INFORMED CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**Spruce Biosciences, Inc. / "A Randomized, Placebo-Controlled, Response-Guided, Intrasubject, Dose Escalation Study to Evaluate the Safety and Efficacy of Tildacerfont in Adult Subjects with Polycystic Ovary Syndrome (PCOS) and Elevated Adrenal Androgens"**
Protocol Number:	**SPR001-210**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

You are invited to be in a research study. This form tells you about the details of this study. Please read this form with care and ask the study doctor or study staff all your questions. When you understand what is in this form, you will be asked to sign and date it to join this study. You will receive a copy of the signed and dated form.

Taking part in this study is voluntary. This means that you can choose if you want to take part in the study or not. You can leave the study at any time, without any reason. Doing so will not change your health care or your rights. If you do not want to join the study, you can talk to the study doctor about your health care.

Spruce Biosciences, Inc. is a drug company focused on developing treatments for disorders like polycystic ovary syndrome (PCOS). This drug company will run and pay for this study. The study doctor is paid by the drug company to conduct this study.

INFORMATION ABOUT THIS STUDY

Why is this study being done?

We have asked you to join this study because you have a condition called PCOS. PCOS is a common endocrine disorder that affects up to 12% of reproductive-aged women in the U.S. and is the most frequent cause of female infertility. PCOS most frequently presents with excessive levels of male sex hormone (testosterone) in females, excess hair growth, acne, irregular periods, and difficulties becoming pregnant.

About 40 women will take part in this study. This study will be conducted at approximately 15 sites within North America.

The study will test a drug called tildacerfont, which is being developed for treating people like you with PCOS. As tildacerfont is not yet approved for treating PCOS, it can only be used in a study like this one. Tildacerfont belongs to a group of drugs known as CRF_1 receptor antagonists. By inhibiting the activity of the CRF_1 receptors on the pituitary gland, tildacerfont has been shown to reduce the excessive production of adrenal hormones in earlier completed studies. This may help reduce the elevated androgen (male hormone) levels and help improve the symptoms experienced by patients with PCOS like excess hair growth, acne, irregular periods, and fertility challenges.

The goal of this study is to test the safety and behavior of tildacerfont in your body. The purpose of this study is to find a safe and acceptable dose of tildacerfont in women with PCOS and to find how the body deals with tildacerfont at different dose levels.

What will happen during the study?

You will be in the study for up to 29 weeks, and you will have to visit the study center 12 times, 3 of which will require you to stay overnight. You will also need to be available for 3 telephone visits.

The study has a screening period of up to 60 days, followed by a study treatment period of 16 weeks, and ends with a follow-up period of 30 days after the last dose. The study treatment period will be further divided into 3 parts: study treatment periods 1 and 2, with a duration of 4 weeks each, and study treatment period 3, with a duration of 8 weeks.

You have been asked to read, sign, and date this form before you have any study tests performed. If you want to be in this study, your study doctor will first check if you are eligible to take part. This is called the screening period, and it must be completed no more than 60 days before you get your first dose of the study drug. Tests and procedures performed during the screening period are provided later in this document.

Because this is a scientific study, it is also important to collect information about subjects who are not receiving tildacerfont. Therefore, some subjects will receive placebo. Placebo looks the same as the study drug but does not contain any tildacerfont or any other active substance. In this study, a computer will decide whether you receive tildacerfont or placebo. Like when you flip a coin, you will have a 50% chance of receiving tildacerfont and a 50% chance of receiving placebo. From this point on, “study drug” will refer to both tildacerfont and placebo.

If you are eligible to enter the study, your study doctor will ask you to stop taking the current drugs you are taking to treat your PCOS for 30 days before you can begin taking the study drug. This time allows for your current drugs to leave your body.

The study drug will be in the form of tablets and should be taken once daily with your evening meal between 6 p.m. and midnight. Your evening meals should contain approximately 25% to 50% fat content. The study team will provide written guidance on how to determine whether your meal contains the appropriate amount of fat.

This is a double-blinded study, which means that neither you nor the study doctor will know if you are receiving tildacerfont or placebo. Both will be packaged the same and will be identical in appearance and taste. If you are receiving tildacerfont, neither you nor the study doctor will know to which dose level you are assigned. Your assigned dose level may also increase during the course of the study depending on how your body responds to the lower dose level. This will be determined by the level of androgens produced by your adrenal glands as measured in your blood. Regardless of your dose level, you will always take 4 tablets once daily. If you are assigned to placebo, you will remain on placebo for the full 16-week study treatment period.

