Novel Combination Therapy for Osteoporosis in Men

NCT03994172

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Department of Veterans Affairs	**INFORMED CONSENT FORM**
Subject Name:	**Date:**
Title of Study: Novel Combination Therapy for Osteoporosis in Men	
Principal Investigator: Dolores Shoback, MD	**San Francisco VAMC**
Research Project Director:	Dolores Shoback, M.D., Professor of Medicine, UCSF, Endocrine Research Unit, Veterans Affairs Medical Center, 1700 Owens Street, San Francisco, CA 94158. Phones: 415-221-4810 ext 23336 or 415-575-0552; e-mail: dolores.shoback@ucsf.edu
Study Coordinator:	Nicole King, CCRP; Clinical Research Coordinator, NCIRE (415) 575-0580

STUDY SUMMARY

Introduction: We are asking you to consider taking part in a research study being done by Dolores Shoback, MD, and Anne Schafer, MD, of the Department of Medicine at UCSF and the San Francisco Department of Veterans Affairs Medical Center.

The first part of this consent form gives you a summary of this study. We will give you more details about the study later in this form. The study team will also explain the study to you and answer any questions you have.

Research studies include only people who choose to take part. It is your choice whether or not you want to take part in this study. Please take your time to make a decision about participating. You can discuss your decision with your family, friends and health care team.

Purpose of the study: The researchers want to find a better medication or combination of medications to treat low bone mass or osteoporosis in men. This study will test the safety and effectiveness of the medication teriparatide compared to the combination of teriparatide with a medication called cinacalcet. We want to find out if the combination produces a stronger effect on bone mineral density. We will also study the safety and side-effect profile for patients of the medications.

Study Procedures: If you choose to be in this study, you will be asked to take a teriparatide injection plus a cinacalcet pill or a placebo pill (no study drug in it) daily for 11 months. The main study procedures include bone density scans, blood draws, and urine collections.

You will be in this study about 12 months total and take the treatment for 11 months and visit the research site about 11 times.

Possible Risks: There are risks to taking part in a research study. Some of the most likely risks of participation in this study include:

- High or low blood calcium level
- Nausea, vomiting, constipation or abdominal pain
- High urinary calcium level
- Dizziness, headaches, weakness, muscle cramps

There are also rare but serious risks of participation, like:

- Very high blood calcium that would require being seen in an emergency room
- Very low blood calcium that would require being seen in an emergency room
- Kidney stone

We'll tell you about the other risks later in this consent form.

Possible Benefits: You may benefit from participating in the study, but this cannot be guaranteed.

Your Other Options: You do not have to participate in this study. Your other choices may include:

- Getting treatment or care for your condition without being in a study.
- Taking part in another study.
- Getting no treatment at all and being observed.

Please talk to your doctor about your choices before agreeing to participate in this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

DETAILED STUDY INFORMATION

This part of the consent form gives you more detailed information about what the study involves.

Research studies include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you are a man with low bone mass.

Why is this study being done?

This study is being done to see if we can find a more effective way to treat men who have low bone density or osteoporosis. Osteoporosis means 'thin bones'. Men with osteoporosis have an increased risk of breaking a bone, and we do not know how best to prevent that from happening. We have treatments, but we do not have the information that will tell us exactly how to use them in the most effective way and how to combine them to get an even greater effect on the bone mass and strength.

One approved treatment for osteoporosis or low bone density in men is teriparatide or parathyroid hormone (1-34) or PTH(1-34). Teriparatide is a piece of a hormone that our bodies normally make. Studies have found that teriparatide stimulates new bone to be made. So it can be used to build up the bone mass in someone with osteoporosis, and it also improves the strength of that bone so it is less likely to break.

All the men in this study will receive teriparatide. Teriparatide is given by a once daily injection to treat people with low bone density or osteoporosis. In studies in the laboratory, we tested the medication teriparatide as a single treatment given to male mice as a daily injection. We compared the bone density responses of the mice to a combination of teriparatide plus another medication called cinacalcet. This is a medicine that can increase the activity of calcium receptors. These receptors on bone cells can increase the ability of those cells to make new bone proteins and form new bone. When we tested the combination of the two medications in mice (teriparatide and a medicine in the same family as cinacalcet), we found that the combined treatments were much more effective at improving the bone density of the mice and making their bones stronger. The combination was better than just giving the mice teriparatide injections alone. This clinical study is to see if we can combine these two approved medications to reach the same improved response in men with low bone mass or osteoporosis.

