

AN OPEN-LABEL PILOT PROSPECTIVE VULVOSCOPY WITH PHOTOGRAPHY  
STUDY OF THE VISIBLE CHANGES IN THE VULVA, VESTIBULE AND VAGINA PRE-  
AND POST- TWENTY WEEKS OF DAILY ADMINISTRATION OF 60 MG  
OSPEMIFENE IN POST-MENOPAUSAL WOMEN WITH DYSPAREUNIA FROM  
VULVAR VAGINAL ATROPHY

NCT 02784613  
March 22, 2016

## Experimental Research Subject's Bill of Rights

California law, under Health & Safety Code 24172, requires that any person asked to take part as a subject in research involving a medical experiment, or any person asked to consent to such participation on behalf of another, is entitled to receive the following list of rights written in a language in which the person is fluent. This list includes the right to:

1. Be informed of the nature and purpose of the experiment.
2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.
3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.
6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
7. Be given an opportunity to ask any questions concerning the experiment or the procedures involved.
8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.
9. Be given a copy of the signed and dated written consent form.
10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

\_\_\_\_\_  
Sign your name

\_\_\_\_\_  
Date

\_\_\_\_\_  
Print your name

Protocol Number: SDSM-2015-02  
Version Date: March 22, 2016

Initials: \_\_\_\_\_  
Page 1 of 11

**APPROVED**  
**March 22, 2016**  
**Aspire IRB**

## **INFORMED CONSENT TO PARTICIPATE IN CLINICAL RESEARCH STUDY**

**An Open-Label Pilot Prospective Vulvoscopy with Photography Study of the Visible Changes in the Vulva, Vestibule and Vagina Pre- and Post- Twenty Weeks of Daily Administration of 60 Mg Ospemifene in Post-Menopausal Women with Dyspareunia from Vulvar Vaginal Atrophy**

**Sponsor:** Irwin Goldstein, MD  
**Protocol Number:** SDSM-2015-02  
**Principal Investigator:** Irwin Goldstein  
San Diego Sexual Medicine  
5555 Reservoir Drive, Suite 300  
San Diego, CA 92120

**24-Hour Telephone Number:** (619)-265-8865

This is a research study. You are being asked to take part in this study because you are in menopause and have symptoms of vulvar vaginal atrophy (VVA) including vaginal dryness, irritation or inflammation, and you also have dyspareunia which is genital pain during sexual activity. This study includes only individuals who voluntarily choose to participate. Please take your time to make your decision. Discuss it in confidence with your regular doctor, friends and family if you want. Be sure to ask questions about anything you do not understand in this document.

### **WHAT IS THIS STUDY ABOUT?**

The study drug ospemifene (Osphena®) has been approved by the Food and Drug Administration (FDA) for the treatment of vulvar vaginal atrophy (VVA) and dyspareunia. The investigational purpose of this study is to examine changes to your genitals visible under magnification and photography before and after use of the study drug, ospemifene. Any changes in the level of genital pain that you are experiencing while on the study medication will also be recorded. All enrolled subjects will be provided with the study drug; there will be no placebo (sugar pill) medication.

### **HOW LONG IS THIS STUDY? HOW MANY OTHER PEOPLE WILL BE IN THIS STUDY?**

A total of 10 women will be enrolled in this study. More than 10 women may be screened in order to get 10 eligible women. You will be in the study for about 20 weeks after screening. Participation requires approximately 7 visits to the clinic.

Protocol Number: SDSM-2015-02  
Version Date: March 22, 2016

Initials: \_\_\_\_\_  
Page 2 of 11

**APPROVED**  
**March 22, 2016**  
**Aspire IRB**

## **WHAT IF NEW INFORMATION BECOMES AVAILABLE?**

If new information in relation to the study drug becomes available that may be relevant to the purpose and safety of the study and your willingness to continue participation in this study, you will be informed by the study doctor.

## **WHAT WILL HAPPEN DURING THE STUDY?**

If you agree to take part in this research study, you will be required to sign this informed consent form before any procedures take place.

