing will be sent to HCW Biologics. If a test cannot be done at HCW Biologic or the University of Minnesota, the blood will be sent to an outside lab.

At the time of study enrollment you are assigned a unique participant code that will be used instead of your name or other identifying information. The research samples are labelled with your unique code making it difficult for anyone looking at the sample to know it belongs to you.

If any blood is left over from the collections described above, the remaining samples may be stored at HCW Biologics and/or the University of Minnesota for additional future research related testing. This may include tests about how HCW9218 works against cancer and its effect on the immune system. At the end of this consent form you are given the opportunity to agree to future use of your leftover samples or indicate leftover samples should be destroyed once study related testing is completed.

If you have a tumor that is easy to biopsy you may be asked to sign a separate research consent form agreeing to a biopsy before the 1st dose of HCW9218 and again before the 3rd dose is given. It is your decision to agree to the additional biopsies if asked, and saying not will not affect your participation in this study.

Information obtained from testing of the samples will be used only for purposes of research and development. None of the research results will affect your care or your participation in this study. You will not be told of the results. The results will not be placed in your medical record and will not be given to your insurance company or employer unless required by law.

Neither you nor your health insurance provider will be charged for the cost of research sample processing, storage or testing.

If the results from this study are published in a medical journal or presented at a scientific meeting, you will not be identified.

Affix Participant Label Here

What are my responsibilities if I take part in this research?

If you choose to take part in this study, you will need to:
- Keep your study appointments.
- Tell your doctor about:
  - all medications and supplements you are taking.
  - any side effects you experience.
  - any doctors' visits or hospital stays outside of this study.
  - if you have been or are currently in another research study.

For women: Do not get pregnant or breastfeed while taking part in this study.

For men: Do not father a baby while taking part in this study.

For all: Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 28 days after your last dose of HCW9218.

What happens if I say "Yes", but I change my mind later?

You can leave the research at any time. Leaving will not be held against you.

If you take part in this research study, and decide you want to stop treatment early, you should tell your study doctor, the study coordinator or a member of the research staff. You can stop treatment at any time; however, you will be asked to complete an End of Treatment Visit.

If you decide not to be in this study or to discontinue treatment early, your decision will not negatively affect your right to any present or future medical care.

If you stop being in the research, information about you that has already been collected may not be removed from the study database.

You will be asked if you agree to be followed through 1 year from the 1st dose of HCW9218 which would be done by reviewing your medical record or contacting your local doctor. The focus would be disease response if you leave the study in the absence of disease progression and survival, as well as, any potential late treatment related side effects.

Affix Participant Label Here

What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)

If you choose to take part in this study, there is a risk that HCW9218 may not shrink or stabilize your cancer or prevent your cancer from coming back or spreading.

You will experience side effects. You may experience all, some, or none of these side effects and the side effects may vary in severity. The severity may be mild, moderate or severe, up to and including death. Also, there is always the risk of a rare or previously unknown side effect occurring.

Other drugs will be given to make side effects less serious and uncomfortable or your doctor may delay and/or skip a dose of HCW9218 if you are not feeling well on the day of planned treated. Many side effects go away shortly after the study drugs are stopped, but in some cases side effects can be serious, long-lasting or permanent, even fatal.

Risks of HCW921
HCW9218 had not been tested or used in humans prior to this study and a pancreatic cancer study being conducted by HCW Biologics Inc.

In May 2023, HCW Biologics reported side effect information after treating 20 patients between the two studies. The most common side effect was mild to moderate injection site reactions in 19 patients and with most participants experiencing mild to moderate flu-like symptoms. Changes in blood work results included mild to severe white blood count decrease (increasing the risk of infection), red blood cell decrease (anemia), low sodium and mild to moderate low magnesium. Of the 1st 11 patients, none experienced a dose limiting toxicity (DLT). Out of the 8 “serious” events reported, two events were felt to be at least possibly related to HCW9218 – fluid collection in the lung (pleural effusion) and a blood clot (thromboembolic disorder).

The table below show the most common and most serious side effects seen in drugs similar to HCW9218. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

The **bold type** side effects in the table below were seen in the 1st 20 patients treated with HCW9218.