You should not take any medication for the treatment of PCOS during the study, including metformin or hormonal contraception.

The information below explains the different periods of the study and what will happen to you during the study.

SCREENING PERIOD

After you have signed and dated the informed consent form, you will be checked by the study doctor for eligibility to participate in the study during the screening period. The screening period lasts approximately 60 days and includes 3 visits.

Screening Visit 1

After you have signed and dated the informed consent form, the study doctor will review your complete health history to make sure you can join the study. You will be asked about any history related to your PCOS (like background and progress of your disease), prior therapies (like other drugs you have received to treat your PCOS) and your response to these treatments, and details of other previous diseases, if any, to understand your health better.

You will be asked about your birth date, gender, and race or background only for clinical research purposes.

You will be asked about the drugs that you are taking or have taken before joining the study. This will include all prescription drugs, over-the-counter medications, herbal products, vitamins, supplements, and any other medications. This will be done at every visit during the study.

The study staff will also complete a psychiatric questionnaire to confirm your eligibility. The questionnaire to be administered is the Columbia–Suicide Severity Rating Scale (C-SSRS) to assess suicidality.

Urine and blood samples will be collected for routine testing to measure various hormone levels. At screening, samples will be collected to screen for drugs as well as Hepatitis B, Hepatitis C, and Human Immunodeficiency Virus (HIV). The study doctor may be required by law to report the result of these tests to the local health authority. You will need to fast for at least 8 hours (nothing to eat or drink except water since the previous midnight) before having urine and blood samples collected at approximately 8 a.m. Based on the results of this testing, you may be asked to come in for an additional visit prior to Screening Visit 2 to determine if this study is a good fit for you.

A blood sample will also be collected for pregnancy testing. If you are pregnant, you will not be allowed to participate in the study.

Your body temperature, heart rate, respiration rate, waist circumference, and blood pressure will be measured.

A physical examination will be performed. Your height and body weight will be measured.

An electrocardiogram will be performed to check the health and rhythm of your heart.

You will be asked to collect 2 late-night saliva samples at home. These are to be collected at approximately 11 p.m. to midnight on separate nights prior to Screening Visit 2 to measure cortisol levels.

Depending on your blood results from Screening Visit 1, you may need to come for an additional visit before Screening Visit 2 in order to complete more tests. These tests will be done to rule out other conditions that could prevent your participation in the study. adrenocorticotropic hormone (ACTH) is a hormone produced by the pituitary gland in your brain that travels to the adrenal glands and tells your body to make cortisol and other hormones. Certain conditions such as adrenal insufficiency and congenital adrenal hyperplasia can also impact your levels of cortisol and other hormones. The high-dose ACTH stimulation test can evaluate if these conditions are present by injecting ACTH into your bloodstream and then measuring the level of cortisol and other hormones your body makes. This test will only be performed if needed to confirm your eligibility to take part in the study.

<u>Screening Visit 2</u>

This visit will include dynamic testing shortly after you start menstruating during your period. If you have not menstruated in 2 or more months, then it may be completed at any time. This dynamic test will help determine the source of your elevated androgens.

Blood samples will be taken to perform 2 tests: a low-dose ACTH stimulation test and a gonadotropin-releasing hormone (GnRH) agonist test. Both are described below:

ACTH is a hormone produced by the pituitary gland in your brain that travels to the adrenal glands and tells your body to make other hormones such as cortisol and androgens. Some women with PCOS make an excess amount of adrenal androgens

when ACTH reaches the adrenal gland. The low-dose ACTH stimulation test evaluates to see if an excess amount of adrenal androgens is present by injecting ACTH into your bloodstream and then measuring the level of adrenal androgens your body makes.

GnRH is a hormone produced in a different gland in your brain called the hypothalamus. Since most women with PCOS secrete and respond to GnRH differently than those without PCOS, the GnRH agonist test is able to see if this difference is present. During the GnRH agonist test, a small dose of GnRH agonist is injected into your blood, and a series of blood samples are collected immediately before the injection and at specific timepoints following the injection to measure how the hormones in your body respond to the GnRh agonist. The final timepoint is at approximately 20 to 24 hours after the GnRH agonist injection, and this blood sample will be collected on the following day during Screening Visit 3. This test determines whether your ovaries are involved in producing excess androgens as part of your PCOS.

During this visit, your body temperature, heart rate, respiration rate, waist circumference, body weight, and blood pressure will be measured.

The study staff will also check and record any medications that you took since the last visit and review if you experienced any side effects.

