Participant Information and Consent Form: FP101A

FP 101A: A Phase I Study of Deflexifol: To determine pharmacokinetic (PK) in patients administered a combined dose of Bolus and continuous 46hr infusion of Deflexifol in patients with advanced malignancy after failure of standard treatment

Sponsor:		Detsamma Investments Pty Ltd
Protocol Number:		FP101A
Principle Investigator:		Associate Professor Daniel Brungs
Location	**:**	Southern Medical Day Care Centre (SMDCC) 410 Crown Street Wollongong NSW 2500 Australia

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Section 1: Participation in the Study – What does it involve?

1.0 Introduction

You are invited to take part in a clinical trial which is a type of research study. This is because you have advanced malignancy which has failed standard treatment. Before you decide whether you would like to take part, it is important for you to understand why the research is being done and what it will involve.

Please take time to read the following information carefully. If there are any words or information that you do not understand, the study doctor or study staff will explain them to you. Reading this form and talking to the study doctor or study staff may help you decide whether to participate or not.
Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor. You may take as much time as you need to make your decision. Participation in this research is voluntary. If you don't wish to take part, you don't have to. If you do not want to participate, your regular medical care and legal rights will not be affected.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests and treatments that are described
- Consent to the use of your personal and health information as described.

You will be given a copy of this *Participant Information and Consent Form* to keep.
Professor Philip Clingan has been actively involved in the development of this drug and should "Deflexifol" become a commercial entity he will receive financial gain from its use.

2.0 Purpose of Study

To determine the PK profile (how the drug is processed in humans) of bolus and Continuous Infusion Deflexifol as a combination therapy in participants who have not responded or relapsed after previous treatment for their disease, and to evaluate the safety of combined bolus and 46hr continuous infusion of Deflexifol.

Deflexifol is a novel combination of 5-Fluorouracil (5-FU), Folinic Acid (FA) and 2-hydroxypropyl-B-cyclodextrin (B-CD), developed at the University of Wollongong (UOW).
Fluorouracil (5-FU) is a chemotherapy drug used for treating a wide range of cancers.
Folinic Acid is used in combination with other chemotherapy drugs to either enhance effectiveness, or as a chemo protectant (an agent that protects against the toxic effects of chemotherapy). 2-hydroxypropyl-B-cyclodextrin B-CD is used as a carrier molecule (an agent to help transport the drug). All of these drugs have been previously approved for use in humans as single agents.

This is the first time that Deflexifol will be used in a human research model as a combined bolus and infusion dose (the 'study drug' or 'investigational drug').

You may not gain benefit from Deflexifol, as it is an experimental treatment. This means that it is not an approved treatment for cancer in Australia or other parts of the world.

The duration of the study is expected to be completed within 12 months.

Detsamma Investments is the sponsor of this study and the manufacturer of Deflexifol. This means Detsamma Investments are providing the experimental drug and financial support to the study centre and the study doctor in the conduction of the study.

Approximately 18 participants are expected to participate in this research study, all will be recruited from Southern Medical Day Care Centre. Your participation in this study is expected to last approximately 3 months from when you begin taking the study drug but may be up to 6 months if you continue on treatment.

3.0 Study Eligibility

On the first visit, your study doctor will examine you and do tests to see if you qualify for this study. To participate in this study, you must be between 18 and 80 years of age with any cancer type. You must have already received what is considered "standard treatment" for your type of cancer. You should discuss t

his with your study doctor before proceeding any further with this study.

If you have previously received 5-FU as part of your chemotherapy treatment, it is possible that you won't benefit from treatment with Deflexifol. In the instance that your disease has progressed on treatments based on 5-FU or Capecitabine, the probability of benefiting from treatment with Deflexifol is likely to be further reduced. You should discuss this with your Oncologist if this statement is applicable to you.

4.0 Description of the Study: Pharmacokinetics (PK) Study

A Phase 1 Study of Deflexifol: To determine pharmacokinetic (PK) in patients administered a combined dose of bolus and continuous 46hr infusion of Deflexifol in patients with advanced malignancy after failure of standard treatment

You will be given Deflexifol as combined continuous infusion(an infusion is a method of putting fluids including drugs into the blood stream) and bolus (a large volume of fluid or dose of a drug given intravenously and rapidly at one time) treatment.

This study is a PK and Safety dose finding study. In a dose finding study participants are enrolled in groups of three. Each group is assessed for toxicity before the next group are enrolled.

