CONSENT FORM

Subject Name _____

Title of Protocol Comparison of dapagliflozin (DAPA) and once-weekly exenatide (EQW), co-administered or alone, combination tablet dapagliflozin/ extended release metformin (DAPA/MET XR) and the weight loss drug, combination phentermine (PHEN)/topiramate (TPM) extended release (ER), on metabolic profiles and body composition in obese PCOS women

Principal Investigators: Renee Harris, MD
Karen Elkind-Hirsch, MS, Ph.D.
Drake Bellanger, MD

Co-Investigator: John Storment, MD

Woman's Metabolic Health and Research Services
100 Woman's Way
Baton Rouge, LA 70817
(225) 231-5275

Drug/Funding Support: Astra Zeneca Pharmaceuticals/VIVUS, Inc.

Please read this form carefully. This consent form contains important facts to help you decide if it is in your best interest to take part in this study. Take time to ask the study doctor or study staff as many questions about the study as you would like. If there are any words or information that you do not understand, please ask the doctor. The study doctor or study staff will explain them to you. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in the research study, you must sign your name to the final page. Your taking part is entirely voluntary.

Purpose of the Study

You are being asked to take part in a clinical research study because you have polycystic ovary syndrome (PCOS). Women with PCOS do not metabolize (digest) enough of the carbohydrates (simple and complex sugars) found in food. This study is being done to compare the ability of different medicines to improve carbohydrate metabolism, body composition, and reproductive function in women with PCOS. You will need to take one of the medicines for about 24 weeks. Expected enrollment at Woman's hospital is 110 women with PCOS. The length of time you will be in this study is about 24 weeks.

Study Procedures

If you volunteer to take part in this research study, you will be asked to read and sign this consent form. You will then have a screening visit. Tests will be done during this visit to

see if you meet all of the entry conditions to take part in this study. These will include:

- review of your reproductive history
- a medical history
- physical measurements of height, weight, and blood pressure

You will also provide information about the following:

- menstrual bleeding cycle length
- race
- current drug use
- cigarette smoking/tobacco use
- alcohol intake

If you are eligible to take part in the study, you will be placed in one of five treatment groups:

i. Exenatide once weekly (EQW; Bydureon),
ii. Dapagliflozin (DAPA; Farxiga),
iii. Dapagliflozin (Farxiga) plus exenatide once weekly(Bydureon)
iv. Combination dapagliflozin/metformin XR (Xigduo)
v. Phentermine/topiramate extended release (PHEN/TPM ER; Qsymia).

Exenatide once weekly (EQW; Bydureon), dapagliflozin (DAPA; Farxiga), and combination dapagliflozin/metformin XR (Xigduo) are marketed in the United States for use in diabetic patients, but are considered investigational drugs in this study.

Your treatment will be chosen on a **randomized** basis, which is similar to rolling dice. A computer will choose which of the medicines you will get. Neither your doctor nor you will be able to choose which treatment you will be given. You have an equal chance of getting placed in any of the five treatment groups. While you will know what medicine you are taking, the principal investigator **will not know** which group you are in.

Once you have enrolled and been randomized to study drug, you will be taught how to take the medicine. You will be instructed when to take the medicine and how many times a day. A research associate who knows which drug you are taking will explain how to take medications. In addition, written instructions will be included with your medicine. The clinic nurse will also see you about 12 weeks after starting the study drug to find out how you are tolerating the medicine. At that time, the research associate will dispense new medicine and get back unused medicine. If there are any questions about the medications and how to take them, you can call the Woman's Metabolic Health and Research Services at 225 924-8947 or the Research Office at 225 231-5275.

Procedures during the Study

You will have a total of 6 visits (3 to the outpatient laboratory and 3 clinic visits) over a 24-week period. The visits are as follows:

Visit 1: baseline lab visit / screening visit (week 1)
Visit 2: first clinic visit (week 2)
Visit 3: lab visit (week 10-12)
Visit 4: clinic visit (week 10-12)
Visit 5: final lab visit (week 22-24)
Visit 5: final clinic visit (week 24)

With each of the clinic study visits, you will have the following clinical measures (vital signs) taken:

- height
- weight
- measurement of your waist and hips with a tape measure
- blood pressure

There will be a baseline lab visit, a 10-12 week lab visit, and a final study lab test visit. These visits will be scheduled before you start treatment (baseline), 10-12 weeks after starting treatment, and during study weeks 22-24. During the baseline and final testing visits, you will need to give blood (around 1 ½ teaspoons) for laboratory tests of your hormones and blood chemistries. This blood test is to find out if your thyroid, liver, kidneys, and lipid levels are normal and to be sure you are not pregnant. At the 10-12 week visit, only a blood test to check that you are not pregnant will be done.

At both the baseline visit and the final study test visit, you will take an oral glucose (sugar) tolerance test. For the sugar tolerance test to work, the night before the test you cannot eat anything after midnight and the only liquid you can drink after midnight is water. This test requires that blood samples be taken when you arrive, 30 minutes, 1 hour and 2 hours after drinking a sugar solution. In total, this test requires that you have your blood taken 4 times within 2 hours. The total amount of blood to be taken during each visit will be about 3 tablespoons. A total of 6 tablespoons of blood will be drawn during your taking part in this study.