Screening Visit 3

As described above, the final blood sample for the GnRH agonist test will be collected at approximately 20 to 24 hours after Screening Visit 2 to complete the dynamic testing.

The study staff will also check and record any medications that you took since the last visit and review if you experienced any side effects.

The study doctor will review the results of all the screening tests to confirm if this research is right for you. If you are not eligible to take part in this study, your study doctor will talk to you about the reasons for this decision and other treatment options.

If you are eligible, you will be asked to collect a 24-hour urine sample anytime starting at least 1 day after Screening Visit 3 but prior to study Day 1. You will also be asked to collect 2 saliva samples on the morning before your Day 1 study visit. One sample must be collected within 30 minutes of awakening, and the other sample must be collected at 8 a.m. (± 1 hour). These samples are collected to measure salivary progesterone and cortisol levels. You will be given clear instructions on how to collect the saliva samples. You will also be provided with the necessary collection and shipping materials, which will allow these salivary samples to be processed and analyzed.

STUDY TREATMENT PERIODS 1, 2, and 3

In Study Treatment Period 1, you will have hospital/clinic visits on Day 1 and at Week 2 and Week 4 (overnight) and a telephone visit on Day 7.

In Study Treatment Period 2, you will have a telephone visit at Week 5 and hospital/clinic visits at Week 6 and Week 8 (overnight visit).

In Study Treatment Period 3, you will have a telephone visit at Week 9 and hospital/clinic visits at Week 10, Week 12, and Week 16 (overnight visit).

During the study treatment period, you will be asked to complete an electronic diary (eDiary) on a daily basis to confirm that you have taken the study drug as directed. You will also use the eDiary to report any menstrual bleeding on a given day by using an illustrated diagram to help you assess your menstrual blood loss throughout the study. The diary should be kept up to date every day during the study treatment period.

During the study treatment period, you will be asked to collect 2 saliva samples on a weekly basis starting at Day 1. One sample must be collected within 30 minutes of awakening, and the other sample must be collected at 8 a.m. (± 1 hour). These samples are collected to measure salivary progesterone and cortisol levels. If you start your period during the study, you should also collect a saliva sample for progesterone on Day 21 of your cycle if this does not overlap with the weekly collection. You will be given clear instructions on how to collect the saliva samples. You will also be provided with the necessary collection and shipping materials which will allow these salivary samples to be processed and analyzed.

At all hospital/clinic visits during the study treatment period:

- Blood samples will be collected for routine testing and to measure various hormone levels. You will need to fast for at least 8 hours (nothing to eat or drink except water since the previous midnight) before having the samples drawn at approximately 8 a.m.

- Your body temperature, heart rate, respiration rate, waist circumference, body weight, and blood pressure will be measured.

- The study staff will check and record any medications that you took since the last visit and review if you experienced any side effects.

On Day 1, in addition to the assessments described above, a physical examination and electrocardiogram will be performed. A urine sample will also be collected, and a urine pregnancy test performed on Day 1. At the end of the visit, you will be given a sufficient supply of study drug to take home. You will need to take your study drug once daily with your evening meal between 6 p.m. and midnight starting on Day 1 and for a total of 16 weeks. You must bring with you all the study drug (including all used and unused study drug blister cards and outer packaging) at every onsite visit thereafter.

On Day 7 and at Week 5 and Week 9, the study staff will contact you by telephone to assess any changes in your symptoms and if you have experienced any side effects since the last visit. The study staff will also confirm compliance with daily intake of the study drug and eDiary completion. The study staff will also check and record any other medications that you took since the last visit.

On Week 4, Week 8, and Week 16, you will need to stay at the hospital/clinic overnight. These overnight visits will last from approximately 6 p.m. on the 1st day to after 6 p.m. on the 2nd day.

During the overnight visits:

- You will receive your study drug dose onsite between 6 p.m. and 7 p.m. with your evening meal.
- The study staff will also complete a psychiatric questionnaire to confirm no significant changes since the last assessment. The questionnaire to be administered is the Columbia–Suicide Severity Rating Scale (C-SSRS) to assess suicidality.
- Blood samples for assessing pharmacokinetics (PK) (what your body does to the drug) will be taken from you before the study drug is given and at different time points after the study drug is given until approximately 6 p.m. the next day.
- Blood samples will also be collected at approximately 8 a.m. on the second day for routine testing and to measure various hormone levels. You will need to fast for at least 8 hours (nothing to eat or drink except water since the previous midnight) before having the samples drawn at approximately 8 a.m.
- A 24-hour urine sample will be collected.
- A urine pregnancy test will be performed.
- Saliva samples will be collected onsite during the morning of the 2nd day. One sample must be collected within 30 minutes of awakening, and the other sample must be collected at 8 a.m. (± 1 hour). It will not be necessary to collect other saliva samples at home for that week.
- Your body temperature, heart rate, respiration rate, waist circumference, body weight, and blood pressure will be measured.
- A physical examination and electrocardiogram will be performed.
- The study staff will check and record any medications that you took since the last visit and review if you experienced any side effects.