3 participants will be assigned to a set dose level of treatment. There are four dose levels in total. 2 weeks from the start dose, the participants will be assessed for toxicity. If there is no dose limiting toxicity observed the next 3 participants receiving Deflexifol will be given treatment at the next dose level up. This dose will be increased by 3 participants at a time dependant on patient toxicities. Once you have been allocated to a dose level it will not be increased.

During your participation in the study your doctor will be assessing your disease progression (status) approximately every 8 weeks. You will be assessed using the same radiological assessment as your baseline (first) scan to show your response to treatment.

You may continue treatment past the initial 8 weeks if you are tolerating the treatment well. You may continue treatment for up to 6 months, without treatment delays as a result of adverse events (An unexpected medical problem that happens during treatment with a drug or other therapy. Adverse events may be mild, moderate, or severe, and may be caused by something other than the drug or therapy being given)

Treatment will continue until the following criteria apply:

- Disease progression (Cancer that continues to grow or spread)
- Intercurrent illness that prevents further treatment (a disease that occurs during the course of another disease)
- Unacceptable adverse event
- You decide to withdraw
- General or specific changes that means your doctor judges that it is unacceptable to continue with the treatment.

Blood tests measuring tumour markers (substances that are released by **cancer** cells or produced by the body in reaction to a tumor that is present) will also be performed if it is appropriate to the type of cancer you have.

5.0 Study Visits and Procedures

After your doctor determines that you meet all the criteria for study participation, the following procedures will be performed at each visit detailed below:

- You will be given this Participant Informed Consent Form (PICF) by the study team and you will review this document in detail.
- You must sign this form (PICF) before any study procedures begin.

Screening Visit:

- The study doctor or study staff will ask you to give personal information, such as your name and date of birth.
- The study doctor or study staff will ask you about your medical history and your current health status.
- You will be asked questions about any drugs, both prescription and over the counter, and supplements that you have recently taken.
- You will be advised not to take aspirin while on treatment.
- You will be asked about any method of contraception that you have been using and will be informed about the contraception required to be in this study.
- You will have a full physical examination, including measurements of your height, weight, blood pressure, and heart rate. You should ask the study doctor about what else will happen during the physical exam in this study. You may be asked to lift your clothing to allow your doctor to access your chest, back and abdomen.
- You will have an electrocardiogram (ECG), a test which records the electrical activity of your heart. For this ECG test, small sticky pads called electrodes will be placed on your chest, arms and legs and connected to a machine by wires.
- You will have scans of your chest, abdomen and other body areas as needed by your doctor. Scans will be done by Computer Tomography (CT scanners that use x-rays to take pictures of your body) or Magnetic Resonance Imaging (MRI; scanners that use magnets to take pictures of your body). The scanner has a round opening in the

centre and a flatbed for you to lie on. While you are lying on the bed, it will slowly move you into the opening where the pictures are taken.

- You will be asked your level of physical activity. How easily you perform daily activities, and which might be giving you difficulty.
- Blood sampling for lab analysis will be done at your hospital or your local laboratory. The staff will take blood by inserting a needle into a vein in your arm. The blood sample results will be reviewed by your study doctor to make sure it will be safe for you to participate in the study.
- If you do participate in the study these blood tests will be used as a baseline to assess any effect the study drug may have on your blood.
- If you are female of childbearing potential, you will have a pregnancy test done. The test will either be a serum test, which means that the research staff will use a portion of the blood collected to determine if you are pregnant, or a urine test, which means that a urine sample will be collected to determine if you are pregnant. You cannot be in the study if you are pregnant.

Your initial screening visit will take approximately 60 mins. Your screening period may last up to 28 days. This time will allow your doctor to review all your test results and confirm you are eligible to continue on the study. You will be officially enrolled into the study if you meet all study entry criteria and agree to participate. If you are not suitable for the study this will be explained to you.

Visit 1 (first day of chemotherapy - study drug)

Pre-treatment:

- You will be asked questions about any changes in your health and in your drugs/treatments since your screening visit.
- You will have a full physical examination, including measurements of your weight, blood pressure, and heart rate.

- **Administration of chemotherapy – study drug**:

  Dose 1/ Week 1/ Day 1

Deflexifol administration:

- Your study drug will be administered via your central venous catheter, port cath or PICC line depending on which device you have.
- Just prior to commencement of treatment blood samples will be taken. You will have additional blood samples taken 6 times in total throughout your treatment time.
- About one teaspoon of blood is collected for this test. This will help your doctor know howthe drug is absorbed.