Affix Participant Label Here

COMMON, SOME MAY BE SERIOUS In 100 people receiving a drug similar to HCW9218, more than 20 and up to 100 may have:	OCCASSIONAL, SOME MAY BE SERIOUS In 100 people receiving a drug similar to HCW9218, from 4 – 20 people may have:	RARE, AND SERIOUS In 100 people receiving a drug similar to HCW9218, 3 or fewer may have:
• **redness, itching and pain or swelling at the injection site** • **infection, especially when white blood cell count is low** • **anemia, which may require a blood transfusion** • bruising, bleeding • nose-bleed • fever, chills, pain • **flu like symptoms** • swelling in arms and legs • pain in belly • pain in joints • loss of appetite • diarrhea • dizziness • shortness of breath • tiredness • high blood pressure which may cause headaches • increase/ decrease in urination • drop in blood pressure • itching • dry skin • nausea, vomiting • **abnormal lab results** • **blood clot** • confusion	• chest pain • skin rash • abnormal eye movement • constipation • bloating • cough • headache • sores in mouth • depression • anxiety/ worry • extreme sleepiness • weight gain • abnormal heartbeat • blurred vision	• skin lesions • allergic reaction • **fluid in the organs** • heart attack • internal bleeding • severe blood infection • damage to multiple organs, heart, kidney, liver, others • swelling, tenderness and/or redness of the veins • stroke

The drug used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

Affix Participant Label Here

Other important things to know about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, and some may never go away.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

Before each planned dose of HCW9218 you will have a brief assessment to make sure you are feeling well, you have no sign of an infection, and any previous treatment side effects have resolved. Treatment may be delayed for 1 week if either you or the study doctor feels it would be of benefit. If after a 1 week delay, you either can receive the HCW9218 injection or it will be skipped until your next planned treatment.

You can ask your study doctor questions about side effects at any time. If you notice or feel anything different, tell your study doctor. They can check to see if it is a side effect.

Blood Draw Risks

Blood samples will be taken for tests throughout this study. The possible risks associated with the drawing of blood are pain, bleeding, fainting, bruising, infection and/or hematoma (blood clot under the skin) at the site where the needle is inserted.

Risks of Completing the FACT-G Quality of Life Questionnaire

You are asked to complete this questionnaire before the 1st dose of HCW9218, every 12 weeks during treatment and at the End of Treatment visit. Completing this questionnaire may remind you of how cancer and its treatment has affected your health and daily activities. You may refuse to answer any question that makes you feel uncomfortable. You also may refuse to complete the questionnaire.

Risks of Genetic Research

The risks to you and your family from genetic research on the tumor and blood samples are very low. The unique participant code assigned at study enrollment will be used instead of your name or other identifying information making it difficult for anyone looking at the sample to know it belongs to you. Testing will be done in batches (more than 1 participant at a time) and no research results will be placed in your medical record.

Affix Participant Label Here

Reproductive Risks

The research may also hurt a pregnancy or fetus in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death. Birth control and pregnancy prevention must be continued by both women and men for 28 days after the last dose of the drug. If you are or your partner is considered to be postmenopausal (no period in the previous 12 month), you are not required to use contraception while participating in this research study. Postmenopausal women rarely become pregnant.

If you are sexually active, both men and women should use at least one effective means of birth control while participating in this research study. Examples of highly effective birth control methods include the following:

- Using twice the normal protection of birth control (i.e., double-barrier) by using a condom AND spermicidal jelly or foam, or a diaphragm AND spermicidal jelly or foam. A spermicidal jelly or foam must be used in addition to a barrier method (e.g., condom or diaphragm).
- Oral contraceptive pills
- Depot or injectable birth control
- Intrauterine Device (IUD)
- Transdermal contraceptive patch
- Vaginal contraceptive ring

Note: Rhythm method or abstinence alone is not considered to be an adequate method of contraception.

Imaging Risks

Tumor reassessments are done according to standard of care and determined by your study doctor based on your diagnosis and the location of your disease. No imaging studies are done solely for research.

Some of the scans that you may get in this study will expose you to low amounts of radiation. Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called “background radiation.” No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT Scans done in this study will expose you to more radiation than you get from everyday background radiation. The amount of radiation from this scan is the same as

Affix Participant Label Here

1 – 3 years of background radiation. Most of the time, this amount of extra radiation is not harmful to you. However, scientists believe that being exposed to too much radiation can cause harmful side effects. This could include getting a new cancer. We estimate that this could happen in about 1 out of every 1000 people who get a very large amount of extra radiation.