- You will be supplied with a sufficient supply of study drug to take home (except at Week 16). You must bring with you all the study drug (including all used and unused study drug blister cards and outer packaging) at every onsite visit.

On Week 12, in addition to the assessments described above, a physical examination and electrocardiogram will be performed.

You will take your last dose of study drug during your final overnight visit on Week 16.

FOLLOW-UP PERIOD

Thirty (30) days after your last dose of the study drug, you will be asked to visit the hospital/clinic for a final follow-up visit. During this visit:

- Blood samples will be collected for routine testing and to measure various hormone levels. You will need to fast for at least 8 hours (nothing to eat or drink except water since the previous midnight) before having the samples drawn at approximately 8 a.m.

- A urine pregnancy test will be performed.

- Your body temperature, heart rate, respiration rate, waist circumference, body weight, and blood pressure will be measured.

- A physical examination and electrocardiogram will be performed.

- The study staff will check and record any medications that you took since the last visit and review if you experienced any side effects.

STUDY PROCEDURES

The list below informs you about the information that will be requested from you and the procedures that will be performed during the study. If you do not know these tests or want to know more about them, please ask your study doctor to explain them.

- **Medical History:** A review of your complete health history to make sure you can join the study. You will be asked about any history related to your PCOS (like the background and progress of disease), prior therapies (like other drugs received for treating PCOS) and your response to these treatments, and details of other previous diseases, if any, to understand your health better. You will be asked about your birth date, sex, and race or background only for clinical research purposes.

- **Physical Examination:** A physical examination will be performed at defined visits. Your height and body weight will also be measured.

- **Vital Signs:** Your body temperature, heart rate, respiration rate, waist circumference, body weight, and blood pressure (in seated position) will be measured. Your vital signs will be measured after a 5-minute rest period.

- **Concomitant Medications:** A review of the drugs that you are taking or have taken before joining the study. This will include all prescription drugs, over-the-counter medications, herbal products, vitamins, minerals, supplements, and any other medications. Certain medications are prohibited and will be reviewed by the study doctor. It is important to let your study doctor know before starting any new drugs or supplements.

- **Electrocardiogram (ECG):** This is a painless test to check the health and rhythm of your heart.

- **Pregnancy Test:** A blood sample will be collected to perform a pregnancy test at screening. A urine sample will be collected for pregnancy testing at defined visits.

- **Adverse Events:** You will be monitored for side effects throughout the study.

- **Blood Tests:** Some amount of blood will be collected from you for tests. The maximum volume of blood taken from you during the entire study will be around 578 mL (approx. 39 tablespoons). A needle will be used to collect blood from a vein in your arm. Sometimes a blood test may need to be repeated. This can be conducted by an unscheduled visit. If this happens, the total amount of blood collected will not exceed the blood limits specified by local regulations. Blood will be collected to assess the following:

    - Complete blood count (white and red blood cells, platelets)
    - Kidney, liver, and thyroid function
    - Cholesterol and lipid levels
    - How your body processes the study drug
    - Hormone levels
    - Screening for Hepatitis B, Hepatitis C, and HIV at the screening visit

- **Urine Samples:** Urine samples will be collected to measure standard parameters and hormone levels at defined visits. A urine drug screen will also be performed at screening.

- **Saliva Samples:** Saliva samples will be collected at defined time points to measure cortisol and progesterone levels.

- **Dynamic Testing:** A low-dose ACTH stimulation test and GnRH agonist test will be performed during the screening period to determine the source of your PCOS: adrenal only or adrenal and ovarian.

- **Participant Electronic Diary (eDiary):** Starting from Day 1, you will be asked if you have taken the study drug as directed in your eDiary. You will also use the

eDiary to report any menstrual bleeding on a given day by using an illustrated diagram to help you assess your menstrual blood loss throughout the study.

- **Columbia–Suicide Severity Rating Scale (C-SSRS):** During Screening Visit 1 and each of the overnight visits, the study staff will complete this questionnaire for baseline suicidality and to confirm no significant changes since the last assessment.