The time required for your first treatment will be approximately 4 hours

- Study drug will be given to you as a bolus (A large dose of a drug given intravenously and rapidly at one time) followed by connection to an infusion delivered by a portable infusion pump which will continue to deliver Deflexifol for a total of approximately 46 hours. This pump is roughly the size of an “ipad mini” and weighs about 500gms. You will be given a pouch to carry the pump in and this can be worn over the shoulder or attached to your belt. You will be given information on who to contact should there be any problems.
- You will be required to return to the clinic after that time so that the pump can be disconnected. An additional blood sample will be collected at 45hours after the start of your infusion. This blood sample will be taken whilst the infusion is still running
- After the blood sample is taken you will be disconnected and will have a two week break prior to the start of your next treatment.
  You will be reviewed by your doctor every two weeks during treatment.
- Treatment time varies across the study. Cycle 1 Day 1 and Cycle 2 Day 1 the approximate time commitment is 4hrs. Cycle 1 Day 3 and Cycle 2 Day 3 the approximate time is 2 hrs.
- Subsequent visits from Cycle 3 onwards will be approximately 2hrs on Day 1 and 90 mins on Day 3 disconnect

Schedule of Procedures	Cycle 1		Cycle 2		Cycle 3		Cycle 4		Cycle 5 through to end of treatment
	Day 1	Day 3	Day 14	Day 16	Day 28	Day 30	Day 42	Day 44	Day 56 -70
Physical examination (Day 1 of each cycle)	x		X		x		x		x
Questions about your health and what medicines you are taking	x	x	X	x	x	x	x	x	x
Vital Signs: Blood pressure, temperature, pulse rate, RR, SPO2 saturation	x		x		x		x		x
Weight	x		x		x		x		x
Blood samples (approximate teaspoons)	Up to 10 tsp	Up to 2 tsp	Up to 10 tsp	Up to 2 tsp	Up to 4 tsp		Up to 4 tsp		Up to 4 tsp
Pregnancy test (if applicable) Prior to day 1 each treatment cycle	x		x		x		x		x
Deflexifol Bolus	x		x		x		x		x
Deflexifol Infusion	x		x		x		x		x
Deflexifol Infusion disconnection 46 hrs		x		x		x		x	x
ECG (Cycle 1)	x								
ECG (Cycle 2)			x						
Week 8 prior to Cycle 4 Tumour Assessment * This will be same as your screening assessment							x		x
Adverse Event (Side effects) evaluated: Questions about any side effects you may have experienced from last treatment.	x	x	x	x	x	x	x	x	x

End of Study Visit

If you are no longer able to take part in this research study, the study doctor will explain to you why an end of the study treatment is necessary. Your doctor will arrange for this visit, which is necessary to ensure your safety and well-being at the end of the study. The following evaluations will be done at your exit visit:

- Questions about your health, medications taken since your last visit including any side effects in which you may have experienced.
- Physical examination including, pulse rate, sitting blood pressure, temperature, respiratory rate and weight.
- You will be asked your level of activity. How easily you perform daily activities and what might be giving you difficulty.
- The end of study visit will take approximately 60 mins

6.0 Participation Responsibilities

As a participant in this study, you have certain responsibilities to help ensure your safety. These responsibilities are listed below:

- Complete all required visits
- Take the study drugs as prescribed
- Agree to have the required blood tests and scans as required
- Report all side effects and medical problems to the study personnel
- Inform the study doctor or staff if you decide to discontinue your participation. You will be required to complete an end of study visit.

7.0 Potential Benefits

You may or may not directly benefit from participating in this study. We hope the information learned from this research study will help doctors learn more about the safety and effect of Deflexifol in participants with advanced metastatic cancer. The information obtained from the study may possibly help provide future cancer participants with a better treatment.

8.0 Potential Risk/s and/or Discomforts

Medical treatments and experimental drugs often cause side effects. There are risks in taking part in any research study. One risk is that you may get a drug or dose of a drug that does not help treat your disease or that makes your condition or disease worse.

Another risk is that there may experience some side effects. All drugs have side effects, which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability among side effects of different drugs and between individuals. For investigational drugs, not all of the risks are known at this time.

You need to tell the study doctor or a member of the study team immediately if you experience any side effects. You should also notify your regular doctor as soon as possible.

