Subject Number: _____

Consent to Participate in a Research Study

Sponsor / Study Title:	**AbbVie / "24-Hour Ambulatory Blood Pressure Monitoring Study in Hypogonadal Men Receiving Testosterone Replacement Therapy"**
Protocol Number:	**M19-161**
Principal Investigator: (Study Doctor)	**Anuj Bhargava, M.D.**
Telephone:	**(515) 329-6800 (24 Hours)**
Address:	**Iowa Diabetes and Endocrinology Research Center 1031 Office Park Rd, Suite 2 West Des Moines, IA 50265**

You are being asked whether you would like to voluntarily participate in a research study of a drug called AndroGel® (testosterone gel)1.62%.

What is a research study?
A research study is an experiment whose purpose is to answer specific questions, such as:

- Does this drug work?
- Is it safe?

To answer these questions, doctors and scientists need volunteers to participate in research studies. These volunteers are called "subjects." The doctor in charge of the study at the study site - is called the "study doctor" or "investigator." The study doctor and scientists who run the research study are called "researchers," and other people who help them run the study are called the "research team."

An Institutional Review Board (IRB) has approved this study. The IRB is a group of people who review research studies to see if they meet federal laws and ethical standards. IRB approval only means it is ok for the study to begin. Only you can decide if being in this study is the right decision. Feel free to talk about this study with your family, friends, and personal doctor before you decide. We will answer any questions you may have so that you can make an informed decision.

The sponsor for this study is AbbVie. AbbVie pays the study site for the study doctor to run the study.

Purpose of Study:
You are being asked to join this study because you may have hypogonadism (a condition where low blood testosterone levels are associated with clinical symptoms). While you may not have the specific causes of low testosterone that AndroGel 1.62% is currently approved for, this study is designed to evaluate the effect of AndroGel 1.62% (testosterone replacement therapy) on blood pressure (ABP) in

hypogonadal men. AndroGel 1.62% is a topical drug approved by the U.S. Food and Drug Administration (FDA) for testosterone replacement therapy in males with low testosterone (hypogonadal). AndroGel 1.62% is currently approved for doses ranging from 20.25 mg up to 81 mg. Only these doses will be used in this trial.

Study Information:
This is a multicenter, phase 4, open-label, single-arm study. "Phase 4" means that AndroGel 1.62% has already been approved by the FDA to treat certain causes of low testosterone, and this is a study to answer further questions about the effect of Receiving Testosterone Replacement Therapy (TRT) on blood pressure, which could not be answered in earlier studies before the drug was formally approved.

"Open label, single arm" means that all study participants will receive the study drug AndroGel 1.62% and no placebo will be used. "A placebo" is not a drug. It is designed to look and feel just like the drug being studied but it is not designed to treat any disease or illness.

If you qualify to participate in this study, on Day 1 you will receive AndroGel 1.62%.The study doctor/study staff will help to show you where and how the study drug will be applied to your skin. All participants will be started at 40.5 mg of study drug. The amount and dose of study drug you will apply may change throughout the study. The study doctor/study staff will discuss any changes with you. No one will be assigned a dose below 20.25 mg or above 81 mg during the course of the study.

We expect that there will be approximately 45 research sites in the U.S., which will include approximately one hundred and ninety (190) men 18 years of age or older.

If you qualify for the study, your participation may last approximately 6.5 months. There are 10 required study related contacts (8 office visits and 2 phone calls). For the phone calls, a study staff member will call you and collect the study information over the phone. You may also be required to come to the office if an Unscheduled Visit is needed (ex. repeat labs or Ambulatory blood pressure monitoring (ABPM)). The study staff will tell you when to come into the office for your study visits. You should ask the study staff how long each visit will last.

This study includes:

- A Screening Period of up to 45 days consisting of 2 visits to determine if you are eligible to participate.
- A Study Treatment Period of at least 16 weeks (4 months) during which you will apply study drug once a day. During this period, the dose of study drug you receive may be adjusted based on your testosterone levels.
- A Follow-up Period of approximately 30 days after your last dose of study drug. If you complete the study entirely or if you discontinue from the study completely (withdraw consent) prior to the last study visit, you will be called on the phone and asked about any ongoing or new medical events since your last visit. All medical events will be followed until they resolve or if they are ongoing at the end of the study, the status of the medical event will be recorded.
- Questions will be asked about any medications you are taking, or changes in medication, and your health at every visit.