You will also undergo a total of 2 whole body "DEXA" (dual energy X-ray absorptiometry) scans. These scans measure your body fat and lean tissue (this is like an x-ray machine). These scans will be performed when you begin the study and at 24 weeks.

In addition to the lab visits, you will see the Metabolic Health Clinic physician before starting the medicine and at the end of the study. The clinic physician and nurse will also see you about 10-12 weeks after starting the medication. These clinic visits are done to find out how you are tolerating the medicine and to give you new medicine.

You will be asked to perform a home pregnancy test every month that we do not test your blood in the laboratory. The test kits will be provided to you at no cost. The study coordinator will make sure you remember to do the test each month by calling you for the result which will

be documented in your chart. It is necessary that you not be pregnant while taking these medications. We need to make sure you are not pregnant every month you are in the study.

A patient flow chart with a review of study visits is shown at the end of the consent form (Figure 1).

Risks/Side Effects

The treatments used in this study may cause some or none of the side effects listed. In addition, there is always the risk of some very uncommon or unknown side effects taking place.

Be sure to tell your physicians and pharmacist that you are taking one of these study medications. This is important so that they can tell you about any drug interactions that may exist with other medicines you may be taking.

Risks Associated with Study Procedures

In this study you will need to have blood drawn from your arm several times. You may have some tenderness from having blood taken from a vein in your arm. You may have to take shots. There may be a risk of infection, mild injection-site bruising related to the injection (shot) method, and local reaction at the injection sites. You may also have unpleasant effects from using the pills.

Possible risks and side effects from each of these tests and drugs are listed below. The risks of drawing blood include local pain, bruising and swelling, bleeding, and infection at the site of the vein puncture. An infrequent risk of lightheadedness, dizziness, and, rarely, fainting is possible.

Risks Associated with Dual Energy X-ray Absorptiometry (DEXA) Scans for Body Composition

This is a painless test that is done on a "DEXA" machine (this is like an x-ray machine). The scan time is 180 seconds (3 minutes). The amount of radiation you will be exposed to from having this scan done is minimal. When the scan is performed, the X-ray exposure is 1.0 mrad, which is the same as about **1/30** the amount of x-ray exposure you would get from having a chest x-ray done.

Risks/Side Effects Associated with Study Medications

Any drug can cause side effects. The drugs used in this study may cause some or none of the side effects listed. This study may also have risks not known at this time. There is always the risk of some very uncommon or unknown side effects occurring which have not been explained in this consent. Risks to subjects are minimized by using procedures consistent with sound research dosing. In addition, a listing of other known side effects of all drugs is on hand through the pharmacy, or from the drug company.

If you do not understand any of the risks you may discuss them with Dr. Harris, Dr. Bellanger, or Dr. Elkind-Hirsch. Although the risks of developing the above complications are small, they do exist. If they occur, Dr. Harris, Dr. Bellanger, Dr. Elkind-Hirsch and their team will watch you closely and take appropriate medical action. This may include stopping the use of the drug. Your primary care physician is still responsible for your medical care.

Possible risks from these medicines are listed below:

Exenatide once weekly (EQW; Bydureon) for injectable suspension

Once-weekly exenatide (Bydureon) is an injectable medicine used to improve blood glucose (sugar) control in adults with type 2 diabetes. It comes in a prefilled injection (shot) pen (pen-injector) that you inject once a week. One pen contains 2 mg of exenatide (as a white to off-white powder) and 0.65 mL diluent (liquid). Exenatide is a peptide (small protein) and therefore cannot be given by mouth. If it were taken in pill form, your stomach would break it down just like the protein in the foods you eat, and it wouldn't work. Bydureon is an extended-release form of exenatide administered as an injection once every seven days. This drug is given by subcutaneous (under the skin) shot that you will learn how to give yourself. You can administer the shot in your stomach area (abdomen), your thigh, or the back of your upper arm. Each week you can use the same area of your body, but be sure to choose a different injection site in that area. If you miss a dose of Bydureon, it should be used as soon as you remember, if the next regularly scheduled dose is due at least 3 days later. If you miss a dose of Bydureon, and the next regularly scheduled dose is due 1 or 2 days later, do not use the missed dose. Use Bydureon on the next regularly scheduled day.

Bydureon should be stored in the refrigerator at 36°F to 46°F (2°C to 8°C), up to the expiration date or until preparing for use. Bydureon is a powder medicine that must be mixed with a liquid (diluent) before using it. You must give the injection right away after mixing. Store unused Bydureon powder in the refrigerator, protected from light. Do not freeze, and throw away any medicine that has become frozen. You may store Bydureon at room temperature for up to 4 weeks.

The most common side effects with Exenatide once-weekly (Bydureon) include::

- nausea
- diarrhea
- vomiting
- dizziness
- constipation
- itching at the injection site
- small bump (nodule) at the injection site,
- headache
- feeling jittery
- acid stomach (indigestion)

Nausea is most common when you first start using Bydureon, but lessens over time in most people as their body gets used to the medicine

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Less common side effects include:

- tiredness
- decreased appetite
- indigestion
- excessive sweating

When taking any drug, there is a risk of an allergic reaction. Since this drug is a peptide, the potential to develop antibodies to exenatide once-weekly following treatment with Bydureon exists. **Some signs of allergic reactions are:**

- skin rash
- fever
- fast pulse
- sweating
- swelling around mouth, throat, or eyes

If not treated quickly, more serious problems such as breathing difficulties or shock could occur. It is not possible to predict if any of these problems will develop. If you have a serious allergic reaction, you may be at risk of death if not treated. Please seek treatment and alert the study doctor and staff right away if you have any of these signs or any other side effects during the study.