Since many drugs used to treat cancer are designed to cause the rapidly dividing cancer cells in your body to slow down or die, these drugs can also effect rapidly dividing normal cells. These include the blood cells that help to fight infection (white blood cells), the blood cells that help the blood clot (platelets), and the blood cells that carry oxygen in your body (red blood cells). When anticancer drugs cause a decrease in these blood cells, it is called bone marrow suppression. While you are participating in this research study, your blood cell levels will be monitored closely

Sepsis, or septicaemia, happens when an infection reaches the blood. It is a life-threatening emergency. If you have the following symptoms: a high fever of 38 degrees and above, faintness and dizziness, and changes in consciousness, seek emergency medical treatment by calling 000 or attending your local emergency department. Please also contact the study team on the emergency number provided.
Please notify the study doctor and your regular doctor if possible, if any of the following occurs:

- A fever of 38 degrees Celsius or above.
- If you have a low white blood cell count, this can be a serious, life-threatening or fatal. You may have to take antibiotics or be admitted to Hospital.
- Low energy or shortness of breath. This could be a sign of anaemia (not enough red blood cells). It this becomes severe; you may need to come into the day surgery or hospital to have a transfusion or red blood cells.
- You bruise easily, or when injured, you do not stop bleeding. This could be a sign that your platelets (blood cells that help with clotting) are low. This can be serious or life-threatening. If your platelets are very low, you may require a transfusion of platelets.
- You will be given an after-hours number to contact the study team if you have any concerns

Many cancer treatments are associated with an increased risk of blood clots forming that could lead to swelling in the legs and arms. These clots may travel to the lungs causing shortness of breath or to the brain causing a stroke. This may become serious and life threatening. This may also happen during treatment with your trial drug. It is important to let your study doctor and regular doctor know if you have increased shortness of breath or difficulty breathing.

Everyone in the research study will be watched carefully for side effects. You will be monitored during your treatment to keep track of your blood counts and organ function, particularly your kidney and liver function. If you experience side effects, they may go away after you stop taking the investigational drug. Some side effects can be mild; but others can

be long lasting and may never go away. Some may be life-threatening or fatal. You should talk to the study doctor about any side effects which you may be experiencing.

During the research study you will be notified of any new information, which may affect your health or willingness to participate. You may be asked to sign a new *Consent Form* that shows that you have been informed of the new information relating to this research study.

Since the effect of the investigational drug taken with other medications may not be known, it is important that you tell the study doctor about all drugs, prescription and non-prescription drugs, herbal preparations and nutritional supplements that you are taking or planning to take.

Risks associated with Deflexifol

The following is a list of possible side effects that you may experience from receiving Deflexifol. The expected frequency of side-effects listed below is based on those recorded from the use of 5-FU and Folinic Acid.

Common side effects include: (Occur in more than 10% of people):

- Tiredness
- Mouth sores
- Dry mouth
- Altered taste
- Nausea
- Decreased appetite
- Vomiting
- Diarrhoea

Less common side effects include: (Occur in less than 10% of people):

- Light headedness (dizziness)
- Decrease in red blood cell count that may lead to anaemia
- Infusion related reaction (breathlessness, chest pain, tiredness, muscle pain, fall in blood pressure, sweating, vomiting, hives, welts during or soon after drug administration)
- Skin rash
- Changes in some liver enzyme levels (which could mean some cells in the liver have been damaged, this may make you feel sick, tired or generally unwell)
- Chills
- Dehydration
- Dry skin
- Dry lips
- Fungal infection of the mouth

- Phlebitis (superficial blood clot)
- Thirst
- Discomfort around the area of injection

Rare but Serious include: (Which may affect between 1 and 10 people in every 10,000):

- Reduced white blood cell (cells that fight against infection) count associated with fever
- Reduced platelet count
- Oliguria (low urine output), low potassium level and fall in blood pressure leading to death

Driving and using machinery

The study drug may influence your ability to drive or use machines. If you feel dizzy, weak or tired while taking Deflexifol, take special care in driving and in the use of tools or machines.

Other potential side effects

There may be other side effects that are unknown at this point in time. You will be informed in a timely manner if additional information becomes available that may be relevant to or affect your willingness to continue to participate in the study.

It is possible that your cancer may get worse or it may not get better at all while using Deflexifol. Your study doctor will carefully look after your health and may decide that you should stop being in the study if it is not safe for you.