What happens to the samples collected from you?

Your blood and urine samples will be sent to a central laboratory to be tested. To protect your privacy, your samples will be labeled with a unique participant code. They will not be labeled with your name or any other personal details.

Your samples will be securely stored for up to 5 years after the end of the study in the laboratory or long-term storage facility designated by the Sponsor in case any samples need to be retested. After this period of time, your samples will be destroyed unless you allow the use of your remaining samples for future research. Anyone who works with your samples will keep the samples coded, and your identity will remain confidential.

During and after the study, you will keep the right to have your samples destroyed if you contact your study doctor. If you leave the study, your samples may not be destroyed. If you want your samples to be destroyed, you will have to ask your study doctor.

All the samples and test results collected before you left the study will still be used for study purposes. After you leave this study, no new samples or test results will be taken from you for the study.

We would like to know if you allow the use of any leftover samples for future research. This means that the samples may be tested to:

- Learn more about the effects of tildacerfont on PCOS,
- Develop new drugs or devices, tests, or processes, including commercial products, or
- Other purposes that are not yet known.

At the end of this form, you will be asked if you allow future research on your samples.

What is expected from you?

While you are in the study you have to:

- Come to all study visits.

- Stop taking the current drugs you are taking for PCOS, including metformin and hormonal contraception, for 30 days before you can start taking the study drug.

- Take the study drug as directed by your study doctor.

- Complete your eDiary entries every day during the study, starting from Day 1.
- Do not give your study drug to anyone else.
- Bring all used and unused study drug blister cards and outer packaging with you to each onsite visit.
- Keep the study drug at room temperature and out of reach of children.
- Do not take any other drugs or remedies unless the study doctor has allowed them first. This includes prescription and over-the-counter drugs (including vitamins and herbal medicines).
- Tell the study doctor about any new treatment or drug you take during the study.
- Give correct and accurate information about your health history and current health.
- Tell the study doctor about any health problems you have during the study.
- Follow appropriate contraception guidelines as discussed with your study doctor. If you become pregnant, tell your study doctor as soon as you know (for additional information, please see the section on “Are there any reproductive risks?” below).
- Avoid grapefruit, grapefruit juice, and other foods that can affect the study drug while participating in the study. Your study doctor will tell you about these.
- Do not use tobacco or nicotine-containing products or drink caffeinated beverages within 30 minutes before any study-related procedure.
- Do not eat or drink caffeine-containing or xanthin-containing products (for example, coffee, tea, cola drinks, or chocolate) within 5 hours (after 3 a.m.) before a blood draw.
- Do not consume alcohol within 12 hours (after 8 p.m.) before a blood draw.
- Do not participate in heavy exercise for at least 8 hours before each study visit.
- Agree to not take part in any other study for 30 days before starting the study or during the study.
- Agree to not post or discuss the study on social media.
- Be in touch with your study doctor or study staff and tell them if you have a change in your contact details or if you no longer wish to be in the study.
- Always carry your patient emergency card.

What will happen at the end of the study or if you stop your participation early?

You will not be able to get study drug after the study is over. Your study doctor will discuss your future health care choices with you.

If, during the study, your study doctor and/or the drug company learn any new information that might make you want to stop taking the study drug or leave the study, you will be told about the new information. You can then decide if you want to still be in the study. If you leave the study, there will be no penalty, and you will not lose any benefits you are entitled to. Leaving the study will not affect the quality of the health care you are given.

The study doctor may stop study drug or end your taking part in this study for any of the following reasons:

- Staying on the study drug or in the study might be harmful for you.
- You need treatment that is not allowed in this study.
- You are having symptoms of severe depression or anxiety.
- You are having suicidal thoughts during the study.
- The study doctor believes that you may have acute adrenal insufficiency with symptoms like, frequent headaches, nausea, and abdominal pain.
- You are having abnormal liver blood test results.
- You are having an abnormal length of time that your heart needs to recharge before the next beat. This interval is determined with an ECG test.
- You are having an abnormal platelet count.
- You are experiencing significant changes in reproductive hormone levels.
- You are experiencing significant side effects.
- You did not follow instructions about what to do in the study.
- The study is cancelled, or your study treatment group is stopped.

The study doctor will tell you the reason(s) why you should stop being in the study.

If you leave the study early or if you stop taking the study drug early and decide to leave the study, the study doctor will ask you to complete an early termination visit (including a final health exam and laboratory tests) for your own safety. If you cannot see the

study doctor in person, someone from the study staff will call you by phone. This is done to have complete data about your health and safety at the end of the study.