Both teriparatide (also called Forteo) and the medication cinacalcet (also called Sensipar) are medications approved by the FDA in the US. Cinacalcet is approved by the FDA for treating hyperparathyroidism, but not to treat low bone density or osteoporosis. It is uncertain whether combining cinacalcet with teriparatide can make teriparatide more effective in men, as it did in mice. This combination of medications has not been given to people in a study before, and that makes this study a research study. Testing this combination therapy together is a research study. In this study, you will get either teriparatide and cinacalcet in combination, or you will get teriparatide and a placebo (an inactive substance). You will not get all three (teriparatide, cinacalcet, and placebo).

This study is being paid for by the Department of Veterans Affairs.

The investigators in this study do not have any financial or proprietary interests in this study or in any of the medications that will be used in this study.

How many people will take part in this study?

About 48 people total will take part in this study at the San Francisco Veterans Affairs Medical Center.

What will happen if I take part in this research study?

Before you begin the main part of the study . . .

You will need to have the following tests and procedures to find out if you can be in the main part of the study. We call these screening procedures.

- **Screening Visit 1**

  - **Bone density (DXA) scan:** Your bone mineral density at your hip, spine, and wrist will be measured by dual-energy X-ray absorptiometry (DXA). You will lie flat on a table in a hospital gown, and a scanning device will pass over your body. This takes about 30 minutes.

- **Screening Visit 2**

  - **Physical examination:** You will have a physical examination, similar to that done for regular medical care. This will include measuring vital signs, weight, and height.

  - **Medical and dietary history:** You will be asked questions about your medical history, medications you take, and the foods you typically eat.

  - **Blood draw:** You will be asked to give a blood sample for measurement of your complete blood count; your electrolytes (blood chemistries); your kidney, liver, and thyroid function; your testosterone, vitamin D, and parathyroid hormone levels; and your diabetes status. Approximately 3-4 teaspoons will be drawn by inserting a needle into a vein in your arm.

  - **Urine collection:** You will be given instructions and the materials for collecting a 24-hour urine sample, which will begin that morning at the Clinical Research Center, continue at home that afternoon and night, and finish the next morning. You will have the option of starting this at home the day before your visit and turning it in at your visit. The urine will be used to measure your urine calcium and sodium levels. Because teriparatide treatment can increase urine calcium, your urine calcium must be below a certain value to continue with the study.

  - **Learn how to do the teriparatide injection:** To be sure everyone coming into the study understands what the daily teriparatide injection will be like, we will teach you how to do the injection using a placebo. You will not yet start doing injections at home.

  - **Start calcium and vitamin D supplements:** You will be provided with and will be asked to start taking calcium and vitamin D supplement pills. The calcium will be at a dose decided on by your study doctor. This will replace any calcium supplement you usually take. The goal of the calcium supplement is to standardize the calcium intake of people participating in the study. The vitamin D will be a standard 1000 IU daily or what is needed to maintain your vitamin D levels in a good range for you.

You will need to complete a log of calcium and vitamin D supplement pill use for 4 weeks in order to continue with the study.

During the main part of the study . . .

If the tests and procedures show that you can be in the main part of the study, and if you choose to take part, then you will need the following tests and procedures, and, as described below, you will take teriparatide and cinacalcet or teriparatide and a placebo for 11 months.

- **Randomization Visit**

  - You will come to the Clinical Research Center in the morning. You will be asked to fast for at least 10 hours before you come in, although you will be able to drink water.

  - **Vital signs, weight, and height** will be measured.

  - **Urine collection:** You will have been given instructions and the materials for collecting a 24-hour urine sample at home, and you will turn it in at your visit. The urine will be used for measurements including urine calcium and sodium levels.

  - We will ask you if you have had any change in your health since your last visit, review what medications you are taking, review your calcium and vitamin D intake, and check to make sure you are taking the calcium and vitamin D supplements correctly.

  - **Randomization:** You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the groups. Neither you nor your doctor can choose the group you will be in. You will have an equal chance of being placed in either group.
  - If you are in group 1: You will inject teriparatide once daily for 11 months, and you will swallow a cinacalcet tablet once daily for the same 11 months.
  - If you are in group 2: You will inject teriparatide once daily for 11 months, and you will swallow a placebo tablet once daily for the same 11 months.
  - To keep the study "blinded"—meaning neither the participants nor the investigators know what people are taking—you will not know which group you are in. The cinacalcet and placebo tablets will be in similar bottles.