Serious side effects that were experienced in the Phase I study resulting in hospitalisation are listed below:

Treatment related grade 3 or 4 adverse events

Adverse Event	Grade	Bolus	Infusion
Diarrhoea	3	7.5%	2.5%
Venous Thrombosis (blood clot in the vein)	3	2.5%	0%
Nausea and Vomiting	3	0%	2.5%

Treatment related side effects commonly experienced in phase one study of Deflexifol:

Most common treatment related AEs		Bolus	Infusion	Total
Nausea	G1/2	8	6	16
Fatigue	G1/2	6	8	14
Diarrhoea	G1/2	6	2	8
Myelosuppression	G1/2	7	-	7
Mucositis	G1/2	4	5	9
Dyspnoea	G1/2	4	5	9
Abdominal Pain	G1/2	2	2	4
Infection	G1/2	2	4	6
Raised LFTs	G1/2	1	1	2
Vomiting	G1/2	2	-	-

Table source: Clingan et al JCO 2017.

Risks of procedures conducted during the study:

Risks from Blood Samples

Blood samples will be collected during this study. A needle is inserted into a vein in the arm and a small blood sample is withdrawn. Although one blood draw is usually sufficient a second one may be necessary if the first is not successful. Collection of blood samples may cause fainting and some pain and/or bruising at the site on your arm where the blood was taken. In rare occasions, infection may occur. Laboratory blood tests will require approximately 27mL (about 6 teaspoons) per week while on treatment.

In addition to the above side effects, routine needle sticks for blood samples may cause pain, bruising and rarely, infection at the site where blood is taken.

Radiation Risks Associated with Scans and X-Rays

Scans will be done by Computer Tomography (CT) or Magnetic Resonance Imaging (MRI).

Computerized Tomography (CT) Scan

CT scans involve exposure to radiation. This research study involves exposure to ionising radiation. This is equivalent to 2-4 milliseverts(mSv). The background radiation from natural sources is about 2 mSv per year.

You will have a CT scan every 8 weeks. These scans will expose you to a medically acceptable dose of radiation.

A typical CT exam usually lasts 30 minutes to an hour. Before your exam begins, a staff member will help you on to the scanning table. Once you are comfortable, the technologist will move you into the scanner and your exam will begin.

It is important that you remain as still as possible throughout the exam, since even slight movement blurs the results. You won't feel a thing, but you will hear the sound of the

scanner working. If you have questions or need assistance at any time, you can communicate with the technologist through an audio system installed in the scanner.

During the exam, an X-ray tube will rotate around you, passing a narrow beam of X-ray from several different angles through the area to be examined. The table will move slightly after each view is taken. Detectors, located opposite the X-ray tube, receive data from inside your body. A computer will analyse the data and create an image. The images can be viewed on a monitor and also will be transferred to X-ray film to become a permanent record.

When the exam is complete, the technologist will help you off the table.
Whilst you are participating in the study you may have 2 scans. One prior to commencing treatment and at the end of 6 doses of treatment.

Magnetic Resonance Imaging (MRI)

An MRI scanner is a machine that uses electromagnetic radiation (radio waves) in a strong magnetic field to take clear pictures of the inside of the body. Electromagnetic radiation is not the same as ionising radiation used, for example, in X-rays. The pictures taken by the machine are called MRI scans. A typical MRI scan takes 30-60 minutes.

Staff will ask you to lie on a table inside the MRI scanner. The scanner will record information about your chest, abdomen and other body areas as needed by your doctor. It is very important that you keep very still during the scanning. When you lie on the table, the study staff will make sure you are in a comfortable position so that you can keep still. The scanner is very noisy, and the study staff can give you some earphones to reduce the noise. Some people may experience symptoms of claustrophobia from lying in a confined space. If you do experience discomfort at any time during the scan, you will be able to alert staff by pressing on a call button provided to you. There are risks involved with an MRI if you are pregnant or have one of the following: an artificial heart valve, metal plate, pin or other metallic objects in your body (including a bullet or shrapnel). During an MRI, you will have to lie still on your back in the MRI scanner in a tight space. This may make you anxious. The MRI scan does not cause any pain and does not expose you to x-ray radiation.

You must tell the study staff if you have metal implanted in your body, such as a pacemaker or metal pins.

These scans are for research purposes. They are not intended to be used like scans taken for a full clinical examination. The scans will not be used to help diagnose, treat or manage a particular condition. A specialist will look at your MRI scans for features relevant to the research project. On rare occasions the specialist may find an unusual feature that could have a significant risk to your health. If this happens, the study staff will contact you to talk about the findings, but they cannot guarantee that they will find any/all unusual features.