Very low blood sugar (hypoglycemia) is an important side effect to consider when taking Bydureon. Exenatide once-weekly (Bydureon) **alone does not cause low blood sugar** but it has been shown to cause hypoglycemia when used with other anti-diabetes drugs. **The warning signs of low blood sugar may include:**

- headache
- drowsiness
- weakness
- dizziness
- confusion
- irritability
- hunger
- fast heartbeat
- sweating
- feeling jittery

You will be trained how to recognize the signs of low blood sugar, and what to do to treat it. It is a good habit to carry glucose (sugar) tablets or gel to treat low blood sugar. If you don't have these forms of glucose, eat a quick source of sugar such as table sugar, honey, or candy, or drink a glass of orange juice or non-diet soda to quickly raise your blood sugar level. Tell your doctor right away about the reaction.

Exenatide once-weekly (Bydureon) causes thyroid C-cell tumors in rodents (mice and rats). The human relevance is unknown. You should tell the study doctor if you experience any symptoms of a thyroid tumor. These symptoms may include a mass in the neck, difficulty swallowing, shortness of breath, or persistent hoarseness.

Exenatide once-weekly (Bydureon) may reduce your appetite, the amount of food you eat, and your weight. Exenatide once-weekly can be used with care if you are taking oral medicines that require rapid absorption through your stomach. Bydureon slows stomach emptying and can affect medicines that need to pass through the stomach quickly. Bydureon can make it harder for your body to absorb other medications you take by mouth. Tell your doctor about all medicines you use, and those you start or stop using.

Exenatide once-weekly (Bydureon) can be used with some other anti-diabetic medicines. Bydureon can interact with other medicines, especially drugs that depend on a threshold concentration to be effective, such as antibiotics. Other drugs may interact with Bydureon, including prescription and over-the-counter medicines, vitamins, and herbal products

If any new risks or side effects are found out that might change your decision to stay in this study, you will be told about it in a timely manner.

Dapagliflozin (Farxiga)

Dapagliflozin works by decreasing the amount of sugar the body absorbs and increasing the amount of sugar that leaves the body in the urine. It is used along with diet and exercise.

In this study, you will be instructed to take one pill the same time every day. Each tablet must be swallowed whole, so do not crush or chew the pills. You should drink plenty of fluids while taking this medicine. Remember to take dapagliflozin on a regular schedule to get the most benefit from it. Taking your pill at the same time each day will help you remember to take it. If you miss a dose of dapagliflozin, take it as soon as possible. If it is almost time for your next dose, skip the missed dose and go back to your regular dosing schedule. Do not take 2 doses at once.

The most common side effects of dapagliflozin include:

- yeast infections of the vagina
- change in urination, including urgent need to urinate more often, in larger amounts, or at night.
- urinary tract infections
- reduced blood pressure
- runny or stuffy nose; sore throat

Dapagliflozin may cause dizziness, light-headedness, or fainting. Alcohol, hot weather, exercise, or fever may increase these effects. This effect may be worse if you take it with alcohol or certain medicines. To prevent them, sit up or stand slowly, especially in the morning. Sit or lie down at the first sign of any of these effects.

Low blood sugar (hypoglycemia) is uncommon when **Farxiga** is taken alone but it may happen if you do not eat enough calories (from food, juices, fruit, etc.). Some of the common signs include:

- chills
- drowsiness

- dizziness
- shaking
- weakness
- fainting
- tingling of the hands or feet

cold sweat
rapid heartbeat
headache
hunger

Low blood sugar makes it hard to think clearly, drive a car, use heavy machinery, or do other unsafe activities where you could hurt yourself or others. Severe cases of low blood sugar could cause loss of awareness, and in extreme cases, death. Tell your doctor right away about the reaction. To help prevent low blood sugar, eat meals on a regular schedule and do not skip meals.
Farxiga will cause your urine to test positive for glucose. Be sure your doctor and lab personnel know you are taking dapagliflozin.

Serious allergic reactions to this drug are unlikely, but seek medical attention right away if it occurs. **Some symptoms of allergic reactions are:**

- rash
- itching
- swelling around the mouth, throat or eyes
- a fast pulse
- sudden drop in blood pressure
- sweating

A severe allergic reaction could be fatal. If you notice other effects not listed above, contact your doctor

Dapagliflozin may be associated with an increased risk of bladder cancer. Tell your doctor right away if you notice symptoms that could be associated with bladder cancer (eg, a red color or blood in the urine, difficult or painful urination, an increased need to urinate). Discuss any questions or concerns with your doctor.

Seek medical help at once if you have any of these serious side effects:

- symptoms of kidney problems or urinary tract infection (eg, blood in the urine, change in the amount of urine produced, difficult or painful urination, unusual or persistent pain in the mid to lower back, unexplained swelling). Urinary tract infections may be life-threatening, leading to sepsis or kidney infections if not treated immediately.
- vaginal discharge, itching, or odor
- feeling short of breath (even with mild exertion), fast or irregular heartbeat, muscle weakness, severe or persistent headache, dizziness, or light-headedness
- severe skin reaction -- fever, sore throat, swelling in your face or tongue, burning in your eyes, very dry mouth or eyes skin pain, followed by a red or purple skin rash that spreads (especially in the face or upper body) and causes blistering and peeling

There have been reports of serious and sometimes life-threatening cases of ketoacidosis in patients treated with dapagliflozin. Ketoacidosis is a condition where the body makes high levels of blood acids called ketones. This condition may lead to hospitalization.