- ABPM: Ambulatory blood pressure monitoring (ABPM) will be collected at beginning and end of study. Each collection will last 24-hours. You will not stay in the hospital during 24-hour ABPM collection. Once the ABPM device is initiated, you will go home and continue your routine activities but should return to the study doctor's office on the next day to remove ABPM device and follow-up procedures.
- Labs will be collected to monitor your health throughout the study.
- At the End of Treatment visit you may be on site for 8-10 hours for 4 separate blood (PK) draws spaced out over several hours.

Study Screening Procedures:
In order to determine if you are eligible to participate in the study, you will complete the following screening procedures (activities, tests and evaluations) described in this form.

- **Informed Consent**: This form will explain the purpose, possible benefits and potential risks of this study.
- **Eligibility Criteria**: Tests will be performed, and questions will be asked of you. You must meet all of the requirements in order to be included in the study. Specific questions will be asked to determine whether you have symptoms related to low testosterone.
- **Medical/surgical / hypertension (high blood pressure) history**: Questions will be asked about your current and past medical conditions and surgeries. Specific questions will be asked whether you have a history of high blood pressure, whether high blood pressure is ongoing and whether you are taking any medications for treating high blood pressure, including the dose.
- **Alcohol and Nicotine Use**: Questions will be asked about your past and current alcohol and nicotine use.
- **Physical Exam**: The exam will be similar to what your regular doctor would do at your annual physical.
- **Vital Signs**: You will have:
  a) your blood pressure checked with an automated device by putting a band (sphygmomanometer) around your arm (this will squeeze your arm for about a minute)
  b) your pulse/heart rate taken (number of heart beats per minute)
  c) your respiration rate taken (number of breaths per minute)
  d) your temperature taken
- **Weight and Height**: Your weight and height will be measured to see how much you weigh and how tall you are.
- **Electrocardiogram (ECG)**: A common heart test, which measures the electrical activity of your heart. Pads will be placed on your chest and arms and a machine will record the heart activity.
- **Blood Tests**: (to check your testosterone levels and monitor your health). Blood samples collected during the study will be used only for research purposes. They will be tested by a central laboratory and may be transferred to third parties for evaluation.
- **Urinalysis**: A test to look at the appearance, concentration and content of your urine.
- **Review of any Medications**: The medications such as over-the-counter medicines, prescription medicines, vitamins, and herbal remedies you are taking or have taken in the past including the dosage.
- **Digital Rectal Exam (DRE)**: It is an exam during which a gloved finger is inserted into the rectum to check for growth, enlargement, or abnormalities of the prostate gland. The results from a DRE

performed within 6 months of the first Screening Visit can be used as long as written documentation of the DRE result is provided.

Study Procedures:
If you are eligible to participate in this study, you will undergo one or more of the study procedures described in this form at each study visit. It is important that you consider whether your schedule will allow for these visits.

- **Clinical Laboratory Blood Testing**: Some blood will be drawn to look at your Testosterone level at some visits. Some blood tests will be repeated at the End of Study or if you decide to discontinue from the study. These blood tests may include hematology, clinical chemistry, and sex steroids (testosterone, free testosterone, dihydrotestosterone [DHT] and estradiol).
  - During the study you may need to have a lab test or tests repeated. If you need to have a lab test or tests repeated, you will be asked to come to the study site to have a blood draw done. You may be asked to stop study drug based on the results of the blood tests.

Please note that the site will NOT store your Blood or Urine samples; the samples will be sent to the central lab, tested and destroyed.

- **Unscheduled Clinical Labs**: May be obtained at any time during the study if your study doctor feels it is necessary as directed by the study plan, these lab sample(s) will be sent to the central lab.
- **Health and Medication Questions:** You will be asked questions during your study visits about your health, medical history, and the medications you take. Please answer these questions to the best of your ability.
- **Vital Signs:** As described above in the Screening section.
- **Physical Exam:** The study doctor may perform an exam if you have any changes in your health or medication.
- **Study Drug:** You will be given a supply of study drug and told how to apply it. You have to bring back all used and unused bottles of study drug to each visit. The first dose of study drug will be administered at the study site on Day 1 after all procedures are completed.
- **ABPM:** Ambulatory blood pressure monitoring (ABPM) is a continuous monitoring of blood pressure by a portable device you must wear for a 24-hour period. The ABPM device consists of an inflatable cuff worn on your upper arm, which is attached to a small monitoring device weighing about 1 pound, which can be worn over the shoulder or on a belt. Application of the cuff/device by the site staff will occur in the office on the first day the ABP monitoring and will be removed by the site staff upon return to the office following 24 hours of collection on the second day. For example, if you start the ABPM at 9:00 am on Wednesday, you will complete it at 9:00 am on Thursday. The device is fully automated and will take BP measurements every 30 minutes over a 24-hour time period. The ABPM procedure will be carried out twice, at the beginning and end of study.