Contrast Dye (MRI, CT scan)

The dye that is injected into a vein for the scan is usually well tolerated. Some people feel dizzy, queasy, or get a headache when given the dye or notice a cold feeling near the injection site. There is a very small chance of having an allergic reaction to the dye that rarely can be serious or life threatening. You must tell your doctor if you have had bad reactions to dyes before. Occasionally, some soreness or swelling may develop at the injection site. These symptoms can usually be relieved by applying moist, warm compresses to your arm.

9.0 Pregnancy & Birth Control

Female Participants:

The risk of Deflexifol to pregnant women or to unborn babies is unknown. However, Deflexifol contains the chemotherapy drug 5-fluorouracil which is known to cause birth defects in animal studies.

For this reason, females of childbearing potential must have a pregnancy test before the study starts and each time before receiving study drug. You must not become pregnant during this study. If you are a female of childbearing potential, you must use an effective form of birth control during this study and for an additional 6 months after the last administration of Deflexifol.

You must use a highly effective contraceptive method that has a less than 1% failure rate per year during the study and for at least 6 months after the last dose of the study. Your Dr should evaluate the potential for failure including non-compliance or any recently initiated relationship prior to the first dose.

Acceptable methods of birth control include consistent use of an approved oral contraceptive (birth control pill), an implantable contraceptive, sterilisation, an injectable contraceptive or true abstinence.

Oral, implantable or injectable contraceptives are only considered effective if used properly and started at least 30 days prior to the screening visit. Some drugs (e.g. antibiotics) may interact with hormonal contraceptives, making them not work properly. Please inform you study doctor of all other drugs you are taking. If you suspect that you may have become pregnant during the study, you must contact the study doctor immediately. You will not be able to continue participation in the study if you become pregnant. In the event you do become pregnant the Sponsor may request that you sign a separate consent form to allow monitoring of your pregnancy and the birth. The effects of Deflexifol on a nursing infant are unknown; if you are breastfeeding, you cannot participate in the study.

Male Participants:

Male participants should be advised that the effects of the study drug on the male reproductive system are not known at this time, and contraceptive methods should be used throughout the study and for 6 months after completion of the study. It is recommended

that both partners use contraception. It is also highly recommended that you inform your partner of your participation in the study and that contraception has been strongly recommended. Further, you must agree that if your partner becomes pregnant while you are on the study, you will advise the study doctor who may then provide you with an authorisation form to present to your partner. If she is in agreement, that authorisation will function as consent to approve the study doctor's access to medical information to allow monitoring of the pregnancy and the birth.

It is recommended that a condom be worn for all sexual intercourse as the study medication may cause harm to your partner through the absorption of the study drug from the seminal fluid.

10. Storage of samples

All your samples will be labelled. All information obtained from your samples will be kept confidential as stated in the Disclosure of Information and Publication (Section 13) of this form.

Your signature at the end of this form means that you allow your study doctor and his/her study staff to complete the set plan of study procedures (called a study protocol), including the collection of samples. Your signature also allows Detsamma Investments and its authorised representatives to use these samples for tests, outlined in the study protocol which will assist in determining if the effectiveness of the study drug, such as antibody samples, tumor assessment measures or for tests necessary to ensure your safety such as laboratory tests. If you stop participating in this study, Detsamma Investments and its authorised representatives may continue to use the samples and scans collected during your participation in the study for tests and procedures described in this form.

Samples collected for testing may be stored for up to 5 years after all the participants have finished the study. Samples for other testing may be stored up to 5 years after all the participants have finished the study. Detsamma Investments and its authorised representatives will make sure your samples are destroyed at the end of the storage period.

You understand that a commercial pharmaceutical or diagnostic product(s) may be developed through the use of your samples or medical information collected during this study. Detsamma Investments, other researchers or research companies may patent or sell discoveries that result from this research. Neither Detsamma Investment nor the study doctor will compensate you. You understand that you do not have any rights to future inventions.

11.0 Reimbursement/Cost for Participation

You will not be paid for participating in this study or for the use of your biologic samples or medical information or for the information or by-products obtained from these. You will only be reimbursed for actual expenses incurred for each visit up to a reasonable amount, (ie petrol/travel) Reimbursement will be payed to you periodically.

You will not have any additional costs if you participate in this study: You will receive the study drug Deflexifol free of charge and there will be no charges for the visits, tests or procedures that are part of this study including the chemotherapy, 5-Fluorouracil. All costs not related to the study, including those related to the normal treatment of your disease, will be your responsibility.

Some of the medical care that you will receive in this study is considered routine care and would be recommended whether you are in the study or not and the cost of this will not be paid for by the sponsor. You can ask your study doctor for more information about this cost.