Seek medical attention immediately and alert us if you experience symptoms consistent with ketoacidosis, such as: nausea, vomiting, abdominal pain, confusion, change in breathing pattern, fruity or acetone smell to your breath, and unusual fatigue or sleepiness.

If left untreated, diabetic ketoacidosis can cause death.

There have been cases of a rare but serious infection of the genitals reported with sodium-glucose cotransporter-2 (SGLT2) inhibitors, like Farxiga. This condition is a serious, rare infection called necrotizing fasciitis of the perineum, also referred to as Fournier's gangrene.

You should seek medical attention immediately if you have tenderness, redness, or swelling of the genitals or the area from the genitals to the rectum, and have a fever above 100.4F, or a general feeling of being unwell. These symptoms can worsen quickly, so it is important to seek treatment right away.

Dapagliflozin plus metformin XR (Xigduo XR)

Combination dapagliflozin plus metformin XR (Xigduo) is a diabetes medicine that helps control blood sugar and insulin levels in patients with type 2 diabetes. This medicine is taken by mouth with meals. Each tablet(s) must be swallowed whole, so do not crush or chew the pills. You should drink plenty of fluids while taking this medicine.

Possible risks and side effects for Xigduo are noted above, under dapagliflozin (Farxiga) and below under metformin XR (Glucophage XR) sections. Please notify your treating physician that you are on Xigduo if you are scheduled for a scan or medical procedure that uses an IV or tests that may use contrast dyes.

Metformin XR (Glucophage XR)

Metformin is an oral medicine that works by decreasing glucose (sugar) production in the liver and decreasing absorption of glucose by the intestines. Inactive parts of the drug may be passed in your stool as a harmless, soft mass that may look like the original tablet. This is normal for this drug. Since this is an extended-release tablet, it lowers the number of times you have to take a pill each day. Extended-release metformin (Glucophage XR) delivers the drug to your body in the same amounts as instant-release metformin over a longer period of time.

The most common side effects of Glucophage XR include:

- nausea
- stomach upset
- diarrhea
- loss of appetite
- acid stomach
- a metallic taste
- increased abdominal gas
- vomiting

Side effects usually decrease over time. Taking metformin right before meals may lessen nausea and vomiting. Food decreases the rate the drug is absorbed, so taking the medicine with food can reduce the side effects of metformin. In this study, metformin will be started at a low dose (1 pill once a day with food) for 4 weeks and increased to 2 pills as you are able to tolerate it.

A rare side effect of metformin use is a condition called lactic acidosis. If the liver is not able to change the lactic acid into sugar, the acid builds up in the blood. If not treated, this acid buildup can lead to coma and death. Lactic acidosis is more likely to occur in patients who:

- have kidney or liver failure
- have low levels of oxygen in their blood (hypoxia) or poor blood flow
- abuse (drink too much) alcohol
- have excess loss of body fluids (dehydration)
- are undergoing X-ray or scanning measures that require an injectable iodinated contrast drug, surgery, or have a serious infection

Seek medical help right away if you develop any of the following signs of lactic acidosis:

- unusual tiredness (fatigue) or severe drowsiness
- cold skin
- muscle pain
- breathing trouble or rapid breathing
- unusually slow or irregular heartbeat

Lactic acidosis is a medical emergency and must be treated in a hospital setting. If you have an illness that results in severe vomiting, diarrhea, and/or fever, or if drinking of fluids is really decreased, you need to call your physician. If your stomach symptoms come back (after you are on the same dose for several days or weeks), tell your doctor right away. A late comeback of stomach signs may be due to lactic acidosis. Alcohol is known to intensify the effect of metformin and you should never drink excess amounts (greater than 2 glasses of wine, or beer, or 2 ounces of hard liquor a day) of alcohol (all the time or "short-term binge") while taking metformin. Taking metformin should be briefly stopped for all surgical procedures that include reducing fluids. You should not take metformin again until normal fluid intake is started again and renal (kidney) function is back to normal.

When taken alone, metformin will not cause low blood sugar (hypoglycemia), but it may happen if you do not eat enough calories (from food, juices, fruit, etc.). Some of the common signs include:

- chills
- cold sweat
- dizziness
- drowsiness
- shaking
- rapid heartbeat
- weakness
- headache

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- fainting
- tingling of the hands or feet
- hunger

Low blood sugar makes it hard to think clearly, drive a car, use heavy machinery, or do other unsafe activities where you could hurt yourself or others. Severe cases of low blood sugar could cause loss of awareness, and in extreme cases, death. Tell your doctor right away about the reaction. To help prevent low blood sugar, eat meals on a regular schedule and do not skip meals.