You may receive a chest X-ray during this study. The amount of radiation from a chest X-ray is the same as 10 days of background radiation.

You may receive an MRI during this study. Because radiation is not used for an MRI, there is no risk of exposure to radiation during the MRI procedure. However, due to the use of the strong magnetic, MRI cannot be performed on certain people. Let your study doctor know if you have any of the following:

- implanted pacemaker
- intracranial aneurysm clips
- cochlear implants
- certain prosthetic devices
- implanted drug infusion pumps
- neurostimulators
- bone-growth stimulators
- certain intrauterine contraceptive devices
- any other type of iron-based metal implants
- internal metallic objects such as bullets, shrapnel, surgical clips, pins, plates, screws, metal sutures or wire mesh

As part of the MRI procedure, you may be injected with a gadolinium-based contrast agent (dye) to improve the imaging of your organs. These agents may increase the risk of a rare but serious disease called nephrogenic systemic fibrosis (NSF) in people with poor kidney function. NSF triggers thickening of the skin, organs and other tissues. There is no effective treatment for this debilitating and sometimes fatal disease.

You may receive a PET scan during this study. As part of this scan, iodine will be injected into your vein. Some people are allergic to iodine. Let your study doctor know if you have an allergy to iodine or seafood or if you have kidney problems.

Affix Participant Label Here

Because this study involves the use of your identifiable, personal information, there is a chance that a loss of confidentiality will occur. There are procedures in place to lessen the possibility of this happening (see "What happens to the information collected for the research, including my health information?" section below).

Duration of Study Treatment:

HCW9218 is given every 3 weeks until it is no longer of benefit (your cancer worsens) however, study treatment may be ended early with or without your consent for any of the following reasons:

- You have unacceptable side effects.
- You require more than a 6 week break from treatment due to side effects or other health issues.
- Your overall medical condition changes significantly.
- You refuse to have tests needed to determine whether the study treatment is safe and effective.
- You require treatment with drugs such as other anti-cancer treatment that are not allowed on this study.

You will be told about any new information that may affect your health, welfare, or choice to stay in the research.

Will it cost me anything to participate in this research study?

HCW9218 is provided without cost by HCW Biologics for the purpose of this study. The cost of collecting, processing, shipping, and testing of any samples collected for research is paid for by study funds.

You and/or your insurance provider will not have to pay for the following standard assessments which are being performed because you are taking part in this research study. Since these tests are performed as it would be for general medical care, the results are placed in your medical record.

- The blood clotting tests at the beginning of the study and during the 1st 6 weeks (through Cycle 3 Day 1).
- The electrocardiogram at the beginning of the study.
- If you could potentially become pregnant, the pregnancy test(s) to confirm you are not pregnant before starting HCW9218.

Affix Participant Label Here

You or your insurance company will be responsible for the remaining costs related to this treatment including but not limited to, clinic visits, routine lab work, scans or imaging for disease assessment, and any medications given to prevent or treat side effects. You will be responsible for any costs your insurance does not cover, such as deductibles and co-payments. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

Taking part in this study means that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

A stipend of $50 will be provided to you on the following schedule:

Cycle 1 Day 1, Day 2, Day 3, Day 5, and Day 8

Cycle 2 Day 1, Day 2, Day 5, and Day 8

An additional stipend will be provided if you complete optional biopsies, up to two possible. $50 per biopsy will be given to you if you participate in this optional portion of the study.

Payment will be made using a pre-paid debit card called Greenphire ClinCard. We will give you a new debit card (Greenphire ClinCard) each time and, the money will be added to the card after each completed visit/procedure.

Beyond the stipend described above, you will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

Affix Participant Label Here

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality.

Organizations that may inspect and copy your information including those that have responsibilities for monitoring or ensuring compliance include:

- Departments at University of Minnesota with research oversight including the University of Minnesota Institutional Review Board (IRB), the committee that provides ethical and regulatory oversight of research;
- The Masonic Cancer Center at the University of Minnesota and their designee;
- Any federal, state, or local governmental agency that regulates the study (such as the U.S. Food and Drug Administration (FDA), the U.S. Department of Health & Human Services (DHHS), and the Office for Human Research Protections (OHRP)).

HCW Biologics Inc. will receive study data and research samples. HCW Biologics will receive a copy of all "serious adverse event" reports as well as a copy of submissions to the FDA. Anything leaving the University of Minnesota is labeled with the unique participant code assigned at study enrollment rather than a name or other identifying information.