12.0 Alternative Treatments

If you do not wish to participate in this study, you will continue to be treated by your doctor and your care will not be jeopardised in any way.

Another choice instead of this treatment is comfort care only, where treatments are used to control symptoms, relieve suffering, and allow the most dignity and control. In comfort care, treatment is unlikely to cure, slow or reverse your cancer.
There may also be other appropriate research studies available to you. You should discuss this with your doctor. Your doctor may continue with your current treatment regimen with modifications that you and your doctor agree are appropriate.

Section 2: Privacy

13.0 Privacy, Disclosure of Information and Publication

Your medical records will be kept confidential as allowed by the applicable laws. If results of the study are published, your identity will not appear. Neither your results nor your samples will be identified with your name. Information about your participation in this study will be associated with you by using a participant number, your date of birth, and your gender. Your study doctor or his/her staff will label all of your samples with the identification number. Only your study doctor and his/her staff will be able to link that number to you at all times. All information obtained from your samples will be kept confidential.

13b. Who will have access to my medical information?

Your participation in this study will be noted in your medical records. If your primary care physician is different from your study doctor, he/she will also be notified.

If you take part in this study, information about your health will be collected and analysed by Professor Clingan, Professor Aghmesheh, Dr Brungs, Southern Medical Day Care Centre, by Detsamma Investments and companies assisting Detsamma Investments with study as well as Ethics committees and regulatory authorities from your country or countries where the information is submitted (such as the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA) or the Australian Government's Therapeutic Goods Administration (TGA)). These agencies will have access to your medical information and see your name, other personal information such as date of birth and gender but will be obliged to keep this information confidential unless required by law or a regulatory authority. If the study is successful some companies assisting Detsamma Investments will receive your information their location may be outside of Australia, such as, but not limited to the United States of America (USA), Europe and countries in Latin America, India, New Zealand and Asia.

Participants should note that some data derived from your participation in this study will be send overseas; the regulatory regimes governing data access and use in other countries may not be the same as those that are in place in Australia. If you have any questions about this direct them to the Principal Investigator.
In accordance with Australian privacy and other relevant laws, you have a right to access your information and a right to correct information which is not correct.
Some of the information collected from you will be analysed by external vendors used by Detsamma Investments (such as a central Laboratory) and may contain encoded confidential information, this means your medical information will be identified only by a code number when sent. Of the people treating you, only the study doctor, nurse and other medical staff involved in your care will know whether or not you are participating in this study and also have access to your personal medical information. Any identifiable information that is collected about you in connection with this study will be your study data. This data will be coded through assignment of a unique participant identification number. This means that participant names are not included in data sets that are transmitted to any location. Also, this information remains confidential and will be disclosed only with your permission, or except as required by law. Only the researcher's names above, the Australian TGA, other overseas government agencies, the study sponsor and the sponsor's authorised representatives, collaborators and licensees will have access to your identifiable details and results which will be held securely at Southern Medical Day Care Centre. Bellberry Human Research Ethics Committee will just have access to your study data. Only non-identifiable information will be sent off site.
An outside laboratory (central vendor) will perform PK analysis on blood samples collected and interpret this information and report the results back to Detsamma Investments. This outside laboratory will be bound by confidentiality obligations.

All reasonable measures to protect the confidentiality of your study records and your identity will be taken to the extent permitted by the applicable laws and/or regulations and will not be made publicly available. Your health records and any information obtained during the research project are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities and authorised representatives of the Sponsor, Detsamma Investments, and the institution relevant to this Participant Information Sheet, Southern Medical Day Care Centre, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

If you withdraw your consent to participate after commencing the study, the data collected up to this time point cannot be deleted on account of the legal requirement to store all study data for a period of at least 15 years.

c. How will my information be used?

The collected medical information will be used to help find out the toxicity of Deflexifol.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

14.0 <u>Voluntary Participation and Termination of Participation</u>

Your participation in this research is voluntary. You can choose not to participate in this study either at the beginning or at any time during the study. There will be no penalty or loss of benefits to which you are otherwise entitled. To ensure your safety, you will be asked to undergo an end of study visit. If you wish to withdraw from the study, you should contact:

Professor Philip Clingan, Dr Daniel Brungs and A/Prof Aghmesheh on (02) 4227 3733 or study personnel at (02) 4228 6200.

Your study doctor will still be able to use the information collected about you prior to your withdrawal from the study. Information that has already been sent to the study sponsor cannot be withdrawn.