### **STUDY PROCEDURES:**

During the screening and, if you qualify and continue, during the study the following procedures will occur:

- Questions about your health, past surgeries, and medications you are taking including requests for your medical records
- Measurement of your height and weight
- Vitals signs (blood pressure, respiration rate, and pulse) will be taken
- Pain scale (a questionnaire to assess your pain)
- Blood samples will be taken to test for specific hormone levels
- Physical examination including vulvoscopy with photography of your genitals and completion of a visual scale
- Q-tip testing of the genitals for pain assessment

Vulvoscopy consists of an examination of your genitals under magnification with a camera attached to photograph the region. You will be asked to undress from the waist down, lie on an exam bed with a sheet over you and your legs frog legged in stirrups. An investigator will examine you looking through the vulvoscope, take several photographs with no identification other than your subject number and date attached to it, and then complete a visual scale to indicate on paper the way your genitals look. The q-tip test, also called the cotton swab test, consists of a q-tip being gently applied one spot at a time around your genitals to check for pain at each location.

The screening visit should take approximately one and a half hours. Each additional visit should take approximately one hour.

The study doctor or his representative will talk to you and give you a list of the things you must do to participate, such as:

- **Pre-study medication:** Any medications that you are currently taking (with some exceptions described below) can continue provided they do not change during the screening and treatment periods. You must inform the study doctor if you need to change your medications once screening begins through the end of the study. Changes to medications include stopping medications, changes in the schedule or quantity of your medications, or starting new medications.
- The following medications are prohibited from 28 days before the first dose of study drug through the end of the study:
  - All forms of testosterone

Protocol Number: SDSM-2015-02  
Version Date: March 22, 2016

Initials: \_\_\_\_\_  
Page 3 of 11

**APPROVED**  
**March 22, 2016**  
**Aspire IRB**

- o All forms of estrogen
- o Over the counter products, vitamins or nutritional supplements
- o Any investigational drug or medical device
- o Any drugs of abuse.

After screening, if you meet all the eligibility criteria, you will be provided with the study drug. You will be asked to take one 60mg tablet of Osphe<sup>na</sup>® once daily as per the approved package insert.

At that visit and at each subsequent visit, every 4 weeks for 20 weeks, you will have your vital signs measured, asked about changes in your health or medication, have an examination of your genitals under magnification with photography, have q-tip testing for pain and complete the pain questionnaire.

Each time you will turn in your medication and diaries and be provided with new diaries and new medication for the next 4 weeks. These visits should take approximately one hour. Medication and diaries will be collected at the last visit. If you decide to stop your participation early, you will be asked to do the same procedures as in the last visit as well as return all medication and diaries.

Please tell your regular health care providers and any emergency care providers that you are participating in this research study.

**WHAT ARE THE RISKS AND DISCOMFORTS OF PARTICIPATING IN THIS STUDY?**

The study drug has been associated with the following side effects: hot flashes, vaginal discharge, muscle spasms and increased sweating. Less common but serious side effects include stroke, blood clots and cancer of the lining of the uterus.

OSPHENA is a medicine that works like estrogen in the lining of the uterus (womb), but can work differently in other parts of the body. Taking estrogen-alone or Osphe<sup>na</sup>® may increase your chance of getting cancer of the lining of the uterus (womb).

Notify your study doctor if you have any unusual symptoms such as vaginal bleeding, change in vision or speech, or a sudden new severe headache.

Do not give Osphe<sup>na</sup>® to other people, even if they have the same symptoms you have. Keep the Osphe<sup>na</sup>® out of the reach of children.

Ask the study doctor for a package insert and patient information sheet for Osphe<sup>na</sup>®. All magnified physical examination findings and photographs will be confidential. There will be no individual identifying features on any genital photographs such as photos of the face. All photographs will be categorized by the subject initials, subject number and date.

**Are there pregnancy risks?**

No. In order to participate in this study you must be post-menopausal.

Protocol Number: SDSM-2015-02  
Version Date: March 22, 2016

Initials: \_\_\_\_\_  
Page 4 of 11

**APPROVED**  
**March 22, 2016**  
**Aspire IRB**

### **ARE THERE BENEFITS TO TAKING PART IN THE STUDY?**

If you agree to take part in this study, you may have improvement in your symptoms of both vulvar vaginal atrophy and dyspareunia. Your condition may stay the same or get worse.

### **WHAT, IF ANY, ARE THE ALTERNATIVES TO PARTICIPATING IN THIS STUDY?**

You could choose to ask your physician for a prescription for Osphe<sup>®</sup> and not get it through this clinical trial. You could also choose to use a form of estradiol. Consult your study doctor for more information on these medications.