Serious allergic reactions to this drug are unlikely, but seek medical attention right away if it occurs. **Some symptoms of allergic reactions are:**

- rash
- itching
- swelling around the mouth, throat or eyes
- a fast pulse
- sudden drop in blood pressure
- sweating
- dizziness
- trouble breathing

A severe allergic reaction could be fatal. If you notice other effects not listed above, contact your doctor

Less serious side effects of metformin may include:

- cold symptoms such as runny or stuffy nose, sneezing, sore throat.
- hepatic (liver) enzyme elevations
- interference with vitamin B12 absorption that is rapidly reversed by taking vitamin B12 supplements

Phentermine/topiramate extended release (Qsymia).

Qsymia is an FDA-approved prescription weight-loss medicine. It contains a combination of phentermine (PHEN) and topiramate in an extended-release capsule (TPN ER). Phentermine is an appetite suppressant similar to an amphetamine. Topiramate is a seizure medication, also called an anticonvulsant. Qsymia is used together with a reduced-calorie diet and increased physical activity for chronic weight management in overweight/obese adults.

You will only need to take 1 capsule a day with or without food in the morning. For the first 14 days you will start on a low dose (PHEN 3.75/TPN ER 23 mg). After 14 days, you will be increased to the final dose (PHEN 7.5/TPN ER 46 mg). Do not crush, chew, break, or open an extended-release capsule. Swallow it whole. You can easily become dehydrated while taking this medicine. This can lead to severely low blood pressure or a serious electrolyte imbalance. Drink plenty of water each day to prevent dehydration or kidney stones while you are taking Qsymia.

Phentermine may be habit-forming and should be used only by the person for whom it was prescribed. Keep the medication in a secure place where others cannot get to it. Do not stop

taking Qsymia suddenly, or you could have a seizure (convulsions). You may need to use less and less before you stop the medication completely. Ask your doctor how to avoid seizures when you stop using Qsymia.

Before you take Qsymia, tell your doctor if you have high blood pressure, heart disease, diabetes, liver or kidney disease, low blood levels of potassium, or if you have had a heart attack or stroke in the past 6 months.

Before taking this medicine

You should not take Qsymia if you are allergic to phentermine (Adipex-P, Oby-Cap, Suprenza, T-Diet, Zantryl) or topiramate (Topamax), or if you have glaucoma or overactive thyroid.

Do not use Qsymia if you have used an MAO inhibitor such as furazolidone (Furoxone), isocarboxazid (Marplan), phenelzine (Nardil), rasagiline (Azilect), selegiline (Eldepryl, Emsam, Zelapar), or tranylcypromine (Parnate) in the last 14 days. A dangerous drug interaction could occur, leading to serious side effects.

You should not use Qsymia if you are allergic to phentermine or topiramate, or if you have:

- glaucoma;
- overactive thyroid; or
- if you are pregnant or may become pregnant.

To make sure Qsymia is safe for you, tell your doctor if you have:

- high blood pressure, heart disease, heart rhythm problems, congestive heart failure;
- a history of heart attack or stroke;
- a history of depression, mental illness, or suicidal thoughts;
- diabetes;
- kidney disease (or if you are on dialysis);
- history of kidney stones;
- liver disease;
- seizures or epilepsy;
- low bone mineral density; or
- if you have ever had metabolic acidosis (too much acid in your blood).

Common side effects of Qsymia include:

- Numbness or tingling in the hands, arms, feet, or face (paraesthesia)
- Dizziness
- Changes in the way foods taste or loss of taste (dysgeusia)
- Trouble sleeping (insomnia)
- Constipation
- Dry mouth

- **Possible side effects of Qsymia include:**
- Mood changes and behavior changes such as new or worse anxiety, irritability, depression, aggression or other unusual changes in behavior or mood
- Concentration, memory, and speech difficulties.

- Increases of acid in bloodstream (metabolic acidosis). Metabolic acidosis can happen with or without symptoms Sometimes people with metabolic acidosis will:
  - Feel tired
  - Not feel hungry (loss of appetite)
  - Feel changes in heartbeat
  - Have trouble thinking clearly

- High blood pressure medicines. If you are taking medicines for your blood pressure, your doctor may need to adjust these medicines while taking Qsymia.
- Central Nervous System (CNS) side effects such as dizziness and light-headedness. Do not drink alcohol with Qsymia.
- Possible seizures if you stop taking Qsymia too fast. Seizures may happen in people who may or may not have had seizures in the past if you stop Qsymia too fast.
- Kidney stones. If you get severe side or back pain, and/or blood in your urine, call your healthcare provider.
- Decreased sweating and increased body temperature (fever). People should be watched for signs of decreased sweating and fever, especially in hot temperatures
- Increases in heart rate. Qsymia can increase your heart rate at rest. Tell your healthcare provider if you experience, while at rest, a racing or pounding feeling in your chest lasting several minutes when taking Qsymia
- Serious eye problems, which include:
  - Any sudden decrease in vision, with or without eye pain and redness
  - A blockage of fluid in the eye causing increased pressure in the eye (secondary angle closure glaucoma) Tell your healthcare provider right away if you have any new eye symptoms.

Call your healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you.

Risks/Side Effects Associated with All Study Medications

Once-weekly exenatide (Bydureon), Dapagliflozin (Farxiga), combination dapagliflozin and metformin extended-release (Xigduo XR), and phentermine/topiramate (Qsymia) can interact with other medicines. This includes some common medications such as certain decongestants, diuretics, cimetidine (Tagamet), corticosteroids, and niacin. Know the medicines you take including prescription and non-prescription drugs, vitamins, and herbal supplements. Keep a list of them to show the study doctor or study staff throughout the time you are taking part in this research study.