The results of this study will be used for teaching, publications, or for presentation at scientific meetings. The results also may be summarized in the background section of future research studies and publications. Results never include information to allow an individual patient to be identified.

A description of this clinical trial will be available at http://www.ClinicalTrials.gov, as required by U.S. Law. This web site will not include information that can identify you. The web site will include a summary of the results after the study is completed. You may search this web site at any time.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.

Affix Participant Label Here

- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Use of Identifiable Health Information

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Those persons who get your health information may not be required by Federal privacy laws (such as the 1099 Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission. Please read the HIPAA Authorization form that we have provided and discussed.

Will I receive research test results?

No, tests done on samples in research studies are only for research and have no clear meaning for health care. The investigator(s) will not contact you or share your individual test results nor will they be placed in your medical record.

What will be done with my data and specimens when this study is over?

We will use and may share data and/or specimens for future research. They may be shared with researchers/institutions outside of University of Minnesota. This could include for profit companies. We will not ask for your consent before using or sharing them. We will remove identifiers from your data and/or specimens, which means that nobody who works with them for future research will know who you are. Therefore, you will not receive any results or financial benefit from future research done on your specimens or data.

Affix Participant Label Here

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

Affix Participant Label Here

Optional Storing of Leftover Samples for Future Research at the University of Minnesota:

There may be some leftover blood or tumor from the samples collected for research purposes. With your permission we would like to store them after the study ends for future analysis as new things are learned.

Storage of Leftover Samples for Future Research

☐ YES, I consent (agree) to the storing of any leftover samples for future research

☐ NO, I do not consent (do not agree) and want any leftover samples destroyed once research directly related to this study is completed.

If neither box is checked, any leftover samples will be destroyed once research directly related to this study is completed.

STATEMENT OF CONSENT

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent

Affix Participant Label Here

Use the signature block only if a witness to the consent process is required
WITNESS STATEMENT:

The participant was unable to read or sign this consent form because of the following reason:
☐ The participant is unable to read the information
☐ The participant is visually impaired
☐ The participant is non-English speaking
☐ The participant is physically unable to sign the consent form. Please describe:

_____

☐ Other *(please specify)*:

_____

For the Consent of Non-English Speaking Participants when an Interpreter is Used:
As someone who understands both English and the language spoken by the participant, I represent that the English version of the consent form was presented orally to the participant in the participant's own language, and that the participant was given the opportunity to ask questions.

_____ _____
Signature of Interpreter Date

_____
Printed Name of Interpreter

OR:

Statement from a Non-Interpreter:
As someone who understands both English and the language spoken by the participant, I represent that the English version of the consent form was presented orally to the participant in the participant's own language, and that the participant was given the opportunity to ask questions.

_____ _____
Signature of Individual Date

_____
Printed Name of Individual

Affix Participant Label Here

Tests and procedures	Baseline / screening	Cycle 1 Study day: 1	2	3	5	8	15	Cycle 2 Study Day: 1	2	5	8	15	Cycle 3 and future cycles (once every 3 weeks)	Every 8-12 weeks per standard of care	End of treatment (EOT) visit about 3 weeks after your last dose of HCW9218	Follow-up every 3 months for 12 months from Cycle 1 Day 1
Written consent	x															
Medical history including prior cancer treatment	x															
Concomitant medications	x	x				x	x	x			x	x	x		x	
Side effect assessment		x	x	x	x	x	x	x	x	x	x	x	x		x	
Physical exam	x	x				x		x					x		x	
Provider assessment	x	x			x	x	x	x								
Vitals signs	x	x	x	x	x	x	x	x	x	x	x	x	x		x	
Weight	x	x				x		x				x	x		x	
Routine bloodwork plus research sample collection*	x	x	x	x	x	x	x	x	x	x	x	x	x		x	
Diagnosis related biomarker (e.g., CA125, PSA)	x													x		x
Tumor assessment by disease appropriate methods	x													x		x
Pregnancy testing (serum or urine)*	x															
ECG and cardiac monitoring	x															
Pulmonary function testing only if medically indicated	x															
Optional tumor biopsy for research	x												Before cycle 3 only			

Affix Participant Label Here

(requires signing of a separate consent)															

* If more than 14 days pass between testing and the 1st dose of HCW9218, the tests will be repeated and they must continue to meet study eligibility criteria.