When ABPM is completed the investigator will assess whether the ABPM collection was successful and there was no device malfunction based on the results that are immediately available on site. If it was not successful you may be asked to repeat the procedure at an Unscheduled visit.

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Risks related to all Study Procedures:

- **Clinical Laboratory Blood Testing**: Taking a blood sample may cause pain, bleeding, and/or bruising at the site where the blood is drawn from. You may feel dizzy or faint and/or in rare instances develop an infection with redness and irritation at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions. The amount of blood that will be taken at the in-person study visits will vary (see activities table in this consent form). The average blood drawn at a scheduled study visit is approximately 2 teaspoons. Only at the End of Study Treatment the amount of blood drawn would be up to 2 tablespoons.
- **Electrocardiogram (ECG**): For the ECG, you will have pads placed on different parts of your body. There is no pain or discomfort during an ECG; however, the gel from the pads or removing the pads may cause some irritation to your skin.
- **Physical Exam:** There are no special risks with an exam.
- **Digital Rectal Exam (DRE**): This procedure may cause mild discomfort, and a small amount of bleeding from the rectum may occur after an examination. In rare cases, you may feel lightheaded and faint.
- **Ambulatory Blood Pressure Monitoring ABPM**: This procedure may cause interference with sleep, skin irritation, bruising and pain due to the cuff inflation.

Subject Responsibilities:
If you choose to participate, you will have certain responsibilities. In order to provide good information about how the study drug works in subjects with your condition, you will be expected to do the following:

- Attend all study visits.
- You will be asked at every visit (both in person and phone contacts) whether you have had any health problems.
- Tell the study doctor if you are feeling bad or worse than before.
- Follow the study drug dosing schedule/notification provided by site.
- You should not have direct skin-to-skin contact with pregnant or nursing women after applying the study drug.
- Follow the below steps after applying the gel to minimize the risk of testosterone transfer to another person:
    - **Apply the study drug only to your shoulders and upper arms that will be covered by a short-sleeve T-shirt.**
    - **Wash your hands right away with soap and water after applying study drug.**
    - **After the study drug has dried, cover the application area with clothing. Keep the area covered until you have washed the application area well or have showered.**
    - **If you expect to have skin-to-skin contact with another person, first wash the application area thoroughly with soap and water.**
- You will need to bring your study drug to the site with you at all of the in-person visits. You should **not** apply the study drug at home before any in-person visits.
- If you are being treated with any antihypertensive medication(s), you will need to bring them to the site with you at all in-person visits and take the medication dose(s) while on site.

- No fasting is required before signing and dating the consent form at Screening Visit 1.
    - All study visits following Screening Visit 1 where you have blood drawn, you should be fasting (no food or drinks except water) for a minimum of 8 hours.
- Tell your study doctor if you have any changes in medications during the study.
- Tell your study doctor if you have any changes in blood pressure medications
- Always tell your study doctor about use of erectile dysfunction medications (tadalafil, sildenafil citrate or vardenafil hydrochloride) and/or if you are taking any form of organic nitrate/organic nitrite.
- Follow the directions of your study doctor and study staff.
- Refrain from participation in other research studies while you are in this study.
- Report any health problems, including hospitalizations, emergency room and physician visits, to the study doctor immediately. If you become sick during the study and cannot report a medical event yourself, ask a family member to report the event to your study doctor.
- While in the study, **do not** take any other testosterone medications including those available without a prescription.
- Contact the study site if you stop your study drug for any reason.
- Notify your doctor if there is an ABPM device malfunction.
    - ABPM days:
        - When a reading is being taken, avoid movement: <u>lie, stand or sit still and relax</u>.
        - <u>Do not</u> engage in strenuous exercise or activities during the ABP monitoring period.
        - <u>Do not</u> take a shower or get the cuff/device wet during the ABP monitoring period.
        - Periodically check the cuff placement. Please adjust the cuff if it slips during the ABP monitoring period.
        - Avoid intake of salty foods.
        - <u>When sleeping</u>, insert the ABPM device between a pillow and its pillowcase and place it in bed with you. **<u>Do not</u>** place the ABPM device on a bed side table.
- End of Treatment Day: You may be on-site for 8-10 hours and will need to be available for 4 separate blood (PK) draws spaced out over several hours.
        - Blood samples to be collected at: 0 hour (immediately before on-site application of study drug), and at 2 hours, 4 hours, and between 6 to 8 hours following study drug application and only after confirmation of a successful Week 16 ABPM 24-hour collection.