Pregnancy

The FDA has created guidelines for drug companies to follow in regards to labeling medications and their impact on pregnancy. The FDA has assigned pregnancy category X to phentermine/ topiramate (Qsymia). **The treatment might harm an unborn child; therefore you should not take part in this study if you are pregnant, breast feeding or you may become pregnant during the study period.** Data indicate an increased risk in oral clefts (cleft lip with or without cleft palate) with first trimester exposure to **topiramate**, a component of Qsymia. These defects can begin early in pregnancy, even before you know you are pregnant. **If you can become pregnant (unless sterilized), you will need to have a negative pregnancy test (blood or urine) before taking Qsymia and take a pregnancy test every month while taking Qsymia. You also must agree to use a reliable form of contraception consistently during the trial (e.g., intra-uterine device (IUD), diaphragm with spermicide plus condom). This should be continued for at least 1 month after the treatment has finished.**

Bydureon, Farxiga and Xigduo are medicines that the FDA has approved for use in diabetic women. These drugs have not been granted marketing authorization for use by pregnant women. A pregnancy test will be done before you start drug treatment and every month of the study. Bydureon, Dapagliflozin, and Xigduo XR are FDA pregnancy category C medications (one in which the risk to the pregnancy cannot be ruled out). There is a chance of fetal harm if the drug is administered during pregnancy.

Patients in all treatment groups will have the same tests done. You will be required to be using contraception (unless you have been sterilized) in order to participate in the study. This contraception method must be maintained during the study. Do not use any of the study medications without telling your doctor if you are breast-feeding a baby. It is not known whether any of the study drugs pass into breast milk or if they could harm a nursing baby.

Benefits

As a result of taking part in the study, you will receive medical care. You will be checked throughout the study. All medicines have been used in diabetic patients and have shown to improve sugar tolerance and result in weight loss. However, this benefit cannot be certain in non-diabetic women with PCOS. It is possible that you may <u>not</u> receive any benefit from this study. Society will gain from learning if the use of certain "anti-diabetic drugs" has a positive influence on sugar metabolism and body composition in women with PCOS.

Alternative Treatment

Caloric restriction, weight loss, and exercise are alternative methods that are used to reduce glucose and insulin levels. A number of other anti-diabetic medicines, like the ones described in this consent form but made by the same or other drug companies, are another choice that may be right for you. You may talk over the use of these with your primary health care professional or the health care professionals in this study. You do not need to take part in this study to receive treatment for your condition.

Costs

There will be no charge for any of the study measurements or blood tests. All study medications and exams will be provided free of charge throughout the time you are in this trial. Test results will be offered to you as well as your private doctor(s) if you give separate written

consent for information to be sent to your doctor(s). You will get $75 after study baseline screening and $75 after the last study testing visit (in which you have a 2-hour lab test at the hospital) to pay for local travel, meals and other costs from your study visit. Your health insurance company or you will pay for all other costs associated with your medical care. Woman's Hospital will be given payment from the study sponsor to cover some of the costs for carrying out the study and data collection.

Confidentiality

The results of this study may be published. Your name and identity will be kept private. Every effort will be made to keep your study information confidential. Absolute confidentiality cannot be guaranteed. Your study records will be part of your medical chart. Your study chart will be kept in a locked filing cabinet. Your study chart and study data will be kept for a minimum of three years. An agent from Astra Zeneca, the company supplying the medicine, may look at your records. The data will not be shared with other researchers. The Woman's Hospital Foundation Institutional Review Board, Woman's Hospital Research and Development Committee, research and clinical study staff, as well as Woman's Health Research Department, and the Food and Drug Administration may also check your study records.

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by 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.

Contacts for Extended Medical Care

If an injury happens while you are taking part in this study, medical care will be given to you. No funds have been set aside to pay your costs in the event of an injury as a result of this study. If an injury does occur, medical care can be gotten easily. The cost of this medical care will be the responsibility of you and/or your insurance company.

If you are hurt while taking part in this study, you should contact the Woman's Metabolic Health Clinic at (225) 924-8550. For more information about this research or patients' rights in research, you may also contact Ericka Seidemann, Human Protections Administrator, at (225) 231-5296.

Termination of Participation

At any time, you may ask that your test results not be used for research. Your decision to not take part will not have a penalty. You can leave the study at any time without changing your further care. Please call Dr. Elkind-Hirsch at (225) 231-5278 if you no longer wish to take part in the study. The researchers may need to stop your taking part in the study for any of the following reasons:

- you become pregnant
- an adverse event that leads to stopping of treatment by your physician
- you develop a related sickness, which increases the risk to you or halts the analysis of the study facts

- you have to take an unacceptable medicine at the same time
- not following study instructions
- finding out that you are not eligible
- new information about the study drug is discovered that may affect your wish to continue taking part
- the study doctor feels it is in your best interest

****

Acknowledgement Of Receipt Of Information And Consent To Participate

I HAVE HAD AMPLE OPPORTUNITY TO ASK ANY QUESTIONS CONCERNING THE STUDY AND MY PARTICIPATION IS VOLUNTARY AS REFLECTED BY THE SIGNED STATEMENT BELOW.