BENEFITS AND RISKS

Are there any possible benefits of being in the study?

Taking part in this study may or may not help to treat your PCOS. Your health could improve, stay the same, or get worse. However, the data we get from you during this study may help doctors and the drug company learn more about the study drug and your disease. If the drug company runs more studies or the study drug is proven safe and effective and approved for use by the Food and Drug Administration (FDA), your data will help these future patients.

What are the potential risks and discomforts?

Risks of Stopping Your PCOS Treatments

You will have to stop taking any medications that you currently use to help control your PCOS symptoms for the entire time you participate in this study. As a result, it is possible that you will have increased hair growth and your periods may become more irregular as a result.

All drugs can cause effects that are not wanted. These are called side effects. So far, tildacerfont has been given to approximately 171 adults in research studies. People who received the study drug in the past most often reported headache, less common were diarrhea, cough, and nausea. Most side effects were mild or moderate in intensity. Your study doctor will discuss these and other side effects reported in tildacerfont studies with you and answer any questions you have.

Elevation of liver enzymes (which can indicate liver damage) has been observed with tildacerfont use at doses higher than those given in this study; this may or may not be associated with a need to scratch (pruritis) or a rash. Your liver function will be monitored throughout the study as part of the laboratory tests, and the study doctor will tell you to stop taking tildacerfont if your liver function is of concern at any time during the study. Restart of tildacerfont dosing is possible if the study doctor and Sponsor approve.

Tildacerfont is a drug that may act on the central nervous system (CNS). Drugs that act on the CNS may have an effect on your mood. Although the study drug has not been shown to be associated with an increased risk of suicidal thinking or behavior in previous clinical trials, it cannot yet be ruled out that there is an increased risk of suicidality in people who take tildacerfont. Suicidal behavior and thoughts will be monitored throughout the study. If you have any suicidal thoughts during the study, please inform the study doctor immediately and seek help. If you feel in crisis, you can call 911 and/or a Nationwide Suicide Hotline that is answered 24 hours a day with a

skilled, trained counselor. One example is the National Suicide Prevention Lifeline at 1-800-273-TALK (8255).

Because of the way the study drug works, it might be possible the study drug could cause adrenal insufficiency, which is when your adrenal glands do not produce enough cortisol. This has not happened to anyone who has already taken the study drug in other completed studies, but it is a possibility. Your study doctor will monitor you carefully, and the study staff will help you if this happens.

Adrenal Insufficiency can be severe enough to require hospitalization. You should contact the study staff promptly if you develop unusual fatigue, headaches, nausea or vomiting, unusual dizziness when you stand up, or muscle cramps.

If any side effects happen to you, tell your study doctor. Because so few people have been exposed to the study drug to date, it is quite possible that there are some side effects that are not yet known. If you notice any symptoms or side effects, even if they are not mentioned here, please tell your study doctor.

You can also experience side effects from the tests done during the study such as the following:

- Blood draw: Drawing blood may cause bruising at the place where the needle goes into the skin. Fainting, and in rare cases infection, may occur.

- Blood pressure: The blood pressure cuff used to take your blood pressure may cause discomfort or bruising to the upper arm.

- ECG: The ECG involves sticking patches on the skin on various parts of your body. The ECG is painless and takes about 5 minutes. The skin may become a little red, irritated, or itchy if you have a reaction to the gel used on the electrode.

- Fasting: You must fast at least three times, overnight, for this study. You may feel lightheaded, or unusually hungry as a result.

- As part of this research, you may be required to use one or more of the following: a phone or web app/ site, an electronic study diary (eDiary), or a device that tracks information about you. While using these, information about you may be collected and shared with the researchers or people outside of the study. This data might include personal health information, location, call logs, text message history, web browsing history, or social media use. A complete description of the data collection and sharing for an app, eDiary, or device can commonly be found in the Terms of Use, End User License Agreement, or Privacy Policy associated with the device. If you would like to read these documents, request a copy or instructions about how to access this information from the study doctor.

  While the Terms of Use, End User License Agreement, or Privacy Policy may include statements limiting your rights if you are harmed as a result of your use of

the app, eDiary, or device in this study, you do not release the study doctor, sponsor, institution, or agents for responsibilities from mistakes. You also do not waive any of your rights as a research subject.

Are there any reproductive risks?

The effects of tildacerfont on an unborn baby, a breast-fed child, and the female egg are unknown. Therefore, you cannot participate in this study if you are pregnant, breast-feeding, or planning to become pregnant during the study. If you are a female of childbearing potential (not postmenopausal or surgically sterilized), your study doctor must confirm you are not pregnant by performing a pregnancy test before you enter the study and start taking the study drug.

After joining the study, you must tell the study doctor as soon as possible if you suspect that you have become pregnant while taking the study drug.

If you are a female of childbearing potential, you must use a birth control method during the study. Birth control methods that can be used while in this study include the following:

- Be abstinent and agree to not have sexual intercourse from screening until 30 days after the last dose of the study drug.
- Any male sexual partner is vasectomized, and an absence of sperm was confirmed.
- Agree to follow any one of the following contraceptive methods, which must be in place at least 1 month before screening until 30 days after the last dose of the drug.
    - Intrauterine Device (IUD): An IUD is a small T-shaped plastic and copper device that is put into the womb (uterus) by a doctor or nurse. It releases copper to protect against pregnancy. You may not use an IUD that releases hormones.
    - Bilateral tubal occlusion.
    - Double-barrier method: A combination of a male condom with either a cap, diaphragm, or sponge with spermicide. This method is only required to be in place starting at screening and until 30 days after the last does of the study drug.

You must discuss with the study doctor the type of birth control method that you use before you begin the study. The study doctor must approve the method you use before you can enter the study.

If you become pregnant during the study, you must tell the study doctor immediately, and you will have to stop taking the study drug. The study doctor will advise you about your health care and will ask about your pregnancy and its outcome.

If you become pregnant, the study doctor will ask you and your partner if it is okay to collect details about the health of your baby for scientific and safety reasons. If required by local law, you and your partner may be asked to sign a new consent form to allow collection of data about the health of your baby.

Are there any other treatments?

Instead of taking part in this study, you may choose to receive standard treatment for treating your PCOS.

The current standard of care for PCOS includes estrogen modulators (used when someone is trying to get pregnant), hormonal contraception (combination or progesterone only birth control pills or injections), antiandrogens(for instance, spironolactone), and metformin.

Your study doctor will explain the risks and benefits of these other treatments before you decide if you want to take part in the study.

COSTS AND COMPENSATION FOR STUDY PARTICIPATION

Are there any costs if you decide to take part in the study?

The drug company that has initiated the study is providing financial support and material for this study. The study doctor and clinic are being paid by the drug company to perform this study.

Taking part in this study will not cost you anything. You will receive the study drug free of charge. You will not be charged for any of the tests that are part of the study.

The drug company will not pay for doctor visits or other treatments or tests that are not part of this study. Your insurance company will have to pay for any procedures unrelated to the study that are considered standard of care. Your study doctor can review these with you.

Your travel expenses to and from the study site may be reimbursed to you. Talk to your study doctor about any costs that might not be paid by the drug company and about any other payment limitations.

Will you receive any payment if you take part in the study?

«Compensation»

For your time and inconvenience related to your participation in this study, you will be paid for the study visits you complete according to the following schedule: [$xx.00] each for Visits [xx], [xx], and [xx]. If you do not complete the study for any reason, you will be paid for each study visit you do complete according to the schedule above.

You will be reimbursed for your time when completing your eDiary at home. You may receive up to $xx.00 for completing your eDiary.

You will be paid by the study site via cash, check, or equivalent (for example, gift card).

If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

You will be paid _____ ***["following each completed visit", "monthly", "quarterly", "at the end of your participation in the research study", "following each completed visit or at the end of your participation in the research study, whichever you prefer"]***.

If you have any questions regarding your compensation for participation, please contact the study staff.

[OR]

You will not receive any monetary compensation for your participation in this study.

Will you receive compensation for injury resulting from the study?

You should inform the study doctor as soon as you feel that you have had an illness or injury related to the study so that you can get proper health care. If you are injured as a result of taking part in this study, the study doctor will recommend or provide medical treatment, including emergency treatment, if necessary. If you are having an emergency, call 911 and/or seek immediate care. Your insurance may be billed for this treatment; however, you should check with your insurance company that taking part in this study will not affect your coverage under your medical insurance policy. Your study doctor will explain more about this to you.

The study Sponsor will pay for the reasonable medical charges that are not covered by your insurance policy or other insurance programs available to you and that are necessary to treat the injury with the standard of care treatment, provided the injury was caused by the study drug or properly performed study procedures. The Sponsor has no plans to reimburse you for medical expenses related to the natural progression of, or failure of the study drug to improve, your disease, illness, or condition; any other pre-existing condition; or any injury or event that would have been expected from the standard treatment for your condition. You will not be reimbursed by the Sponsor for any injury that was caused by you or a third party.