  - **Review how to do the teriparatide injection:** We will review with you how to do the teriparatide injection.

8-hour pharmacodynamic study: You will undergo testing to determine exactly how calcium-related minerals and hormones change in response to the first dose of each of the study medications. A small catheter (tube) will be placed in a vein in your arm, wrist, or hand. A needle will be used to place this IV catheter. First, approximately 4 teaspoons of blood will be drawn. Next, you will receive your first injection of teriparatide and swallow your first tablet of cinacalcet or placebo. The volume of teriparatide that will be injected (per injection) is about 86 microliters, which is just under 0.1 or 1/10 or a milliliter, which is a very small drop of liquid. Then, blood will be drawn through the catheter 1, 2, 4, and 8 hours later.

  - **Start study medications:** After the randomization visit, you will start the study medications. The injections should be done every day in the morning. On the days you

have study visits, wait until after your study visit blood draw to do the injection. The cinacalcet or placebo should be taken once daily by mouth.

- **Week 1 Telephone Visit & Labs (with optional in-person visit)**
  - **Blood draw:** Approximately 4 teaspoons of blood will be drawn for testing to include calcium and related hormones, kidney function, bone turnover markers, and blood cells
  - We will call you one week after you begin taking the study medications. We will ask you if you have had any change in your health since your last visit, review what medications you are taking, review your calcium and vitamin D intake, and check to make sure you are taking the study medications correctly. This phone visit will take about 15 minutes of your time.

At each of the subsequent study visits, you will come to the Clinical Research Center in the morning, fasting. You will be able to drink water during the fasting period. We will ask you if you have had any change in your health since your last visit, review what medications you are taking, review your calcium and vitamin D intake, and check to make sure you are taking the study medications correctly.

Other measurements are as follows:

- **4 Weeks (Approximately Month 1) Visit**
  4 weeks (approximately one month) after you begin taking the study medications, you will undergo:
  - **Vital signs, weight, and height** will be measured.
  - **Blood draw:** Approximately 4 teaspoons of blood will be drawn for testing to include calcium and related hormones, kidney function, bone turnover markers, and blood cells.
  - **Urine collection:** You will have been given instructions and the materials for collecting a 24-hour urine sample at home, and you will turn it in at your visit.

- **8 Weeks (Approximately Month 2) Visit**
  8 weeks (approximately two months) after you begin taking the study medications, you will undergo:
  - **Vital signs, weight, and height** will be measured.
  - **Blood draw:** Approximately 4 teaspoons of blood will be drawn for testing to include calcium and related hormones, kidney function, bone turnover markers, and blood cells.
  - **Urine collection:** You will have been given instructions and the materials for collecting a 24-hour urine sample at home, and you will turn it in at your visit.

- **12 Weeks (Approximately Month 3) Visit**
  12 weeks (approximately 3 months) after you begin taking the study medications, you will undergo:
  - **Vital signs, weight, and height** will be measured.
  - **Blood draw:** Approximately 4 teaspoons of blood will be drawn for testing to include calcium and related hormones, kidney function, bone turnover markers, and blood cells.

- **Urine collection:** You will have been given instructions and the materials for collecting a 24-hour urine sample at home, and you will turn it in at your visit.

- **<u>20 Weeks (Approximately Month 5) Visit</u>**
  20 weeks (approximately 5 months) after you begin taking the study medications, you will undergo:
  - **Vital signs, weight, and height** will be measured.
  - **Blood draw:** Approximately 3-4 teaspoons of blood will be drawn for testing to include calcium and related hormones, kidney function, bone turnover markers, and blood cells.

- **<u>24 Weeks (Approximately Month 6) Visit</u>**
  24 weeks (approximately 6 months) after you begin taking the study medications, you will undergo:
  - **Vital signs, weight, and height** will be measured.
  - **Blood draw:** Approximately 4 teaspoons of blood will be drawn for testing to include calcium and related hormones, kidney function, bone turnover markers, and blood cells.
  - **Urine collection:** You will have been given instructions and the materials for collecting a 24-hour urine sample at home, and you will turn it in at your visit.