Contraception Requirements

If you are sexually active with a female partner of childbearing potential you must agree to use condoms, even if you have undergone a successful vasectomy, from the beginning of the study through at least 30 days after the last dose of study drug.

AndroGel 1.62% Risks:

AndroGel 1.62% is a testosterone hormone replacement prescription medicine and should only be used while you are under the care of a health care professional.

AndroGel 1.62% contains testosterone and you should tell your doctor or the investigator if you have a history of any of the following:

- Breast or prostate cancer

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- Polycythemia/Erythrocytosis (increased red blood cell count)
- Pulmonary embolism/Deep vein thrombosis (blood clots)
- Problems urinating due to an enlarged prostate
- Heart problems
- Swelling or fluid retention due to heart, liver or kidney problems (edema)
- Problems breathing while you sleep (sleep apnea)
- Have any other medical conditions

AndroGel 1.62% medicinal products is supplied as a gel that is applied on the skin, it is possible ***that the study drug could be transferred to another adult or child through skin-to-skin-contact*.** Refer to the information you received with your AndroGel 1.62% prescription for where AndroGel 1.62% should be applied to your body or apply as directed by your study doctor.

The most common side effects (Adverse Events) reported in men during clinical trials with AndroGel 1.62% that may be caused by testosterone include:

- A rise in PSA levels (a blood test) used to screen for and monitor patients with prostate cancer
- Mood swings such as anger, aggression or depression
- Slight rise in red blood cell count
- Slight rise in blood pressure

In rare instances, blood clots in the veins were reported in men during clinical trials of AndroGel 1%. These events were not reported during clinical trials of AndroGel 1.62%.

Side effects (Adverse Events) reported by people prescribed and using AndroGel 1.62% since the drug was approved include:

- Abnormal blood tests including sugar, cholesterol, other lipids, and tests checking function of kidney and liver.
- Acne
- Blood clot (deep vein thrombosis and pulmonary embolism)
- Breast enlargement or breast tenderness
- Decrease in sperm count
- Difficulty emptying the bladder
- Dizziness, nausea, and headache
- Fluid retention or edema
- Heart attack (myocardial infarction) and stroke
- Increase in body hair
- Prolonged erection

Skin reactions have been reported by some men at the site where AndroGel 1.62% was applied. All of these reactions were mild and did not lead to stopping treatment in the clinical studies.

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Application of Study Drug to Minimize Risk of Transfer:

Study drug is supplied as a gel that is applied on the skin. It is possible that the study drug could be transferred to another adult or child through skin-to-skin-contact. You should follow the important instructions on how to avoid transferring study drug to others through skin-to-skin contact as described in the "Subject Responsibilities" section above.

Transfer of AndroGel 1.62% could lead to unwanted health effects in women and children who come in contact with the gel. You should avoid direct skin-to-skin contact with women and children after applying AndroGel 1.62%. A t-shirt may be worn to cover the application site once the application site is dry. A woman or child who accidentally comes into contact with the site where AndroGel 1.62% was applied should shower or wash the area with soap and water as soon as possible.

The following precautions are meant to be strictly followed by others in your household to minimize the risk of study drug transfer to them:

- Women and children should avoid contact with unwashed shirts or exposed skin at the application site(s) of men using study drug.
- If a woman or child's skin comes in contact with study drug, either directly or by touching your skin where the study drug was applied, he/she should wash the areas that have been exposed to the study drug thoroughly with soap and water to remove the study drug as soon as possible.

You are responsible for letting others (women and children) know that you may be using AndroGel 1.62%, of the risks mentioned above regarding transfer of study drug to a woman or child and what to do if they accidentally come into contact with study drug either directly or by touching your skin.

Below are some of the signs and symptoms of secondary exposure to testosterone in women and children. If any of the below are seen in a woman or child in your household, you should stop using study drug and should contact the study doctor right away:

- In women: changes in hair distribution, increase in acne, or other signs of testosterone effects such as abnormal hair growth on the face, or deepening of the voice.
- In children: unexpected sexual development including inappropriate enlargement of the penis or clitoris, premature development of pubic hair, increased erections, and aggressive behavior.

Risk to Pregnancy

Exposure to AndroGel 1.62% should be avoided in pregnant women. Testosterone may cause harm to the fetus when administered to pregnant women based on the way it works and data from animal studies. The side effects of AndroGel 1.62% on an unborn or nursing baby are unknown. There is a possibility that AndroGel 1.62% may be transferred from a man to a pregnant or nursing mother through direct skin-to-skin contact. There may be harm to the baby if a pregnant or nursing woman comes into contact with AndroGel 1.62%.