### **CONFIDENTIALITY**

Your personal information will be kept confidential to the extent permitted by law. We cannot guarantee absolute confidentiality. By signing this document, you give permission to access your medical records, including after withdrawal, for data verification purposes.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as:

- The study staff and other researchers involved in the study
- Shionogi, Inc that provided a grant and medication for this study
- The Food and Drug Administration (FDA)
- Aspire Independent Review Board (IRB)

The results from the study, including photographs, may be published for scientific purposes, but your identity will be kept confidential.

In the rare event that your information is required to be disclosed by law to another entity, privacy laws may not apply, and neither the Sponsor nor Aspire IRB can protect your information.

### **WHAT ARE THE COSTS?**

There are no additional costs associated with being in this study. You are responsible for your regular health care while in this study. You will not have to pay for study drug, study visits, or tests/procedures that are part of the study.

After the study is over, the study drug will no longer be provided to you.

### **INVESTIGATOR PAYMENT**

The Sponsor is the study doctor so he is not being paid for conducting this study. The research is being supported by a grant from Shionogi, Inc.

Protocol Number: SDSM-2015-02  
Version Date: March 22, 2016

Initials: \_\_\_\_\_  
Page 5 of 11

*APPROVED*  
*March 22, 2016*  
*Aspire IRB*

### **WILL YOU BE COMPENSATED DURING THE STUDY?**

You will be compensated for participating in this research study. You may receive up to \$425.00. This amount is prorated as follows and reflects each completed visit:

- You will receive \$100.00 if you complete the screening and \$75.00 when you are enrolled.
- You will be paid \$50.00 for the completion of each of the 5 additional study visits.

### **WHAT HAPPENS IF YOU HAVE COMPLICATIONS OR ARE INJURED?**

If you have serious side effects, complications or are injured because of participating in this study, please contact the study doctor promptly. The study doctor will provide any necessary medical treatment to help you promptly recover from the injury. If you require care outside of San Diego Sexual Medicine, your insurance will be billed for the medical treatment.

### **YOUR RIGHTS AS A RESEARCH SUBJECT**

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to the study doctor and your regular doctor first.

### **YOUR RESPONSIBILITIES AS A RESEARCH SUBJECT**

You will be asked to adhere to all instructions issued by the study doctor and other study staff including the following:

1. Answer all medical questions completely and truthfully
2. Arrive at all study visits on time
3. Take study drug at home per the instructions provided by the study staff
4. Complete a sexual event diary every time you have a sexual event
5. Report any changes in your medications while on the study to the study doctor or staff
6. Adhere to the instructions on prohibited medications and supplements
7. Inform your regular healthcare provider about your participation in this study

Should you not comply with instructions, the study doctor may stop your study participation. Your study doctor may also exclude you from this trial if he deems it beneficial for your health, or if you do not meet the study requirements.

Your participation in this study may be ended if the study is stopped for any reason. If your participation in the study is ended before you complete all the visits, doses, and tests, you will be asked to visit the study center to return your medication and diaries and have some final tests done.

Protocol Number: SDSM-2015-02  
Version Date: March 22, 2016

Initials: \_\_\_\_\_  
Page 6 of 11

**APPROVED**  
**March 22, 2016**  
**Aspire IRB**

**WHOM TO CALL IF YOU HAVE QUESTIONS**

For questions, concerns or complaints about the study or a research-related injury, contact Dr. Irwin Goldstein, 619-265-8865.

This study was reviewed by Aspire Independent Review Board (IRB). An IRB reviews research to protect the rights and welfare of study participants. If you have problems, concerns, complaints, questions or information about the study, and for information regarding research subject's rights, please call Aspire's Subject Participant Advocate at 1-877-366-5414 (toll free).

Although Aspire IRB has approved the information provided in this informed consent form and has granted approval for the study doctor to conduct the study this does not mean Aspire has approved your participation in the study. You must evaluate the information in this informed consent form for yourself and decide whether or not you wish to participate.

***PRIMARY CARE PHYSICIAN / SPECIALIST NOTIFICATION OPTION***

Please indicate below whether you want us to notify your primary care physician or your specialist of your participation in this study.

- Yes, I want the study doctor to inform my primary care physician/specialist of my participation in this study.
- No, I do not want the study doctor to inform my primary care physician/specialist of my participation in this study.
- I do not have a primary care physician/specialist.
- The study doctor is my primary care physician/specialist.