- **<u>36 Weeks (Approximately Month 9) Visit</u>**
  36 weeks (approximately 9 months) after you begin taking the study medications, you will undergo:
  - **Vital signs, weight, and height** will be measured.
  - **Blood draw:** Approximately 4 teaspoons of blood will be drawn for testing to include calcium and related hormones, kidney function, bone turnover markers, and blood cells.
  - **Urine collection:** You will have been given instructions and the materials for collecting a 24-hour urine sample at home, and you will turn it in at your visit.

When you are finished receiving study medication, this will occur at the 48 Week (Month 11) Visit:

- **<u>48 Weeks (Approximately Month 11) Visit</u>**
  48 weeks (approximately 11 months) after you begin taking the study medications, you return for a final visit:
  - **Physical examination:** You will have a physical examination, similar to that done for regular medical care. This will include measuring vital signs, weight, and height.
  - **Medical and dietary history:** You will be asked questions about your medical history, medications you take, and the foods you typically eat.
  - **Bone density (DXA) scan:** Your bone density at your hip, spine, wrist, and whole body, as well as the amounts of muscle and fat in your body, will be measured again by DXA.
  - **Blood draw:** Approximately 4 teaspoons of blood will be drawn for testing to include calcium and related hormones, kidney function, bone turnover markers, and blood cells.
  - **Urine collection:** You will have been given instructions and the materials for collecting a 24-hour urine sample at home, and you will turn it in at your visit.

- We will ask you if you have had any change in your health since your last visit, review what medications you are taking, review your calcium and vitamin D intake, and check to make sure you took the study medications correctly.

If you are not able to finish the study and withdraw before the end, you will be asked to complete the study procedures that would have been done at the 48 Week (Month 11) Visit.

The total amount of blood to be collected for the study is approximately 44 teaspoons, or a bit less than a cup (spread out over the course of the study).

Vials of blood and urine labeled with codes (not with your name, date of birth, or social security or medical record number) may be sent to external laboratories for analyses that cannot be performed locally.

Study locations: Some study visits will be performed at the UCSF Radiology Center at China Basin, and some study visits will be performed at the San Francisco VA Medical Center in the Clinical Research Center. The visits that must be done at the UCSF Radiology Center are the Screening Visit and Week 48 (Month 11) Visit, because of the bone density (DXA) scan. Parking at or transportation to and from the study sites will be provided, using parking validation, vouchers, reimbursement, or the UCSF/VA shuttle system.

Study Plan

Another way to find out what will happen to you if you participate in the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.

DXA Scan – done to see if you qualify for the study (Screening Visit 1)

↓

Screening Visit 2

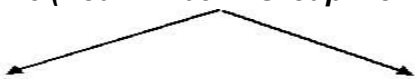
↓

<u>Medicines Used in This Study</u>
Teriparatide by injection daily and cinacalcet by mouth daily over a 48-week (approximately 11-month) period

<u>Supplements Used in This Study</u>
Daily calcium and vitamin D3 supplements by mouth daily according to your needs over a 52-week (approximately 12 month) period

↓

Randomize (You will be in Group 1 or Group 2)



Group 1	***Group 2***
Teriparatide by daily injection and cinacalcet tablet by mouth daily for 48 weeks (approximately 11 months)	***Teriparatide by daily injection and placebo tablet by mouth daily for 48 weeks (approximately 11 months)***
Study visits as described above	***Study visits as described above***

How long will I be in the study?

You will be in the study for approximately 12 months. The visits over that time will take a total of about 20 hours. Additional time will be required at home to take the medications daily. Including the at-home procedures, it is estimated that full participation in the study will last up to 80 hours over the 12 months.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor(s) if you are thinking about stopping or decide to stop. She will tell you how to stop your participation safely. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side-effects or risks can I expect from being in the study?

You may have side-effects while on the study. Everyone taking part in the study will be watched carefully for any side-effects. However, doctors don't know all the side-effects that may happen. Side-effects may be mild or very serious. Your health care team may give you medicines to help lessen side-effects. Many side-effects go away soon after you stop taking the medications. In some cases, side-effects can be serious, long lasting, or may never go away. Risks and side-effects related to the procedures and study medications in this study include those listed below.

You should talk to your study doctor about any side-effects you experience while taking part in the study.

Risks and side-effects related to **teriparatide** include those which are:

Likely
This means occurring in 20% or more of research participants. We feel that there are no side-effects or risks that occur at that rate due to teriparatide.

Less Likely
This means occurring in less than 20% of research participants.

- High blood calcium level
- Injection site reactions
- Fatigue
- Headache
- Joint or body pain
- Nausea
- Low blood pressure

Rare but potentially serious
This means side-effects that may require hospitalization or may be irreversible, long-term, life threatening or fatal.

- Kidney stone

More information:

- Increase in blood calcium level – Teriparatide briefly increases the calcium level in the blood, with the peak 4-6 hours after each daily injection. In the setting of a clinical trial, 6% of men taking teriparatide had an increase to above the upper limit of normal range, and 1% of men in the trial had an increase that was still there when measured a second time. Mildly increased blood calcium level may cause no symptoms, but symptoms of high blood calcium can include fatigue, frequent urination, thirst, nausea, vomiting, constipation, or confusion. Very rarely, blood calcium can increase enough to require treatment in the hospital.
- Increase in urine calcium level – Teriparatide increases urine calcium level, although in clinical trials urine calcium has not been above the upper limit of normal range any more frequently with teriparatide than with placebo. High urine calcium can cause kidney stones, although in clinical trials kidney stones have been no more common with teriparatide than with placebo in clinical trials.
- Injection site effects – Injections under the skin can cause pain, bruising, or bleeding.
- Other possible risks – Other uncommon side-effects that have been seen with teriparatide treatment include body or joint pain, nausea, vomiting, fatigue, headache, and dizziness.
- Low blood pressure can occur after taking an injection of teriparatide. If it were to happen, it would only be expected after the first few injections of the teriparatide. This short-lived effect might be noticed upon changing position such when you are going from lying down to standing up. It might cause dizziness or lightheadedness. It generally goes away with time and may happen right after (a few minutes or a few hours) taking the medication.
- In rats given very large doses of teriparatide every day for most of their lives, a rare bone cancer (called osteosarcoma) was seen. This led the FDA to place a warning on the teriparatide label about these animal studies. To date, such cancers have not been seen in over 250,000 people treated with teriparatide for 2-year treatment courses. However, if

you are at risk for osteosarcoma on a genetic or hereditary basis, you should not take teriparatide.

Risks and side-effects related to **cinacalcet** include those which are:

Likely
This means occurring in 20% or more of research participants.

- Nausea

Less Likely
This means occurring in less than 20% of research participants.

- Vomiting
- Diarrhea
- Low blood calcium level
- Muscle cramps
- Dizziness
- Numbness and tingling around the mouth or in the fingers and toes

Rare but potentially serious
This means side-effects that may require hospitalization or may be irreversible, long-term, life threatening or fatal.

- Seizure

More information:

- Decrease in blood calcium level – Cinacalcet decreases calcium level in the blood. Mildly decreased blood calcium level may cause no symptoms, but symptoms of low blood calcium can include difficulty concentrating, poor memory, fatigue, muscle cramps, or numbness or tingling around the mouth and in the fingertips. Very rarely, low blood calcium can be severe enough to require treatment in the hospital.
- Gastrointestinal symptoms – Cinacalcet can cause nausea, which is usually mild. Rarely, it can cause vomiting. Patients with known risk factors like stomach or esophagus ulcers or inflammation may have greater risk of gastrointestinal bleeding with cinacalcet.
- Other possible risks – Other uncommon side effects that have been seen with cinacalcet treatment include muscle or joint pain, fatigue, headache, and dizziness.

Other Possible Side-Effects During the Study from Study Supplements or Study Procedures

- **Calcium and vitamin D pills:** In the doses used in this study, calcium and vitamin D have minimal side-effects. Some individuals will note constipation or stomach upset with calcium supplements. Very rarely, if a person is over-supplemented with calcium, a kidney stone could result.

- **Blood drawing (venipuncture) and IV insertion risk:** Drawing blood or inserting an IV may cause temporary discomfort from the needle stick, bruising, and, rarely, infection.

- **Blood and urine tests done outside the UCSF and the San Francisco VA Medical Center**: Some of the tests that will be done on the blood and urine samples from this study will be sent to a reference laboratory for specialized testing. These tests will be done by our research collaborators. Your samples will not be identified with your name or any information that can be traced to you. Your samples will have an identifying number on them so that we will track them in that way.

- **Radiation risk**: This research study involves exposure to radiation. Not all this radiation exposure is necessary for your medical care and is for research purposes only. The additional amount of radiation that you will receive as a result of participating in this study will be less than the yearly natural background of radiation in the US, which is 3 mSv (a mSv, or milliSievert, is a measurement of radiation). This amount of radiation involves minimal risk. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting the study.

- **Randomization risks:** You will be assigned to a treatment program by chance, and the treatment you receive may prove to be less effective or to have more side-effects than the other study treatment or other available treatments.

- **Inconvenience:** You may find the 24-hour urine collections inconvenient.

- **Sensitive topics:** We will ask questions about alcohol intake, and this could cause stress or embarrassment in some people.

- **Incidental findings:** It is possible that the lab tests or DXA scan done as part of this study will reveal new information about your health. Should this happen, important results will be discussed with you, and you may be referred to your doctor.

- **Confidentiality:** Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible.

- **Unknown risks:** The experimental treatments may have side-effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

- For more information about risks and side-effects, ask your study doctor.

Are there benefits to taking part in the study?

When given alone, teriparatide has been shown to increase bone density and reduce fracture risk. Thus, your bone health might benefit from your participation in the study, but it is not guaranteed. If you are in the group that receives cinacalcet in combination with the teriparatide, and if the combination turns out to improve bone health more than teriparatide alone, then that

could result in an additional benefit, but whether that will be the case will not be known until all participants finish the study and the data are analyzed.

You will be offered the results of tests that may be useful to you. Specifically, you will be given a copy of the DXA bone density report, and if you wish, a copy of some of your lab test results. We encourage you to share this information with your physician, and to contact Dr. Dolores Shoback at (415) 221-4810 x23336 or 415-575-0552 if you have any questions.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- Getting no treatment for low bone mass
- Getting standard treatment for your condition without being in a study
- Getting a different experimental treatment/taking part in another study

There are several medications besides teriparatide available by prescription for the treatment of osteoporosis. Dr. Shoback can discuss these in more detail if you would like. Please feel free to talk to your doctor as well about your choices before deciding if you will take part in this study.

How will my specimens and information be used?

Researchers will use your specimens and information to conduct this study. Once the study is done using your specimens and information, we may share them with other researchers so they can use them for other studies in the future. We will not share your name or any other personal information that would let the researchers know who you are. We will not ask you for additional permission to share this de-identified information.

There will be no direct benefit to you from allowing your data to be kept and used for future research. However, we hope we will learn something that will contribute to the advancement of science and understanding of human health and disease. If the data or any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits. If you decide later that you do not want your information to be used for future research, you can notify the investigator in writing at:

Endocrine Research Unit, San Francisco Department of Veterans Affairs Health System-Mission Bay, 111N, 1700 Owens Street, Room 369, San Francisco, CA 94158

If you notify the investigator, any remaining data and specimens will be destroyed. However, we cannot retract any data or specimens that have been shared with other researchers.

How will information about me be kept confidential?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. If you do not have a VA medical

record, one will be created for you. Your signed consent form and some of your research tests will be added to your UCSF medical record and your VA medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Department of Veterans Affairs
- University of California
- US Food and Drug Administration (FDA)

Are there costs to me for taking part in this study?

No. The sponsor (the Department of Veterans Affairs) has agreed to pay for all items associated with this research study; you or your insurer will not be billed. **Will I be paid for taking part in this study?**

In return for your time, effort, and travel expenses, you will be paid up to a total of $630 for taking part in this study. Each participant will be paid for completing the study visits and the study procedures as outlined below.

Study Visit	Amount to be paid
Screen Visit 1	$40
Screen Visit 2	$40
Randomization Visit (with pharmacodynamic study)	$200
Randomization Visit (without pharmacodynamic study	$40
Week 1 Phone/Lab Visit	$25
Month 1 Study Visit	$25
Month 2 Study Visit	$25
Month 3 Study Visit	$25
Month 5 Study Visit	$25
Month 6 Study Visit	$25
Month 9 Study Visit	$25
Month 11 Study Visit	$200

Total Payment (with pharmacodynamic study)	$655
Total Payment (without pharmacodynamic study)	$495

The Department of Veterans Affairs issues payments for research studies using the electronic fund transfer (EFT) rather than a paper check or a Direct Express card. In order for us to send this payment to you, we will need your social security number and your bank account number. It can take the Department of Veterans Affairs up to 30 days to complete an EFT. Parking or transportation assistance will be supplied in addition to this payment.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Dr. Dolores Shoback, if you feel that you have been injured because of taking part in this study. You can tell Dr. Shoback in person or call her at (415) 221-4810 x23336 or 415-575-0552.

Treatment and Compensation for UCSF Research Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at (415) 476-1814.

Treatment and Compensation for SFVA Research Injury:
If you are experiencing a medical emergency, please call 9-1-1. If you incur an injury or illness as a result of being in this study, the Department of Veterans Affairs (VA) will ensure that treatment is made available at a VA medical facility or non-VA facility, as appropriate. If you were following study instructions, the costs of such treatment will be covered by the VA or the study sponsor (if applicable). If you were NOT following study instructions, the costs of such treatment may be covered by the VA or the study sponsor (if applicable), or may be billed to you or your insurer just like any other medical costs, depending on a number of factors. The VA and a study sponsor do not normally provide any other form of compensation for injury or illness. For further information about this, call the study team at the number(s) provided.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. You may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your study doctor, Dr. Dolores Shoback, at (415) 221-4810 x23336 or 415575-0552. If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Institutional Review Board of the University of California, San Francisco at (415) 476-1814.

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.

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Optional Research:

Please note: This section of the informed consent form is about an optional research study that is being done with people who are taking part in the main study. You may take part in this if you want to. You can still be a part of the main study even if you say "no" to taking part in this optional study.

You can say "yes" or "no" to each of the following studies. Please mark your choice for each study.

Blood and Urine Specimen Banking

If you participate in the main study described above, you also have the option to allow the researchers to store blood and urine samples for future research. Future testing of your stored blood and urine samples may be funded by various agencies or institutions. All participants in the main study are being asked to allow the storage of blood and urine for this research.

What will happen if I agree to donate my specimens?

If you agree to let the study team store your specimens for future research, the following will happen:

- After all routine tests required for the main study are finished, instead of discarding your leftover specimens, we will save them in what is called a “bank” for possible future research. The “bank” is located in the Metabolism Unit in Building 2 of the San Francisco VA Medical Center. We will label the vials containing your blood and urine with codes (not with your name, date of birth, or social security or medical record number), although we on the study team will be able to connect your coded specimens with some of the clinical information we

collect during your participation in the main study, including things like your age, medical history, laboratory values, and bone density results. You will not undergo any additional blood draws or urine specimen collections (beyond those in the main study).

- We will not give your specimens to any researchers outside of the study team.

- We do not know for sure if your specimens or medical information will be used, but they might be used in research about what causes osteoporosis, or how osteoporosis responds to treatment. They may be used to develop new drugs, tests, treatments, or products. In some instances these may have potential commercial value.

- Results from any future research using your specimens will not be given to you or your doctor. The research will not change the care you receive.

- Your specimens will be kept indefinitely. If you decide later that you do not want your specimens and information to be used for future research, you should call Dr. Dolores Shoback at (415) 221-4810 x23336 or 415-575-0552, and we will destroy any remaining identifiable specimens. However, if any research has already been done using portions of your specimens, the data will be kept and analyzed as part of those research studies.

- If research results using a participant's stored sample results in a commercially valuable product, a participant will not benefit financially from that event.

What risks are involved with donating specimens for research?

- Confidentiality: Donating specimens may involve a loss of privacy, but information about you will be handled as confidentially as possible. Your name will not be used in any published reports from research performed using your specimen. The members of the study team will not release any identifying information about you to other researchers. The UCSF Institutional Review Board, the San Francisco VA Health Care System Research Office, and other University of California or VA personnel may see information about you to check on the specimen "bank."

What are the benefits of donating specimens for research?

There will be no direct benefit to you from allowing your specimens to be kept and used for future research. However, we hope we will learn something that will help treat future patients.

What financial issues should I consider before donating?

You will not be charged for donating your specimens. You will not be paid for donating your specimens. If any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits.

What alternatives do I have?

If you choose not to donate your specimens, any leftover blood and urine that is not needed for the main study will be thrown away.

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CONSENT

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you. You have been given copies of this consent form and the UCSF Experimental Subject's Bill of Rights to keep.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

Please read each sentence below and think about your choice. After reading each sentence, put your initials in the "Yes" or "No" box. If you have any questions about this study, please talk to the study doctor or coordinator. No matter what you decide to do, it will not affect your care.

1. I would like to participate in the main study described above.

YES	*NO*

2. My specimens may be kept for use in future research to learn about, prevent, or treat osteoporosis.

YES	*NO*

3. Someone may contact me in the future to ask me to take part in more research.

YES	*NO*

If you wish to participate in this study, you should sign below.

_____ _____

Date Participant's Signature for Consent

_____ _____

Date Person Obtaining Consent