You should not enroll in this study if your wife, partner or significant other is pregnant, plans to become pregnant or nursing.

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Please follow the directions in the above section titled "Subject Responsibilities" to minimize the transfer of testosterone to the pregnant woman.

While participating in this study you should not have direct skin-to-skin contact with a pregnant or nursing woman.

If your partner becomes pregnant while you are in this study, you must inform the study doctor. If she agrees, she may be asked questions about the outcome of the pregnancy and the health of the baby.

You are responsible for letting your partner(s) know that you may be using AndroGel 1.62% and of the risks mentioned above regarding pregnancy. If your partner(s) become pregnant, a Consent Form will be provided to her to request information about her pregnancy and the health of the baby at birth, and this information may be shared with the Sponsor.

Allergic Reactions

As with any study drug, allergic reactions may occur, including:

- Fast heart rate
- Having a hard time breathing
- Wheezing when you breathe
- Hives
- Rash
- Sudden drop in blood pressure
- Sweating
- Swelling around the face, mouth, lips, tongue, throat or eyes

If you feel that you have any of the above allergic reaction symptoms, call your doctor immediately or go to the hospital emergency room.

It is possible that not all of the risks and side effects associated with the use of AndroGel 1.62% are known at this time. If you experience any of the symptoms mentioned or are having any unusual symptoms, you should notify your study doctor immediately.

Prostate cancer: About half of the men over age 65 have tiny areas of cancer in their prostate glands that appear not to hurt them. It is unknown if testosterone study treatment in this study could change these harmless tiny prostate cancers into harmful ones or increase the frequency of identifying the cancers that appear not to hurt men due to increased monitoring. When testosterone was given in previous studies to men over the age of 65, there was no increase in prostate cancer, but not enough men participated in those studies to know for sure if using testosterone will affect the chance of prostate cancer. Also, some men who have prostate cancer have an improvement in the cancer if their blood testosterone is lowered.

Men who have had prostate cancer will not be allowed to take part in the study. Also, men who have a prostate lump or hardness on the rectal examination will not be permitted to join the study, unless a previous biopsy shows that the lump is not cancer. If a prostate lump or hardness is detected during

the screening period, these abnormalities will be evaluated further in order to determine if you qualify for the study.

If your study doctor notices changes in your prostate such as a prostate lump (nodule) or prostate enlargement during the study, he/she may ask you to see a urologist (a doctor who specializes in the urinary system) to discuss whether you should have a prostate biopsy (a procedure to take small samples of prostate tissue and study them under a microscope). If a prostate biopsy is performed and prostate cancer is confirmed, you may need to discontinue from the study participation.

Enlarged prostate (Benign prostatic hyperplasia/BPH): Testosterone dosing of older men might also increase the size of the prostate and cause a decrease in urine flow. Other studies of testosterone have not shown worsening of urination problems, but the number of men studied so far is too small to know for sure. To reduce the chance of urination problems in this study, only men who do not have a lot of difficulty urinating will be eligible.

High red blood cell count: Testosterone may increase the number of red blood cells, which is why men may have higher red blood cell counts than women. If a man had a high red blood cell count when his testosterone was low, increasing the blood testosterone level with a TRT may increase his red blood cell count to higher than normal. This might increase the chance of a blood clot. For this reason, only men with red blood cell counts below a certain value will be allowed to be in the study and blood cell counts will be looked at periodically during your participation in the study.

Venous Thromboembolism (blood clots): There have been reports of blood clots in the legs and lungs in men prescribed testosterone products such as AndroGel 1.62%.

Cardiovascular (CV): Long term clinical safety trials have not been conducted to assess the cardiovascular outcomes of testosterone replacement therapy in men. To date, studies have been unable to determine whether or not TRT increases the risk of CV events, such as heart attack and/or stroke.

Sleep apnea: Testosterone may increase the risk of sleep apnea, a condition in which not enough oxygen gets into the blood during sleep, resulting in excessive sleepiness during the day. Although it is not certain that testosterone has this effect, men who have been diagnosed with sleep apnea will be eligible only if they are being treated for it.

Alternatives to Participation:

You have the option not to participate in this study and to receive the standard of care treatment from your regular doctor who can discuss the potential benefits and risks for these treatments with you.