Your participation in this study may be discontinued without your consent by the study doctor or the sponsoring company at any time. Some of the reasons this could happen include: failure by you to follow your study doctor's instructions, or if in your study doctor's opinion, Deflexifol is harmful, or has medically unacceptable side effects, or for other reasons at the discretion of the sponsor or study doctor. If you are withdrawn from the

study, or the study otherwise ends, you will stop receiving the study drug and may be asked to have appropriate medical tests and follow-up to evaluate your health and safety.

15.0 Injury Compensation

If you are injured as a result of your participation in this trial, you have a legal right to seek compensation. It is the recommendation of the independent ethics committee responsible for the review of this trial that you seek independent legal advice before taking any steps towards compensation for injury.

Sponsors of clinical trials in Australia have agreed that the guidelines developed by their industry body, Medicines Australia, will govern the way in which compensation claims from injured participants are managed by sponsors.

However, as guidelines, they do NOT in any way dictate the pathway you should follow to seek compensation. The sponsor is obliged to follow these guidelines.

These guidelines are available for your inspection on the *Medicines Australia Website* (www.medicinesaustralia.com.au) under - Policy – Clinical Trials – Indemnity and Compensation Guidelines. Alternatively, your study doctor can provide you with a hard copy of the guidelines.

It is the recommendation of the independent ethics committee responsible for the review of this trial that you seek independent legal advice.

16.0 Who to Contact to Ask Questions or Report a Possible Research Related Injury or Reaction

If you have any questions concerning your participation in this study, or if you feel you have experienced a research-related injury or a reaction to the study drug, you should contact: Associate Professor Daniel Brungs on (02) 4227 3733 or study personnel at (02) 4228 6200 or Sue Parker on (02) 4228 6200/ 0407 786 403 (mobile/ after hour's emergency number).

17.0 Who to Contact to Report a Breach of Confidential Information

If you feel there has been a breach of your confidential information, you should contact the principal study doctor for this study:

Associate Professor Daniel Brungs on (02) 4227 3733

18.0 Who to Contact to Ask Questions about Your Rights as a Research Participant

The ethical aspects of this research project have been approved by Bellberry Human Research Ethics Committee. (HREC)

The Belberry Human Resarch Ethics Committee has reviewed this study in accordance with the National Statement on Ethical Conduct in Human Research (2007) including all updates. If you have questions about your rights as a research participant, you may contact: The Operations Manager, contact Bellberry by telephoning 08 8361 3222 or Postal: 123 Glen Osmond Rd,Eastwood SA 5063

Patient Information and Informed Consent Form
Deflexifol – FP101A

I _____the undersigned hereby voluntarily consent to my involvement in the research project titled:

Phase I Study of combined Infusion and Bolus Deflexifol in Patients with advanced malignancy after failure of standard treatment.
I acknowledge that the nature, purpose and risks of the research project and alternatives to participation have been fully explained to my satisfaction by Dr/Prof/ A/Prof_____. I have also been provided with an *Information Sheet* regarding the research.

Specifically, the details of the procedure(s) proposed and the anticipated length of time it will take, the frequency with which the procedures(s) will be performed and an indication of any discomfort that may be expected have been explained to me.

- Although I understand that the purpose of this research study is to improve the quality of medical care, it has also been explained that my involvement may not be of any direct benefit to me.
- I have been given the opportunity to have a member of my family or another person present while the study is explained to me.
- I have been told that no information regarding my medical history will be divulged to unauthorised third parties and the results of any tests involving me will not be published so as to reveal my identity.
- I understand that access will be required to my medical records for the purpose of this study as well as for quality assurance, auditing and in the event of a serious adverse event.
- I understand that if I become pregnant during the study I will be invited to consent to access to information regarding any pregnancy and its outcome.
- I understand that I am free to withdraw from the study at any stage without prejudice to future treatment. If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.
- I am between the ages of 18 and 80.
- I consent to my GP being notified of my participation in this study and of any clinically relevant information noted by the trial doctor in the conduct of the trial.
- I declare that all my questions have been answered to my satisfaction.
- I have read or have had read to me in my first language and I understand the *Participant Information and Consent Form FP101A*. Version 1 20 September 2019.

SIGNATURE OF
STUDY PARTICIPANT: DATE:

INVESTIGATOR STATEMENT

The person signing this consent form has had the study fully and carefully explained and has been given an opportunity to ask any questions regarding the nature, risks and benefits of the participant's participation in this research study.

NAME OF INVESTIGATOR:

SIGNATURE OF
INVESTIGATOR: DATE: