INFORMED CONSENT AND AUTHORIZATION FORM

Study Title: A randomized, double-blind, placebo-controlled, phase 2b dose-ranging study to assess the efficacy and safety of OBE2109 in subjects with endometriosis associated pain

Study #: 15-OBE2109-001

Sponsor: ObsEva S.A.

Study Doctor: Michael L. Twede MD

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For California participants: Before you read this consent form, you should read and sign a copy of the California Experimental Subject's Bill of Rights. Ask the study staff for a copy of this document if you haven't already received one.

You should keep a copy of this form.
If you have any questions or problems during the study, call the phone number(s) above.

SUBJECT INFORMATION

1. Introduction

You have been invited to participate in a clinical research study. This study is testing whether an investigational drug called OBE2109 being developed by a Swiss company, ObsEva, can reduce endometriosis-related pain in women.

An investigational drug is one that is being tested and has not been approved for sale in the United States by the U.S. Food and Drug Administration (FDA).

To be eligible for this study, you must be premenopausal between the ages of 18–45 inclusive, your endometriosis must have been confirmed surgically, and you must have moderate to severe endometriosis-related pain.

ObsEva is the Sponsor of this study and pays the study doctor to perform the study.

Before you can make an informed decision to participate in this research study, you should understand the possible risks and benefits of this study. This process is known as informed consent.

Quorum Review has reviewed this study. Quorum Review is a group of medical and non-medical experts set up to help protect the rights and welfare of research subjects. This does not mean your participation in the study is approved. It also does not mean the study is without risk.

This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not understand.

Take as much time as you need to make a decision about joining the study. You may take home an unsigned copy of this consent form to think about or discuss with family, friends, or anyone you choose before making your decision.

If you decide to participate in this study, you will be asked to read and sign this consent form to confirm that you have had the study explained to you, and you have agreed to participate. You will receive a copy of the signed consent form.

2. General Information

Endometriosis is a hormone-dependent condition in which tissue that normally grows inside the uterus grows outside the uterus. Clinical symptoms can include painful menstruation, chronic pelvic pain, pain with defecation (bowel movements), and pain during intercourse.

OBE2109 is a new oral drug that is being developed as a possible treatment for pain associated with endometriosis. OBE2109 reduces the production of sex hormones such as luteinizing hormone and estradiol. The level of hormone reduction is dependent on the dose of OBE2109.

To date, about 200 women, including healthy women and women with endometriosis, have received at least one dose of OBE2109. Doses and duration of dosing has varied across the different studies conducted to date. One study already tested a 200 mg dose for up to 3 months.

It is important that you are not intending to become pregnant and will take precautions not to become pregnant while taking the study drug.

Being in this study does not replace your regular medical care.

3. What is the purpose of this study?

The purpose of this study is to test the safety and effectiveness of different doses of OBE2109 compared to placebo (a tablet that looks like a drug but has no drug in it) in women with moderate to severe pain associated with endometriosis.

Be aware that this form refers to OBE2109 and placebo as “study drug.”

4. Study Information

This study is expected to enroll 330 women across approximately 60 study sites in the U.S. and Europe.

The study consists of four periods:

1. Screening Period (11 weeks plus/minus 5 weeks) – no study drug given
2. Dosing Period A (12 weeks) – study drug (OBE2109 or placebo) taken once daily

3. Dosing Period B (12 weeks) – study drug (OBE2109) taken once daily
4. Follow-up Period (24 weeks) – no study drug given

Your participation in this study could last just over one year (between 54 and 64 weeks) and will include approximately 12 study visits to the research center.

If you decide to be in this study, you will have to stop taking your regular oral contraceptives or other sex hormones during the entire study. This is known as a “wash-out.” You may be required to stop taking oral contraceptives or other sex hormones for a period of up to 6 weeks between signing the informed consent and starting the screening period.

Recruitment of subjects will be competitive between the participating study sites. If the target number of 330 subjects has been reached, and you are in screening, there is a possibility that you will not continue in the study.

If you qualify for the Dosing Period of this study, you will be randomly assigned by chance (like the flip of a coin) to one of six study dosing groups.

During Part A of the study, you will take either OBE2109 (50, 75, 100, or 200 mg per day) or placebo tablets for 12 weeks. If you are in the sixth group, you will start taking 75 mg of OBE2109 per day, after which the dose may go up to 100 mg, down to 50 mg, or stay the same. Neither you nor the study doctor or study staff will be able to pick which study group you are in.

Placebo looks the same as OBE2109 but does not contain any active drug, and is used to make it possible to assess OBE2109’s effects.

You have an equal chance of being in any of the six study groups. You will have an 83 percent chance (five chances out of six) of receiving OBE2109 and a 17 percent chance (one chance out of six) of receiving placebo for the first 12 weeks.

In Part B of the study, all subjects (including those who received placebo in Part A) will receive OBE2109 for 12 weeks. Furthermore, the Part B daily dose of OBE2109 may or may not change compared to the dose received in Part A. Neither you nor your study doctor will be informed if your dose has been changed.

This is a double-blind study, which means that throughout the study, neither you nor your study doctor will be informed which study drug (OBE2109 or placebo) you will receive. In case of an emergency, your study doctor can get this information.

You will receive study drug tablets with instructions how to take them during this study. You will take two tablets of the study drug once a day for 24 weeks. Both tablets should be taken at about the same time every morning. The dosing will start between the first and seventh day of your menstrual cycle after the screening period (i.e., from the 1st day of menstruation up to the 7th day of the cycle).

Because this is a research study, the study drug will be given to you only during this study and not after the study is over. However, for subjects who complete the Parts A and B dosing periods and are willing to continue dosing with OBE2109, an extension might be proposed. The extension would consist of a further 28 weeks of dosing with OBE2109 (no placebo) and a 24-week Follow-up Period. A separate consent form will be provided to you if you wish to participate in the extension.

5. What will I have to do?

If you agree to participate in this study, you will first have some tests and evaluations to determine if you are eligible for this study. These activities take place during a Screening Period, before participation in the main part of the study.

1. Screening Period

The Screening Period will last about 11 weeks (plus/minus 5 weeks) depending on the length of your menstrual cycle. It must include at least two full spontaneous menstrual cycles. During this time, you will be asked to visit your study site two or three times.

The following activities, tests, and procedures will be done initially to determine if you qualify to continue in this study:

- Informed Consent – please note that the Informed Consent may be signed at a prior date than the screening visit if wash-out of oral contraceptives or other sex hormones is required.
- Review that your endometriosis is surgically confirmed. Your study doctor may ask for medical reports from your regular treating physician.
- You will be asked about your past and present health and any medications you are and were taking, including your history of endometriosis diagnosis and treatments. If you are currently taking any therapies that are not allowed during this study, your study doctor may ask you to stop taking these for a specific time and wait until you can continue in the study.
- Demographic data collection (e.g., age, date of birth)
- Physical examination (check-up) including measurement of your weight and height
- Your blood pressure and heart rate will be measured
- TransVaginal UltraSound (TVUS) of the uterus and ovaries to measure the thickness of the endometrium (womb lining) and to rule out any clinically significant gynecological conditions
- Gynecological examination, including assessment of pelvic pain severity
- Screening procedure for cervical cancer (PAP smear), unless you have had a PAP smear within the past 12 months showing no clinically significant abnormalities requiring surgical intervention and for which results are available
- Sampling of cells (biopsy) from your endometrium, unless a sample was taken within the past six months showing no malignancy and for which results are available
- Manual breast examination (by palpation)
- Blood sampling (approximately 4 teaspoons or 20 mL in total) to check your blood parameters including hormone levels.
- Urinary protein dipstick (to quantify proteins in your urine)
- Collection of a urine sample for a pregnancy test. The study doctor or study staff will tell you if the pregnancy test results are positive. The result of the pregnancy test must show that you are not pregnant for you to participate in this study.

- Birth Control Counseling/Contraception Dispensing. The study doctor or study staff will review with you the methods of birth control considered effective for use during this study.
    - You will be provided free of charge with condoms with spermicide for the duration of the study, if you wish.

You will be provided for free a limited amount of ibuprofen and/or acetaminophen as standard pain medications to be taken when required to treat pain (but not to prevent anticipated pain). You are asked to take only these pain medications and avoid taking other pain medication if possible. However, if the provided pain medications are not suitable for you, you are allowed to take another pain medication brand. In any case, you must not take long-acting pain medications (that require dosing once a day or longer). All intake of the provided standard pain medication, including the amount you took, needs to be recorded by you in your electronic diary (eDiary, see below).

Pain Medication Paper Diary

You will be provided with a pain medication paper diary to report any intake of pain medications other than the standard ones provided (ibuprofen, acetaminophen), or to record the reason for which you took the standard ones provided in case you didn't take them for endometriosis-related pain.

Electronic diary (eDiary)

Your study doctor will give you an electronic diary (eDiary) and instructions to take home. You will be trained on how to correctly use and complete the eDiary.

It is important that you complete your eDiary every day, because it will determine whether you are eligible to continue in the study and it will help to assess your endometriosis symptoms.

You will need to start using your eDiary as soon as possible and keep using it daily until the Week 36 visit.

You will need to record the following in your eDiary:

- **Daily** (at about the same time each evening):
    - Intake of study drug
    - Responses to questions about your endometriosis-related pain and difficulty doing your daily activities
    - Pain medication use (if any)
    - Occurrence and severity of vaginal bleeding
- **Weekly** (at the same time as the daily assessments that day):
    - Pain with defecation (bowel movements)
- **Every Four Weeks** (at the same time as the daily assessments that day):
    - Severity of your endometriosis condition over the past 28 days

2. Dosing Period

You are not allowed to get pregnant while taking the study drug (i.e., during the Dosing Periods). You will be asked to use double-barrier, non-hormonal methods of contraception (e.g., condoms or diaphragm, each with spermicide) during the entire Dosing Period. Condoms with spermicide will be provided to you at no cost, if you wish.

Baseline Visit (Day 1)

The Baseline Visit will be scheduled between the 1st and 7th day (inclusive) of your menstrual cycle directly after the two Screening menstrual cycles. You should let your study site know as soon as your period starts.

For the Baseline Visit, you will need to come to the study site in the morning and to bring your eDiary. You will be asked not to eat or drink anything, except water, before you come to the study site in the morning and up to the time of the blood sample collection for checking your blood parameters.

During the Baseline Visit, you will have the following assessments and procedures:

- Your study doctor will make sure you still satisfy the study requirements.
- Your eDiary and pain medication paper diary will be checked for good completion and eligibility.
- You will be asked about your health since the last visit and any changes in your medications.
- A physical examination (check-up) will be done.
- Your blood pressure and heart rate will be measured.
- A urinary protein dipstick will be done (to quantify proteins in your urine).
- Urine pregnancy test and contraception counseling will be performed.
- You will be asked to answer questions about your quality of life and overall status over the previous four weeks.
- Your bone mineral density (BMD) will be assessed using dual-energy X-ray absorptiometry (DXA) of the femoral neck (the region just below the ball of the hip joint), hip, and spine. You may be asked to return another day for these tests.
- Fasting blood samples will be taken (approximately 4 teaspoons or 20 mL in total) to check your blood parameters, including hormone levels.

If all these tests confirm your eligibility to continue in the study, you will be randomized to one of the six study groups. You will be given a three-month pack of the study drug together with instructions on how and when to take the tablets. You will take the first two tablets of the study drug under supervision at the study site.

- Blood samples will be taken (approximately 2 teaspoons or 10 mL in total) to determine the amount of study drug in your blood. You will have one blood sample taken before taking your first dose of study drug at the study site, and then another blood sample will be taken about 1.5 – 2 hours after study drug administration.

Study drug administration (until the end of Week 24)

You will have to swallow two tablets – one from the yellow blister pack and one from the blue blister pack – at about the same time each morning.

Note that, at Week 4 and Week 16, you will be asked to not take your study drug at home but wait until you are at the study site.

Your study doctor will give you condoms with spermicide, if you wish, and additional pain medications (if required) to be used during the study.

You will be given a Subject Card stating that you are participating in the study and including emergency contact numbers to dial immediately in case of a medical emergency. You must carry the card with you as long as you are in the study and show it to any medical staff who may be involved in your healthcare.

The study staff will schedule your next visits with you.

Every-four-week visits during Dosing Period A (Weeks 4, 8, 12) and Dosing Period B (Weeks 16, 20, and 24)

During Dosing Periods A and B, you will come to the study site 6 times (once a month) for regularly scheduled visits.

At the Week 4 and Week 16 visit days, you will need to take the study drug when told to do so by study staff during the visit to the study site. On the other dosing visits (Weeks 8, 12, 20, 24), you will take your daily dose of study drug at home at the usual time in the morning.

The following tests and procedures will be performed at each of the regularly scheduled every-4-week dosing visits, unless indicated otherwise:

- eDiary check and pain medication paper diary check
- You will be asked about your health since the last visit and any changes in your medications
- Physical examination (check-up) at Week 12 and Week 24 (including measurement of your weight at Week 24)
- Blood pressure and heart rate measurement
- Gynecological examination including assessment of pelvic pain severity (Week 12 and Week 24)
- TVUS of the uterus including endometrium (womb) and the ovaries (Week 12 and Week 24)
- Sampling of cells (biopsy) from your endometrium at Week 12 and Week 24 may or may not be required, depending on results of the TVUS.
- Blood samples (approximately 5 teaspoons or 25 milliliters) to check your blood parameters including level of hormones and to measure the study drug in your blood.
- Urine protein dipstick (to quantify proteins in your urine)
- You will be asked to answer questions about your overall status and your quality of life for the past four weeks, and about your change in overall status since the beginning of the study (Week 12 and Week 24)

- Bone mineral density (BMD) measurement using dual-energy X-ray absorptiometry (DXA) of the femoral neck, hip, and spine (Week 12 and Week 24). You may be asked to return another day for these tests.
- Urine pregnancy test and contraception counseling will be performed.
- Return of unused study drug from Part A and receipt of the Part B three-month pack of study drug (Week 12)
- Return of unused study drug from Part B (Week 24)

3. Extension Study

If you complete Dosing Periods A and B, you may be invited to continue in an extension to the study. If you accept and are eligible, you will need to sign a new consent form to enter the extension to continue taking OBE2109 for 28 weeks, followed by a 24-week drug-free Follow-up Period. You do not have to agree to participate in the extension of the study in order to participate in the main study.

If you do not take part in the extension of the study, you will directly enter the 24-week drug-free Follow-up Period after the Week 24 Visit.

4. Follow-up Period

During the Follow-up Period, you will not receive study drug. However, you will continue to make the recordings in your eDiary and pain medication paper diary as before (up to the study visit Week 36).

Contraception is not mandatory during the Follow-up Period. However, hormonal contraception (e.g., contraceptive pills) is not permitted up to the Week 36 visit. If you wish to use a contraceptive method, non-hormonal contraception should be used during this time. You may continue to use the provided condoms with spermicide.

During the Follow-up Period, you will visit the study site 3 times for scheduled visits.

The following tests and procedures will be performed at the Weeks 28, 36, and 48 visits, unless indicated otherwise:

- eDiary check and paper pain medication diary check (Weeks 28 and 36)
- You will be asked about your health since the last visit and any changes in your medications.
- Physical examination including measurement of your weight (Week 36)
- Blood pressure and heart rate measurement (Weeks 28 and 36)
- Blood samples (approximately 4 teaspoons or 20 milliliters) to check for your blood parameters including hormones (Weeks 28 and 36)
- Urine protein dipstick (Weeks 28 and 36)
- Gynecological examination including endometriosis pain assessment (Week 36)
- A sampling of cells (biopsy) from your endometrium may or may not be done at Week 36 depending on previous results.
- TVUS of the uterus including endometrium (womb) and the ovaries (Week 36)
- Manual breast examination (by palpation) at Week 36

- Urine pregnancy test and contraception counseling (Weeks 28 and 36)
- At week 36, you will be asked to answer questions about your overall status and quality of life for the past four weeks and about your change in status since the beginning of the study.
- Return of eDiary and paper pain medication diary to study personnel (Week 36)
- BMD assessment using dual-energy X-ray absorptiometry (DXA) of the femoral neck, hip, and spine (Week 48)
- Completion of a study exit form (Week 48)

Will I need time to recover after my participation in the study?

Ask the study doctor or study staff for the estimated recovery time of your participation in this study.

Withdrawal from the Study

Participation in this study is voluntary. You can stop participating in the study at any time. If you decide not to participate in the study or to withdraw from the study, the quality of your regular medical care or any benefits to which you are otherwise entitled will not be affected and there will be no penalty to you.

Your study doctor may also end your participation in the study, even if you want to stay in the study, if he/she believes that it is in your best interest or if you are unable to follow the requirements of the study. In addition, your participation may be ended early without asking for your consent if the sponsor makes a decision to temporarily or permanently discontinue the study for safety, ethical, compliance or other reasons.

When you withdraw from the study for any reason, all study drug and study drug packaging, including unused and empty blister packs, the eDiary device, and the paper pain medication diary must be returned to the study site. You will also be asked to return to the study site so that the study doctor may perform a final evaluation. If you discontinue participation in the study between Day 1 and the Week 24 visit, you will undergo the procedures required at the Week 24 visit. If you discontinue between the Week 24 and Week 36 visits, you will undergo the procedures required at the Week 36 and Week 48 visits. If you discontinue between the Week 36 and Week 48 visits, you will undergo the procedures required at the Week 48 visit.

If you leave the study, the study doctor and study staff will still be able to use your information that they have already collected.

6. What are your responsibilities?

In order for this study to provide good information about how OBE2109 works in subjects with moderate to severe endometriosis pain, you will be expected to do the following:

- Follow the instructions of your study doctor, including requirements to use appropriate birth control methods;
- Come to all of your scheduled study visits and procedures (e.g., DXA scan, TVUS);

- You may be required to stop certain medications and supplements you are currently taking. Certain medications you are taking or have taken in the past may keep you from being in the study. Please review all of your medications with your study doctor. Some procedures/conditions you may have had in the past may keep you from being in the study as well;
- Take and store your study drug as instructed and return all of the unused study drug and empty blister packs to the study site at each visit;
- Do not share your study drug or pain medications with anyone. You are the only person allowed to take the study drug or pain medications;
- Keep the study drug and study supplies out of the reach of children and persons of limited ability to read or understand;
- Take only the pain medication provided in this study and avoid taking other pain medication if possible. However, in any case, you must not take long-acting pain medications (that require dosing once a day or less frequently). All intake of the standard pain medication, including the amount you took, needs to be recorded by you in your eDiary;
- Please don't take the pain medication as a preventive measure (because you expect pain on this day).
- Complete your electronic daily diary (eDiary) and the pain medication paper diary completely, honestly and as instructed by the study staff. Bring the eDiary device and pain medication paper diary to the study site at each visit. Handle the eDiary device with care. Return the eDiary device and the paper pain medication diary at the Week 36 visit;
- Tell your study doctor or study staff about any problems with your health even if you do not think they are important. Failure to report symptoms may be harmful to your health. Tell them if you are hospitalized for any reason during the study, or if you stop taking the study drug, even if you do not think the problems are caused by the study drug;
- Tell the study staff if you wish to stop your participation in the study;
- Do not participate in any other research studies during your participation in this study;
- If of childbearing potential, follow contraception counseling and use double non-hormonal barrier contraception such as condoms or diaphragms, each combined with spermicide, to prevent pregnancy during the entire Dosing Period of the study. The provided condoms with spermicide are suitable as contraceptive and free of charge for you;
- Tell the study staff about the type of birth control methods used and if you had any problems with them.
- The timing of your visits is very important, and you should understand that you must try to make all your scheduled appointments. You might have to come to the study site more often than if you were not participating in a clinical trial.

7. What are the possible risks and discomforts?

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought before agreeing to participate in any scientific trial.

1. What are the known risks and discomforts?

OBE2109 risks

Like all drugs, OBE2109 can cause side effects, although not everybody experiences them. Your study doctor will be monitoring you for side effects from the study drug. It is important you report any side effects that you have to your study doctor right away. Your study doctor may give you other drugs to help with side effects. If you or your study doctor think you cannot tolerate the side effects, the study drug may be stopped altogether and you will be withdrawn from the study.

Ask the study doctor if you have questions about the signs or symptoms of any side effects you read about in this consent form.

Please tell the study doctor or study staff right away if you think you have any symptoms or side effects. Failure to report symptoms may be harmful to your health. Also, tell them if you have any other problems with your health or the way that you feel during the study, if you are hospitalized for any reason during the study, or if you stop taking the study drug, even if you do not think the problems are caused by the study drug.

All drugs can have side effects. The possible side effects and risks associated with OBE2109 are described below.

Common side effects associated with OBE2109 during Clinical Studies

The most common side effects of OBE2109 observed in women include:

- Disturbances or changes in the menstrual cycle (irregular vaginal bleeding) or absent menstrual periods
- Hot flashes

Effects on ovulation and risk of pregnancy

OBE2109 is not a contraceptive, that is, it does not prevent pregnancy. One subject in a previous study became pregnant while receiving OBE2109.

Studies in animals have shown that animals receiving OBE2109 have lower pregnancy rates, which is explained by the mechanism of action of OBE2109 (i.e., suppression of sex hormones). However, these effects were reversible when dosing was stopped.

If you decide to participate in this study, you must use birth control measures as instructed by your study doctor, and take every precaution to avoid becoming pregnant during the entire dosing duration. You will be provided free of charge with condoms with spermicide for the duration of the study, if you wish.

If you think that you may be pregnant, decide to become pregnant, or have a positive pregnancy test at any time during the study, it is important that you tell the study doctor immediately. If you become pregnant, you must stop taking the study drug, and you will not be allowed to continue in the study. However your study doctor will request some information on your pregnancy up to the birth if applicable and may share this information with the study sponsor.

In this case, you may request to know exactly what study drug group you were assigned to during the study (also known as un-blinding). Your study doctor will discuss your options and next steps with you. You will be asked to provide information about your pregnancy, your delivery, and about your baby (for example, sex, birth weight, and if there were any birth defects).

Bone Mineral Density and the risk of fractures

Similar to other drugs that reduce female hormone levels in the body, particularly estrogen levels, OBE2109 could increase the risk of reduced bone mineral density. Higher doses and longer exposure to OBE2109 may result in greater bone loss. Lowering of bone mineral density can place a woman at risk for osteoporosis (softening of the bones) and fractures (broken bones). Inform the study doctor if you or family members have been diagnosed with osteoporosis, if your mother had a hip fracture, if you have used or are now using drugs such as corticosteroids or drugs to treat epilepsy (convulsions or seizures), and if you have ever had any fractures.

Because the risk of fractures depends on many factors (including your age, overall health status, bone mineral density, and smoking habits), you should discuss the possible risk of fractures specific to you with your study doctor.

Effects on liver enzymes

While you are on OBE2109, the amount of certain liver enzymes in your blood may change. These effects are usually reversible. During the Dosing Period and Follow-up Period (until the Week 36 visit), your liver enzyme levels will be monitored.

Effects on lipids

Lipid changes, such as increases in total cholesterol, triglycerides, and low density lipoprotein cholesterol are associated with lower levels of estrogen, whether this occurs naturally at menopause, surgically (with removal of the ovaries), or medically (varying pharmaceutical agents). Similar changes in serum lipids have occurred in clinical studies with OBE2109. While the significance of these lipid changes in healthy young women is unknown, your levels will be monitored during this study.

Drug Interaction

To date, clinically significant drug interactions have not been identified. However, it is very important that you tell the study doctor about any vaccines, medicines (either prescription or over-the-counter), or supplements such as vitamins or herbs that you are taking.

Allergic reaction risks

There is always a possibility of an allergic reaction to any drug.

Some allergic reactions to drugs could become severe or life-threatening. To date, no such reaction has been reported with OBE2109. Symptoms of a severe or life-threatening allergic reaction include:

- difficulty breathing
- fast pulse
- rash
- sudden drop in blood pressure (feel dizzy or lightheaded)
- sweating
- a feeling of dread
- swelling around the mouth, tongue, lips, throat, or eyes
- wheezing when you take a breath
- inability to breathe without assistance

If you have any of the above symptoms, get medical help and/or go to the emergency room, and contact your study doctor.

Inform the study doctor if you have had any allergic reaction to drugs in the past, or if you know that you have an allergy or are sensitive to any other drugs like OBE2109, e.g., gonadotropin releasing hormone (GnRH) antagonists such as cetrorelix (Cetrotide®) or ganirelix (Antagon®) or gonadotropin releasing hormone (GnRH) agonists such as leuprolide acetate (Lupron®), nafarelin acetate (Synarel®), or goserelin acetate (Zoladex®).

2. What are unknown risks and side effects?

OBE2109 is an experimental drug that is being developed for the possible treatment of women with endometriosis-associated pain. Not all of the side effects are known at this time. For this reason, you will be watched for known and other unknown, possibly serious side effects. You will be told if there is new information that may change your willingness to stay in this study, as it becomes available.

You might have side effects or discomforts that are not listed in this form, which may include your condition getting worse or even death. Some side effects may not be known yet. Please tell the study doctor or study staff right away if you have any symptoms or side effects; this includes your condition getting worse. Failure to report symptoms may be harmful to your health. Also, tell them if you have any other problems with your health, change in the way you feel during the study, if you are hospitalized for any reason during the study, or if you stop taking the study drug, even if you do not think the problems are caused by the study drug.

Pregnancy testing and birth control counseling

Taking OBE2109 may involve unknown risks to a pregnant woman, an embryo, a fetus, or a nursing infant. Some drugs cause premature (early) birth or birth defects. The potential risks of OBE2109 on an unborn child are unknown.

You will be tested regularly throughout the study for pregnancy. You must have a negative pregnancy test at all times during the Dosing Period of the study. In addition, you will be

counseled at every visit throughout the study (until Week 36 inclusive) on the importance of pregnancy prevention and the use of appropriate and effective methods of birth control.

If you qualify for and decide to participate in this study, you must use one of the following birth control methods during the entire Dosing Period of the study (until the end of Week 24) and take every precaution to avoid becoming pregnant:

- Sexual abstinence;
- Partner with a vasectomy performed at least 6 months prior to the study and confirmed azoospermia (no measurable level of sperm in the semen);
- Double non-hormonal barrier contraception such as condoms or diaphragms, each combined with spermicide.

If you are sterilized, you must have had tubal ligation sterilization at least two months before the first screening visit.

If you are already using a method of birth control, the study doctor or study staff will discuss with you whether your current method of birth control is acceptable for use during this study.

After the end of the Dosing Period (end of Week 24), contraception is no longer mandatory. However, hormonal contraceptives (e.g., oral contraceptives) are not permitted up to Week 36. If you wish to use a contraceptive method, non-hormonal contraception should be used up to Week 36.

3. What other risks are related to study procedures?

- **Washout risk:** If you stop your regular medication or supplement to be in the study, your condition may become worse or stay the same. Please tell the study doctor or study staff right away if you have any problems when you stop or change your regular medication or supplement.
- **Placebo risk:** Some people in Part A of the study will get placebo instead of OBE2109. If you receive placebo during Part A, it is possible that your endometriosis pain will not be relieved or get worse. Please ask the study doctor or study staff if you have any questions about placebo.
- **Gynecological examinations (breast and pelvic examination/PAP Smear):** There may be mild discomfort or pain associated with the gynecological examinations. Some women experience discomfort from the pressure applied on the breast, discomfort from the pressure applied during the pelvic examination when the speculum is inserted into the vagina, or when the cervix is scraped to take a PAP smear. There may be temporary spotting or bleeding after the PAP smear.
- **Transvaginal Ultrasound (TVUS):** Ultrasounds are usually a painless procedure; however, there may be varying degrees of pressure or discomfort as the probe is inserted into the vagina and moved around to allow for the uterus and ovaries to be examined until desired pictures are captured. TVUS may cause mild vaginal spotting. Ultrasounds do not use x-rays.
- **Blood sample collection:** During the study, you will have multiple blood samples collected. You may experience some pain and/or bruising on your arm where the blood is collected. In some instances, a blood clot near the collection site may form or an infection may occur. Some people experience dizziness or faintness during or shortly

after having blood drawn. If you feel like you may faint, you should notify the study staff and lie down immediately to avoid a possible injury caused by falling. Although one attempt at blood collection is usually all that is necessary, additional attempts may be needed if the first attempt is unsuccessful.

- **Dual Energy X-ray Absorptiometry (DXA):** DXA is a noninvasive procedure. The amount of radiation used is small – less than one-tenth the dose of a standard chest x-ray, and less than a day's exposure to natural radiation which you experience on an everyday basis. Women should always inform their study doctor or x-ray technologist if there is any possibility that they are pregnant.
- **Endometrial biopsy:** The risks of endometrial biopsy include bleeding, infection, minor discomfort, pain, and risk of uterine perforation (tearing or making a hole). Perforation may require hospitalization, antibiotic therapy, or additional procedures necessary to repair the perforation site. If a sedative is used during the biopsy, the study doctor will describe its risks to you (which could include an allergy to the anesthesia used).
- **Pain medication (analgesics) risks:** The standard pain medication you may take in this study may cause side effects. Ask your study doctor about the risks of your analgesic rescue medication(s).
- **Questionnaires:** Filling out questionnaires or answering the study doctor or study staff's questions could lead you to feel uncomfortable or upset. Please tell the study doctor or study staff if you feel uncomfortable or upset while filling out a questionnaire or answering questions. You have the right to refuse to answer any question.
- **Loss of Confidentiality:** There is a risk of loss of confidentiality of your information. You will read more about the protection of your information later in this form. Please ask the study doctor or study staff if you would like to know more about how your information will be protected while you are in this study.

8. What happens with my blood and urine samples?

The blood and urine samples collected during the study will be used exclusively during the study and will be destroyed after the analyses. Blood and urine samples will be analyzed at laboratories identified by ObsEva.

Your samples will not be labeled with your name or other directly identifying information. Your samples will have a code instead (a subject identification number). The list that matches the code with your name and information will be stored separately from your samples. The samples and reports of the analyses will not identify you.

If you change your mind later, be aware that your samples may or may not be withdrawn from the research, depending on the sponsor's policies. You can ask the study doctor or study staff about this.

9. What are the costs and compensations?

Study participation will be free of charge for you. You will not be charged for the required study drug (OBE2109 or placebo) or procedures during the study. You and/or your health-care payer/insurer will be billed for the cost of your regular medical care. You can ask the study

doctor or study staff to find out more about costs. You will be provided free of charge with condoms with spermicide for the duration of the study, if you wish.

Before you agree to be in this study, you should contact your health-care payer/insurer to see if your plan will cover any costs required as part of your participation.

Compensation and Reimbursement for participation

You will be paid at a rate of $50 for each Study visit you finish to cover any inconvenience and out of pocket expenses.

In addition to payment for being in this study, you may be reimbursed for travel and parking costs. The study doctor or study staff can tell you more about this reimbursement and when you will receive it.

10. What are the potential benefits of Study participation?

The information that is obtained during this study may be useful scientifically and thus be helpful to others with the same condition in the future.

You may or may not receive any direct medical benefit from being in this study. Your condition may get better, it may get worse, or it may stay the same.

You may get placebo for part of the study, which is a tablet that looks like a drug but has no drug in it.

11. What alternatives to Study participation exist?

You do not have to participate in this study to receive treatment for your condition.

Alternatives for your condition include:

- Non-steroidal anti-inflammatory drugs (NSAIDS) (such as ibuprofen or naproxen): the potential benefit is relief of pain; risks of NSAIDS include stomach upset, inflammation, or ulcers;
- Hormonal therapy (such as oral contraceptive pills or hormonal blockers): the potential side effects and risks of hormonal therapy vary according to the type of drug, and include changes in or irregular menstrual bleeding, nausea, skin changes, blood clots, or heart attacks. Ask your study doctor if you have any questions about hormonal therapy.

Radical surgery (surgery to remove the uterus and ovaries) may be performed if the above treatment options are unsuccessful: the potential benefit is treatment of endometriosis lesions; the potential risks include complications from having a surgical procedure performed such as infection, bleeding, and scar tissue formation, possibly requiring treatment; in addition, radical surgery removes the option for future pregnancy.

Your study doctor will discuss the risks and advantages of these alternatives methods with you. In addition, you may discuss your options with your general practitioner or anyone you choose

before making your decision. If you decide to participate in the study, you will be asked if you authorize your study doctor to notify your general practitioner of your study participation.

New information

You will be told if there is new information that may change your willingness to stay in this study. You will be informed in writing in a timely manner and will be asked to sign a new (revised) informed consent form if new information that could affect your willingness to continue participation in this study becomes available.

12. What if I get hurt or sick while I am in this study?

If you are injured during this study, your study doctor will discuss with you the available medical treatment options.

You do not give up any of your legal rights by signing this form.

Be aware that your health care payer/insurer might not cover the costs of study-related injuries or illnesses.

13. Who can I talk to about this study?

In the event of an emergency, dial 911 immediately.

If you require emergency care, be sure to tell the emergency care provider about your participation in this study. Contact the study doctor or study staff as soon as possible.

You can ask questions about the study at any time. You can call the study doctor or study staff at any time if you have any concerns or complaints. You should call the study doctor or study staff at the phone number listed on page 1 of this form if you have questions about the study procedures, study costs (if any), study payment (if any), or if you get hurt or sick during the study.

Quorum Review reviewed this study. Quorum Review is a group of people who review research studies to protect the rights and welfare of research participants. Review by Quorum Review does not mean that the study is without risks. If you have questions about your rights as a research participant, if you are not able to resolve your concerns with the study doctor or study staff, if you have a complaint, or if you have general questions about what it means to be in a research study, you can call Quorum Review or visit the Quorum Review website at www.quorumreview.com.

Quorum Review is located in Seattle, Washington.
Office hours are 8:00 AM to 5:00 PM Pacific Time, Monday through Friday.
Ask to speak with a Research Participant Liaison at 888-776-9115 (toll free).

14. What about my confidentiality?

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.

What data do you collect from me?

Your personal health information from your original medical records and all data resulting from your participation in this research will be collected during the course of this study. Your study doctor may ask you to sign a separate authorization to obtain some or all of your original medical records. Your personal health information could include any of the procedures outlined in this consent.

An eDiary device will be used to collect your answers to questions regarding your health. This eDiary will not capture any information that can identify you. Your answers to questions will be transferred to a storage facility via a secure internet connection and will be viewed by the study site and the sponsor.

How will my data appear?

Your identity and contact details will not be disclosed except as described in this form, unless required by law. Rather, your identity and contact details will be replaced by a code, such as a subject identification number.

Why are my data collected?

Your personal health information will be used for clinical research and may also be used for seeking approval from regulatory authorities to market the study drug OBE2109. It may also be used in study reports or for scientific presentations, but in a way that will not identify you by name. Your personal health information will be kept confidential and, unless required by law, will not be made publicly available.

After this study has been completed, it is possible that your coded health information will be used for future research concerning the study drug OBE2109 and other reproductive diseases.

Who will see my data?

The only people with access to your personal health information in identifiable form will be the study doctor, personnel helping the study doctor conduct the study at the study site, sponsor representatives who are checking that the study is conducted properly, Quorum Review, and regulatory authorities where required by law.

You may not participate in this study unless you give your permission to use and disclose your personal health information. By signing this document, you are allowing the study doctor and personnel at the study site to permit Sponsor and others described in this form to have access to your personal health information for the purpose of collecting data, verifying the data are correct, and checking that the study is conducted properly.

In order to complete the research, Sponsor and its representatives, the study doctor and personnel at the study site, Quorum Review, and domestic and foreign regulatory authorities responsible for overseeing research studies (including the U.S. Food and Drug Administration [FDA], S. Department of Health and Human Services, and/or equivalent government agencies in other countries) will have access to your coded health information.

Additionally, your personal health information may no longer be protected by HIPAA (Health Insurance Portability and Accountability Act) once it is disclosed to Sponsor and others as described in this form. However, Sponsor will take reasonable measures to keep your personal health information confidential. However, absolute confidentiality cannot be guaranteed.

Your HIPAA authorization will expire 50 years from the date you sign it unless you revoke (cancel or withdraw) it sooner, since information collected for research purposes continues to be analyzed for many years. If the results of the study are published, your identity will remain confidential.

Can I take back my permission to use or disclose my personal health information?

Yes. To take back your permission to use or disclose your personal health information at any time, you must write to your study doctor at the address listed on Page 1 of this consent form. If you do this, you will no longer be

allowed to be in this study. Any information that has already been collected at the time you take back your permission will be kept and, where the law allows, your personal health information will continue to be used by the study doctor or Sponsor and parties hired by Sponsor or collaborating with Sponsor, or other parties involved with the study.

Rights to my data

You may have the right to access, correct, and make a copy of your medical and/or clinical study records as allowed by applicable privacy laws. You may ask to see your records by requesting such records from the study doctor or the study site(s) where the study is being conducted. However, to ensure the valid results of the study, you agree that you may not be able to review or make a copy of some of your records related to the study until after the study has been completed.

When you sign this document, you agree to the access, collection, processing, and transfer of your personal health information as described in this informed consent document. If you do not sign this form, you cannot be in the study.

Signature of Participant Date

CONSENT

By signing this form:

1. I confirm that I have read and understood this consent form and have been given the opportunity to ask questions and discuss this study. I have received satisfactory answers to my questions.
2. The study doctor has explained the nature and purpose of the study to me.
3. I agree to participate in the above study, which is being conducted on behalf of ObsEva (who is the Sponsor of this study).
4. It has been explained to me that the drug being tested in this study (OBE2109) may involve risks to me which are currently unforeseeable.
5. By signing this form, I am authorizing access, use, and transfer of my personal data as described above.
6. I understand that I may request to see any data stored with regard to me, and request any errors to be corrected.
7. I have been told that the potential risks of study drug (OBE2109) on an unborn child are unknown and therefore I must not get pregnant during the entire Dosing Period of the study (until the end of Week 24). I agree to consistently use contraception as described above.
8. I understand that, having signed this consent form, I can still withdraw at any time without giving a reason and without affecting my future care.
9. By signing this consent form, I am not giving up any of my legal rights.
10. I will get a signed copy of this consent form.

Printed Name of Participant

Signature of Participant Date

I, the undersigned, declare that I have explained the nature, goal, and risks of this clinical trial, and that the individual providing consent had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to participation in this study.

Printed Name of Person Explaining Consent

Signature of Person Explaining Consent Date