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ACTIVITY SCHEDULE

Visit Windows Baseline ABPM (+ 7 days) Week 2 (± 4 days) Week 4 (± 7 days) Week 10 (+ 7 days) Week 16 ABPM (+ 7 days) Follow-Up (± 7 days) *Visit timing based on time elapsed from the Day 1 Visit*	SV1	SV2	Baseline ABPM	Day 1	Week 2 - Titration	Week 4 - Titration	Week 10 - Phone Call	Week 16 ABPM	End of Treatment	Premature Discontinuation	Unscheduled	30-Day Follow Up Call
INTERVIEWS												
Informed consent	✓											
Eligibility Criteria	✓	✓	✓									
Subject/medical/surgical/hypertension history	✓		✓									
Alcohol and Nicotine Use	✓											
Adverse Event Assessment	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Prior/Concomitant Medication Assessment	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Phone Call							✓					✓
EXAM												
Height, weight, and BMI		✓										
Vital signs (include oral temperature, HR and RR)	✓	✓	✓					✓	✓	✓	✓	
Office blood pressure measurements (cuff)	✓	✓	✓		✓	✓		✓		✓	✓	
Physical examination (full)		✓										
Physical examination (symptom directed)			✓					✓	✓	✓	✓	
Digital Rectal Exam		✓										
12-Lead ECG (after 5 minutes of supine rest)		✓										
Cuff size measurement	✓		✓					✓			✓	
Dispense/Collect ABPM device			✓	✓				✓	✓		✓	
Pre-ABPM Assessment			✓					✓			✓	
ABPM (24-hour collection)			✓					✓			✓	
ABPM Assessment (validity confirmation of ABPM collection)				✓					✓			
CENTRAL LABS												
Testosterone	✓	✓		✓	✓	✓				✓		
Dihydrotestosterone (DHT)				✓					✓	✓		
Estradiol (E2)				✓					✓	✓		
Prostate-specific antigen (PSA)		✓							✓	✓	✓	
Hematocrit											✓	

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Visit Windows Baseline ABPM (+ 7 days) Week 2 (± 4 days) Week 4 (± 7 days) Week 10 (+ 7 days) Week 16 ABPM (+ 7 days) Follow-Up (± 7 days) *Visit timing based on time elapsed from the Day 1 Visit*	SV1	SV2	Baseline ABPM	Day 1	Week 2 - Titration	Week 4 - Titration	Week 10 - Phone Call	Week 16 ABPM	End of Treatment	Premature Discontinuation	Unscheduled	30-Day Follow Up Call
Hematology (without differential)		✓							✓	✓		
Hemoglobin A1c		✓										
Chemistry (including serum creatinine for eGFR assessment by CKD-EPI equation at SV2 only)		✓							✓	✓		
Urinalysis (without microscopy)		✓										
Serial PK blood samples following ABPM assessment obtained at 0, 2, 4, and 6 - 8 hours									✓			
℞ TREATMENT												
Enrollment			✓									
Subject applies study drug on site				✓	✓	✓		✓	✓			
Dispense study Drug				✓	✓	✓						
Collect Study Drug					✓	✓			✓	✓		
Study Drug Adherence Check					✓	✓			✓	✓		

ABPM = ambulatory blood pressure monitoring; BMI = body mass index; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; HR = heart rate; PK = pharmacokinetics; RR = respiratory rate; SV1 = Screening Visit 1; SV2 = Screening Visit 2

Use of Biological Samples

The biological samples (such as blood, urine, stool, and tissue) that we collect from you will be stored, processed, and used as described in this document. Biological samples collected during the study will be tested by the central laboratory, AbbVie, and/or companies or people working with AbbVie. Unless otherwise specified, samples will be destroyed once all required tests and analyses are completed. AbbVie will not sell your biological samples to other people or companies. All biological samples collected from you will be given a unique code to protect the confidentiality of your Personal Data. Please refer to the section entitled, "Information About Confidentiality and HIPAA Authorization," for more details. In addition, in the "Voluntary Participation and Withdrawal" section, you can find information about what to do if you no longer want AbbVie to use your biological samples.

New Information

You will be informed in writing in a timely manner and will be asked to sign and date a new (revised) informed consent if new information that could affect your willingness to continue participation in this study becomes available

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Benefits
Although you may not directly benefit from being in this study and from the ABPM procedure, your participation may benefit to future patients with your disease or condition and contribute to scientific advances in the area of ABPM research and its clinical practice, as well as provide valuable information for the medical community. Your condition during and after the study may get better, it may get worse, or it may stay the same.

Costs
Neither you nor your insurance company will have to pay for the study drug or procedures that are done only for the study.

You or your insurance company will be responsible for the costs of your regular medical care. Regular medical care costs are the costs for medications, treatments, procedures, and testing that you would have had if you were not in the study.