I have read the preceding description and have heard the verbal explanation of these procedures from my doctor. I freely give my consent to participate in this research. I have the right to ask questions and may refuse to continue in the study any time. If I refuse to participate or if I withdraw from the study, the doctors will continue to care for me and treat me as necessary for my condition

During the course of the research study, I will be informed of any new significant findings that may relate to my willingness to continue to participate.

At any time during treatment I am free to discuss with my doctor or his/her designee or the WHF Human Protections Administrator my rights as a participant and any side effects that might occur.

I AM MAKING A DECISION WHETHER OR NOT TO PARTICIPATE IN THIS STUDY. MY SIGNATURE INDICATES THAT I HAVE DECIDED TO PARTICIPATE, HAVE READ (OR BEEN READ) THE INFORMATION PROVIDED HEREIN, AND THAT I HAVE RECEIVED A COPY OF THIS INFORMED CONSENT FORM.

_____

Patient Name Date

_____

Patient Signature Date

_____

Signature of Person Administering Consent Date

_____

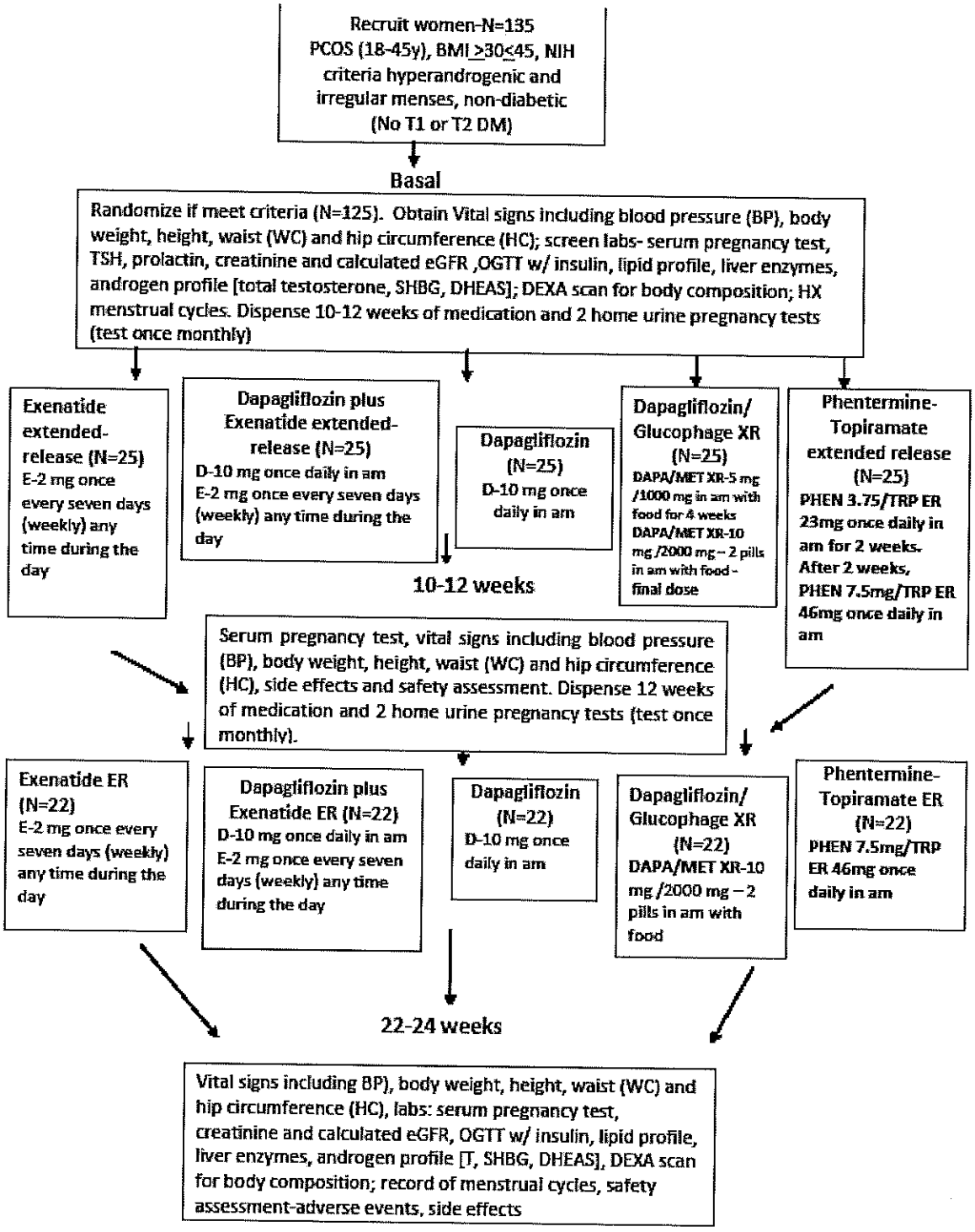
Investigator Signature Date

Woman's IRB

Approved 8/31/18

Expires 8/6/19

Figure 1: Flow of Patients Through Study Trial



Woman's IRB

Approved 8/31/18

Expires 8/6/19

RP-15-008

WOMAN'S HOSPITAL *Medical Record Number:* _____

Authorization to Release Health Information from Woman's Hospital

Patient's Name_____ Patient's Date of Birth_____

I hereby authorize appropriate personnel at **WOMANS HOSPITAL** to release my health information to, and/or allow my records to be reviewed by:

Recipient(s)	Study doctors, nurses, and personnel; Public health agencies and government agencies as required by law; Woman's Hospital Foundation Institutional Review Board; and Woman's Hospital Research and Development Comittee; study sponsor (AstraZeneca) personnel
Recipient's Address	
Attention:	

Purpose of Release

- ☐ for Treatment at Another Facility
- ☐ for Treatment by a Physician
- ☐ for Processing of my Insurance Claim
- ☐ for an Interview
- ☐ for Publication, Broadcast, or Other Dissemination by the hospital or media
- ☐ Other Reasons; Specify: _____
- ☐ for Application for Insurance
- X for Research
- ☐ Personal (at my request)

Specify information to be released by placing a check mark in the appropriate box(es):

Dates of Services	

- X Entire Record
- ☐ Diagnosis
- ☐ History & Physical Examination Reports
- ☐ Physician's Progress Notes
- ☐ Physician's Orders
- ☐ Nurse's Notes
- ☐ Discharge Summary
- ☐ Operative Report
- ☐ Consultation Reports; Specify by Doctor _____
- ☐ Other Records; Specify_____
- ☐ Information Concerning Illness, surgery, or events surrounding the birth of my child
- ☐ Treatment Room Record
- ☐ Clinic Record
- ☐ Entire Billing Record
- ☐ Itemized Bill
- ☐ Demographic Information
- ☐ X-Ray Reports
- ☐ Lab Results
- ☐ Photograph/Video

Woman's IRB Approved 8/6/15 Expires 8/6/15 Sib

Special consent is required to release the following information. Indicate Your Authorization by placing a checkmark in the appropriate box(es). NO INFORMATION WILL BE RELEASED IF BOX IS NOT CHECKED

- X Alcohol abuse records/test results/diagnosis
- X Drug Abuse records/tests results/diagnosis
- X HIV or AIDS test results
- X Mental Disorder records/test results/diagnosis

GENETIC TEST RESULTS – You must specify the test results to be released by checking or writing below:

Chromosome Analysis (specify below):
X Blood X Bone Marrow X CVS X Amniotic Fluid X Tissue

X Factor V Leiden
X Prothrombin DNA
X Cystic Fibrosis

X Methylenetetrahydrofolate Reductace
X Her2/neu Fish for breast cancer
X Other _____

Marketing

If I am providing authorization for marketing purposes, I understand that

☐ Woman's Hospital will not receive a monetary benefit from a third party for the use of my patient information.

☐ Woman's Hospital will receive a monetary benefit (directly or indirectly) from a third party for the use of my patient information.

Authorization Expiration Date or Event

Unless otherwise revoked, this authorization will expire on the indicated date, event or condition. If an expiration date, event or condition is not specified below, this authorization will expire six (6) months from date of signature. For genetic information, the expiration date must be sixty days or less from date of signature. If no expiration date is specified, the authorization will expire sixty days from date of signature . The statement "end of research," "none," or similar language is sufficient if disclosure is for research, (except for research on genetic information) including the creation and maintenance of a research database or repository.

Expiration (Month,Day,Year / Event / Condition) ____End of study_____

REQUIRED STATEMENTS

I understand that:

1. Authorizing the release of this health information is voluntary and I can refuse to sign this authorization.
2. I have the right to revoke this authorization at any time (upon written notification to the Health Information Management Department at Woman's Hospital) except to the extent that Woman's Hospital has already released the health information before receipt of the revocation. For genetic information, I have the right to revoke the authorization at any time before the disclosure is actually made or when I am made aware of the details of the genetic information.
3. If the authorization is for research, the researcher may continue to use and disclose the health information collected prior to the receipt of the written revocation.
4. Woman's Hospital cannot condition treatment, payment, enrollment, or eligibility for benefits on the patient providing this authorization.
5. If the authorization is for research-related treatment, Woman's Hospital may condition the provision of research-related treatment on provision of an authorization for the use or disclosure of protected health information for such research.
6. Any release of information carries with it the potential for an unauthorized redisclosure by the Recipient and the information may not be protected by federal law.
7. The authorization shall be invalid if used for any other purpose other than the described purpose for which the disclosure is made.
8. A photocopy of this authorization may serve as an original.

_____ _____

Patient's Signature Date

_____ _____

Personal Representative's Signature (if necessary) Date

Personal Representative

If it is necessary for a personal representative to sign and date this authorization due to lack of capacity of the patient, including minority, interdiction or any other legal reason, indicate below how the person signing as representative has authority to do so:

- ☐ The court appointed person acting for the patient, if one has been appointed.
- ☐ An agent acting pursuant to a valid mandate, specifically authorizing the agent to make health care decisions.
- ☐ The patient's spouse not judicially separated.
- ☐ An adult child of the patient.
- ☐ Any parent, whether adult or minor, for his minor child.
- ☐ The patient's sibling.
- ☐ The patient's other ascendants or descendants.
- ☐ Any person temporarily standing in for the parents, whether formally serving or not, for a minor under his care and any guardian for his ward.
- ☐ Other (Please specify): _____

Woman's IRB Approved 8/6/12 Expires 2/6/13

For Office Use Only: Date copy of authorization given to patient _____

Date copy of authorization mailed to patient _____

Date records sent _____