It is important that you are careful to follow all the instructions given by the study doctor and study staff for this study.

By signing and dating this form, you are not giving up your legal rights and are not releasing the study doctor or drug company from their legal and professional responsibilities.

CONFIDENTIALITY

What happens to the data collected about you?

The information below explains how your health records and the research data we get from the samples collected from you during the study may be used and shared with others.

The study site will record basic personal details about you, including your name, contact details, sex, height, weight, and racial origin (to be used only for study purposes), as well as data on your health history and any study data collected about you during the study.

The following people may review your health records to make sure that the study is being run as planned and that the data collected about you are correct:

- Government health agencies and their staff
- Drug company staff observing the study (monitors and auditors)
- Members of the ethics committee/Institutional Review Board
- Contractors and consultants working for the drug company and for health authorities
- Other representatives of the drug company
- Employees of the drug company or its authorized agents, who may be with the study monitors and auditors for quality and training purposes.

All staff with access to your records are required to keep your data private.

To ensure your privacy, you will only be identified by a code. Your name and other data that can identify you will not be attached to records or samples released to the drug company and its service providers. Only the study doctor and allowed staff will be able to connect this code to your name with a list that will be kept safe by the study site for 5 years. If allowed by local laws, your birth date may also be recorded to help identify your study records.

After your coded data are sent to the drug company, the results of the study will be analyzed and reported. The drug company may use your coded information to get the study drug approved for use in this country and/or different countries.

The results may also be analyzed again at a later date or may be combined with the data of other studies. The drug company and people who work with the drug company may use the results of this study to understand the disease better, to review the safety or effectiveness of the study drug, or for other research purposes.

Your personal data will be shared with the drug company if you agree to take part in the study.

You have the right to access, correct, and limit the access to your personal data at any time during the study. You can exercise those rights by telling the study doctor.

However, in order to protect the scientific value of the study, your right to access these data may be delayed until the study data are analyzed, unless required to be made known earlier by local law.

What if you change your mind and do not want your data to be used or disclosed?

If you leave the study early, data obtained while you were in the study may still be kept with other data obtained as part of the study. Normally, no new data will be obtained for the study unless you clearly agree to that. However, the law requires that you report side effects that you experience even after you leave the study.

Will information about this study be publicly available?

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

After this study is over, a brief report of the overall results will be prepared for the general public. The study results may also be shared with scientific journals and the scientific community. Whenever the results of the study are shared or published, your identity will remain private.

CONTACTS

Whom to contact about this study?

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00057328.

Statement of Consent

- I have read and understand the statements in this informed consent form.
- I have had the chance to ask questions, and I am satisfied with the answers given to me.
- I understand that this study may only be performed by collecting and using my health data. Therefore, by signing and dating this form, I specifically give permission for my data to be checked, transferred, and processed as follows:
  - The authorized representatives of Spruce Biosciences, Inc., the ethics committee, and inspectors for regulatory authorities may review my health data by directly accessing my health records.
  - Study data, including my coded health data, may be used and shared for legitimate study and scientific purposes.
- I agree to take part in this study of my own free will.
- I understand that I will receive a copy of this signed and dated written informed consent form.

Spruce Biosciences, Inc. would like you to allow them to use your blood samples for future research that may help understand more about PCOS:

☐ _____ Yes, I agree to have my sample(s) used for future research related to PCOS.
Initial

☐ _____ No, I do not agree to have my sample(s) used for future research related to PCOS.
Initial

_____

Printed Name of Subject, in full

_____

Signature of Subject **Date (dd-Mmm-yyyy)**

- I have presented the study and answered the subject's questions.
- I will give the subject a copy of this signed and dated informed consent form.

_____

Printed Name of Person Obtaining Consent (Investigator/Delegate), in full

_____

Signature of Person Obtaining Consent **Date (dd-Mmm-yyyy)**

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the study doctor and study staff will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the study staff may share health data about you with authorized users. Authorized users may include:

- Representatives of Spruce Biosciences, Inc.
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Governmental agencies of other countries.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this study, if applicable.
- A data safety monitoring board which oversees this study, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the study drug works and is safe.

- To compare the study drug to other drugs.
- For other research activities related to the study drug.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____

Printed Name of Subject, in full

_____

Signature of Subject **Date (dd-Mmm-yyyy)**