Reimbursement and Payments
You will be paid for in-person study site visits you complete according to the following schedule:

- Baseline ABPM Visit: $50
- Day 1 and Week 16 Visit: $75 each visit
- Weeks 2 and 4 Visit: $50 each visit
- End of Treatment Visit: $125
- Unscheduled Visits (up to 3 visits, during Treatment): $50 each visit

You will be paid after you have completed each visit. If you do not complete the study for any reason, you will be paid for each study visit you do complete according to the schedule above. If you have any questions regarding your compensation for participation, please contact the study doctor at the telephone number listed on page one of this consent document.

You will not be paid for telephone visits.

We may have to report this payment to the IRS.

AbbVie and people or companies working with AbbVie may use your biological samples when developing new tests, procedures, and commercial products. If this happens, AbbVie does not plan to share any profits with you.

Research Related Injuries
Treatment for injuries that result from the study drug or study procedures is available. Your study doctor will discuss with you the available medical treatment options. You may arrange to have treatment performed by the study doctor or a licensed doctor selected by you.

If you experience any injuries that result from the study drug or study procedures, AbbVie will provide reimbursement for reasonable medical expenses that are a direct result of such injuries.

Subject Number: _____

AbbVie makes no commitment to provide compensation except as described above. You will not lose any of your legal rights or release AbbVie, the study doctor, the research team, or study site from liability for mistakes or intentional misconduct by signing and dating this consent document.

INFORMATION ABOUT CONFIDENTIALITY AND HIPAA AUTHORIZATION

The Privacy Rule of the federal Health Insurance Portability & Accountability Act (HIPAA) is a law that protects the confidentiality of your personal health information. This confidentiality section describes your rights and explains how your personal health information will be used and disclosed.

Why is access to my personal health information being requested?

To help answer the research questions, the study doctor and research team will collect, use, and store personal health information about you. We are asking your permission to use and share it with others, as explained below. If you don't give this permission, you won't be able to take part in the research study.

What information about me will be collected and used?

If you decide to participate in this study, the study doctor and research team will collect personal health information about you that also includes your name, address, or other data that could identify the information as yours. Under HIPAA, this personal health information is protected and can't be used without your permission, unless otherwise permitted by law. The study doctor and research team may collect this information about you from your existing records (including medical records), so they can understand your medical history. During the study, they may also collect information self-reported by you by answering questions and/or completing questionnaires, as well as their observations of you.

The following are examples of personal health information that may be collected:

- your name, address, telephone number, date of birth, race/ethnicity, medical record numbers, and/or other identifying information
- results of examinations, laboratory tests, and procedures such as physical examinations, blood tests, ABPM, or other medical procedures
- information about your medical conditions and history, including information derived from your biological samples (for example, blood and urine), health conditions, treatments and medical procedures, including related dates

Subject Number: _____

Who will see my personal health information?

The study doctor and the research team will use your personal health information to carry out this study. By signing and dating this authorization, you allow access to your personal health information (including direct access to your medical records at the study site or any other facility where the study is conducted) to the following:

Who may have access:	**Purpose:**
AbbVie and its representatives	To oversee the study and make sure the information is correct and to report to government agencies as required by law
The study doctor and the research team	To determine if you can participate in this study, conduct the study, make sure the study information is correct, provide you with reimbursement of your travel expenses and/or compensation for your time and inconvenience to attend study visits, and to follow up with you if needed for safety reasons after the study is completed
The FDA and government agencies that regulate research in the US and other countries	To make sure applicable laws are being followed, ensure that the study is being conducted properly, and verify that the study data is being reported accurately
IRB	To protect the rights and safety of subjects, make sure applicable laws are followed, ensure that the study is being conducted properly, and verify that the study data is being reported accurately
Centers for Medicare & Medicaid Services (the agency that runs Medicare)	To determine if Medicare should pay for services related to the study, including diagnosis and treatment for research-related injuries

If AbbVie is going to pay for healthcare services that you receive in connection with the study, we may also need to disclose your personal health information to AbbVie and its representatives in order for AbbVie to comply with a Medicare reporting requirement.

After the study has been completed, it is possible that your coded data will be used for future research relating to the study drug, your disease, similar diseases and medical conditions, or analysis of how AbbVie can improve its clinical research processes.

Will you keep my personal health information confidential?
We will keep your personal health information as confidential as possible. While it is unlikely that your personal health information will be given to others without your permission, we can't control how it is used once it leaves the study site, and it will no longer be covered by the HIPAA Privacy Rule.