Protocol Number: SDSM-2015-02  
Version Date: March 22, 2016

Initials: \_\_\_\_\_  
Page 7 of 11

***APPROVED***  
***March 22, 2016***  
***Aspire IRB***



**SIGNATURE AND CONSENT TO BE IN THE STUDY**

Your signature below means that you have read the above information about this study and have had a chance to ask questions. Your questions have been answered to your satisfaction. Your signature means that you voluntarily agree to participate in this research study. Your signature notes you have also received and read a copy of the California Experimental Bill of Rights. Your signature also means that you have been told that you can change your mind later if you want to. You will be given a signed and dated copy of this agreement. By signing this consent form you are not giving up any of your legal rights.

\_\_\_\_\_  
SIGNATURE OF SUBJECT

\_\_\_\_\_  
DATE

\_\_\_\_\_  
PRINTED NAME OF SUBJECT

I confirm that a copy of this consent form has been given to this person to read and that this person has been told about the study. The contents of the consent form describing the study has been discussed with this person. All questions have been answered to his or her satisfaction. I have watched this person sign the consent form.

\_\_\_\_\_  
SIGNATURE OF PERSON OBTAINING CONSENT

\_\_\_\_\_  
DATE

\_\_\_\_\_  
PRINTED NAME OF PERSON OBTAINING CONSENT

Protocol Number: SDSM-2015-02  
Version Date: March 22, 2016

Initials: \_\_\_\_\_  
Page 8 of 11

***APPROVED***  
***March 22, 2016***  
***Aspire IRB***

## Authorization to Use and Disclose Your Personal Health Information

Name of Study: **An Open-Label Pilot Prospective Vulvoscopy with Photography Study of the Visible Changes in the Vulva, Vestibule and Vagina Pre- and Post- Twenty Weeks of Daily Administration of 60 Mg Ospemifene in Post-Menopausal Women with Dyspareunia from Vulvar Vaginal Atrophy**

Principal Investigator: Irwin Goldstein, MD  
IRB Study Number: SDSM-2015-02

### **What is private health information?**

*State and federal privacy laws protect the use and release of your private health information.*

Private health information is any information that can be traced back to you. We need your authorization (permission) to use your private health information in this research study. If you decide to give your permission to participate in the study, you must sign this form as well as the Consent Form. *If you refuse to give permission, you will not be able to be in this research.* The private health information that we will use and share for this study includes:

- *your past and present health information (medical records)*
- *research records*
- *records about phone calls made as part of this research*
- *information obtained during this research, such as laboratory and other test results*
- *information that could be used to identify you*

### **Who else will see my information?**

If you give your permission and sign this form you are allowing Dr. Goldstein and the research team to share your Personal Health Information with:

- All groups that work with the investigators, including government agencies such as the Food and Drug Administration. These organizations and their representatives may see your Personal Health Information. They may not copy or take it from your medical records unless permitted or required by law.
- The Aspire IRB committee that reviews research to help protect people who join research studies.

Protocol Number: SDSM-2015-02  
Version Date: March 22, 2016

Initials: \_\_\_\_\_  
Page 9 of 11

**APPROVED**  
**March 22, 2016**  
**Aspire IRB**

Once we have shared your information we cannot be sure that it will stay private. If **you share** your information with people outside the research team, it will no longer be private. Your name will not be used in any report that is written.

**How long will you use and share my information?**

This permission to release your Personal Health Information expires 50 years from when you sign this authorization unless you revoke it sooner. Research reports can be used forever.

**What if I change my mind about sharing my research information?**

You can cancel your permission at any time. You can do this in two ways but you have to do it in writing. You can write to the researcher or you can ask someone on the research team to give you a form to fill out to cancel your permission. If you cancel your permission, you may no longer be in the research study. You may want to ask someone on the research team if canceling will affect your medical treatment. If you cancel, information that was already collected and disclosed about you may continue to be used. Also, if the law requires it, the sponsor and government agencies may continue to look at your medical records to review the quality or safety of the study.

**Do I have the right to see and copy my research information?**

You can see your research information that is also being used for your health care. Some research information may not be available to you because of the design of the study or because the tests have nothing to do with your health care. You can talk to your study doctor about this.

If you have questions or concerns about your privacy and the use of your personal medical information, please contact your research doctor at the phone number in the Informed Consent form.

If you agree to share your information please sign this form below. You will be given a copy of this form.

\*\*\*\*\*

***I agree to share my information as described in this form***

\_\_\_\_\_  
Sign your name Date

\_\_\_\_\_  
Print your name

Protocol Number: SDSM-2015-02  
Version Date: March 22, 2016

Initials: \_\_\_\_\_  
Page 11 of 11

***APPROVED***  
***March 22, 2016***  
***Aspire IRB***