Your study records and biological samples will receive a unique code in place of information that can be used to identify you (such as your name or address). In addition, any features that can identify you during ABPM recording as part of your participation in the study will be blocked or masked. AbbVie and its affiliates and the people and companies involved in the study conduct will have access to and use these coded records, samples and accompanying data to conduct the research described in this form and to learn more about the disease(s) or health condition(s) and the study drug that are the subject of the study. However, they will not be able to see the key that links the code to you. AbbVie will only receive coded data and will not be able to directly identify you.

The results of this study may be published in study reports or scientific presentations. Information that identifies you or that reasonably could be used to identify you will not be included in such publications. Your health records taken as part of your participation in the study may be used in study publications or educational materials relating to the study drug. Any features that can identify you will be removed to protect your identity.

How long will my personal health information be used?
Access to your personal health information begins as soon as you sign and date this form. This authorization expires fifty years after the date that you sign and date this form, unless you revoke it sooner.

If you don't want us to collect, use, and share your personal health information anymore, you must let the study doctor know in writing. There will not be any penalty or loss of benefits to which you are otherwise entitled, but you will not be able to continue in the research study. We will stop collecting new information about you, but will still use, analyze, and disclose any information that we gathered before you revoked your permission. You should understand that personal health information that has

already been collected cannot be deleted from study records due to regulatory requirements that are designed to safeguard scientific integrity. The study doctor and research team and AbbVie may be required to include your information in analyses and aggregate research results, but in a way that will not identify you.

Can I see my records?

You may have the right to see and get a copy of your medical records as allowed by applicable privacy laws. However, by signing and dating this form, you agree that you may not get to see your records relating to the study until after the study is over. You may ask to see your records by requesting such records from the study doctor.

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.

STATEMENT OF AUTHORIZATION

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

_____

Printed Name of Subject

_____ _____

Signature of Subject Date

_____

Printed Name of the Person Obtaining the Authorization

_____ _____

Signature of the Person Obtaining the Authorization Date

Subject Number: _____

Voluntary Participation and Withdrawal

Do I have to participate in the study?

You do not have to be in this study. There is no penalty or loss of benefits if you don't want to participate, and your decision won't affect your regular medical care.

Can I change my mind about participating in the study?

If you start participating in the study, you may stop at any time without further explanation. If you want to stop participating in the study for any reason, you must let the study doctor know in writing. You will not be punished or lose any benefits to which you are otherwise entitled.

The study may be stopped early by AbbVie, the study doctor, the IRB, or the FDA. You could be withdrawn from the study without your consent, at any time and for any reason.

If you withdraw from the study for any reason, all study drug bottles, including those unused and empty must be returned to the study site. You will also be asked to return to the study site if you discontinue from the study completely so that the study doctor can perform a final evaluation, which may include a physical examination and/or laboratory tests.

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

If you sign this form and participate in the study, the study personnel will be authorized to use the information described above to carry out the purposes of the research study.

What will happen to my biological samples if I stop participating in the study?

If you withdraw or are withdrawn from participating in the study, the biological samples that we have collected from you as part of the study will continue to be stored and analyzed as described in this document unless you specifically take back your permission to use your biological samples. If you want to take back your permission to use your biological samples, you must let the study doctor know in writing. If you take back your permission to use your biological samples, no new research work will be started, and your biological samples will be destroyed unless a regulatory authority requires AbbVie to keep them. If AbbVie and/or other researchers did any testing of your biological samples before you took back your permission, AbbVie will still use and disclose the test results and keep the data generated from your biological samples due to regulatory requirements that are designed to safeguard scientific integrity.

What will happen to my personal health information if I stop participating in the study?

Unless you have specifically revoked your permission for us to collect your personal health information as described in the "How long will my personal health information be used" section above, we may continue collecting your personal health information if you withdraw or are withdrawn from the study. If you are withdrawn from the study, we may continue to follow up with you. If you do not want to be contacted by the study doctor, you should inform the study doctor about this when you are withdrawn from the study.

Subject Number: _____

Whom to Contact About To Study

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

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

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00040458.

CONSENT

For Research Subjects in California: Before you sign this informed consent, you should read and sign a copy of the California Experimental Subject's Bill of Rights. Ask the study staff or the Investigator for a copy of this document if you have not already received one.

Printed name of Subject: _____

- I have read this form and the research study has been explained to me.
- I have been given the chance to ask questions, and my questions have been answered.
- I voluntarily agree to be in the research study described above.
- I will receive a copy of this consent form after I sign and date it.
- I authorize the collection, use, and sharing of my personal health information and biological samples as described in this form.
- I am not giving up any of my legal rights by signing and dating this form.

_____

Signature of Subject Date

_____

Printed Name of Person Conducting Informed Consent Discussion

_____ _____

Signature of Person Conducting Informed Consent Discussion Date