



**PARTICIPANT INFORMATION SHEET & INFORMED CONSENT**  
**AMG 785/Placebo in Postmenopausal Women With Osteoporosis**  
**Protocol Number: 20070337**

Sponsor (a for-profit drug company): Amgen Inc.

We would like to invite you to take part in our research study. Before you decide, we would like you to understand why the research is being done and what it would involve for you. One of the research team will go through the information sheet with you and answer any questions you have. You will be given at least 24 hours and more time if you need it to consider whether or not you wish to take part. Talk to others about the study if you wish. This patient information sheet is split into 2 parts:

Part 1 tells you the purpose of this study and what will happen to you if you decide to participate.

Part 2 provides detailed information about your rights as a research participant.

**PART 1**

**1. WHAT YOU SHOULD KNOW ABOUT THIS STUDY**

**a. Why is this study being done?**

The purpose of this study is to find out more about AMG 785 in women with postmenopausal osteoporosis. This study will see if AMG 785 prevents fractures of the bone and whether it causes any side effects. To do this, AMG 785 will be compared with a placebo over the course of one year. The placebo will look like AMG 785 but it will not contain active ingredients. Taking placebo is the same as not taking anything for osteoporosis. AMG 785 and placebo are both called investigational product in this form. In addition, all study participants will be required to take vitamin D and Calcium daily, which is important for your bone health.

AMG 785 is still experimental and is not approved by any regulatory health agency (like the US Food and Drug Administration [FDA] or European Medicines Agency [EMA]).

After taking AMG 785 or placebo for one year, all study participants will be taking denosumab for the following year. Denosumab (also known as Prolia®) is a medication to treat postmenopausal osteoporosis that has been approved by many regulatory health agencies worldwide (for example by the US Food and Drug Administration [FDA] and the European Medicines Agency [EMA]). While taking denosumab, all study participants will be required to continue taking daily vitamin D and Calcium.

You are being invited to take part in the study because your details have been reviewed by your personal doctor (GP), and by a doctor at the hospital or Dedicated Research Centre (DRC), who believes that you may be eligible to participate in this study. We believe this study may be of importance to patients with osteoporosis.

**b. How many people will participate in this study?**

The study will take place in approximately 175 centres in North America, Europe, South America and Asia/Pacific. A total of approximately 5,600 people are expected to participate in this study.

**c. How long will you be participating in this study?**

If you choose to participate, you will be in this study for about 25 months. Your study doctor will inform you if additional follow-up is needed after these 25 months to monitor your safety.

**d. Do you have to take part?**

No. It is up to you to decide whether or not to take part and this choice will not affect your current or future care. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form of which you will be given a copy.

**e. What is the product being tested?**

The investigational product being tested in this study is a protein called AMG 785. This is a new medicine, which has been shown in animal studies to stimulate the formation of new bone and to accelerate the healing of fractures. AMG 785 is not approved by any regulatory organizations (such as the European Medicines Agency [EMA]) for the treatment of people with postmenopausal osteoporosis. In this study, investigational product will be administered by injection once a month for one year at a dose of 210 mg.

After the first year, all participants will stop receiving the investigational product and will receive denosumab (also known as Prolia®) instead. Denosumab is a medication to treat postmenopausal osteoporosis, which has been approved by many regulatory health agencies worldwide (including the EMA). Denosumab will be administered by injection twice during this study, once at 12 months into the study and once at 18 months into the study.

**f. What are the chances that you will get AMG 785?**

You will be randomized into one of two groups; AMG 785 or placebo. Randomized means that you are being put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in either group. Neither you nor the study doctor can choose the group you will be in.

It is important to understand that, for the first year only, you may be assigned to the placebo group. Placebo is the same as taking nothing at all for your osteoporosis. Even if you are assigned to the AMG 785 group, this is an investigational product and is not yet approved for the treatment of osteoporosis. Therefore, for the first year of the study you may be at a greater risk of fracture than if you were receiving a standard approved treatment for osteoporosis.

**g. Will you know which investigational product you are receiving?**

Neither you nor the study doctor nor his/her study staff will know which investigational product you are receiving in the first year of the study. In an emergency, the study doctor can find out what you are receiving. For the second year of the study, you and your study doctor and his/her staff will know that you are receiving denosumab.

**h. Can you stop participating in the study?**

You are free to stop participating in this study at any time. If you stop, you will not lose any medical benefits. All information and samples collected from you before you stop the study may still be used by Amgen to understand more about the investigational product(s), and/or bone disease, and/or mechanism of action.

If you want to stop participating in the study, please tell the study doctor. He/She can tell you about stopping all or part of the study activities and what other care is available for you.

The study doctor or Amgen may stop your participation at any time. The study doctor will tell you if this happens. Some reasons this could happen include:

- Staying in the study could be harmful to you.
- You need treatment not allowed by the study.
- You are not able to complete the study procedures as required.
- The study is stopped by Amgen for reasons not related to you.

There may be other reasons to stop your participation in this study that are not known at this time. If you stop participating in the study, or the study ends, you will stop receiving the investigational product(s) and may be asked to come back for final tests and procedures.

If you choose to stop taking the investigational product before the study ends, you should discuss the following options with the study doctor:

- You can stop taking the investigational product but continue to visit the study doctor for study related procedures or tests.
- You can completely leave the study and have no more contact with the study doctor and his/her study staff for study related procedures or questions as of the date of your request.

**2. WHAT WILL HAPPEN IF YOU PARTICIPATE IN THIS STUDY**

**a. What will you be responsible for if you take part in this study?**

If you decide to participate in this study, you will be asked to attend a screening visit during which the study doctor and his/her study staff will do some tests to see if you meet the study requirements. Once it is confirmed that you meet the requirements

you will be asked to attend all scheduled study visits: every month for one year and then 4 visits during the second year (see table 1 below for details). Prior to some visits, you may be asked to fast overnight, where you should not eat or drink anything, but you are able to drink water.

While participating in the study, you will not be allowed to take certain medications such as bisphosphonates, parathyroid hormone, strontium fluoride if prescribed for the treatment of your osteoporosis, cinacalcet, tibolone, calcitonin, estrogen, oral glucocorticoids, androgen deprivation therapy or hormone ablation therapy. The study doctor can give you more details about which medications you may take or not take.

You will be given a patient card to carry with you at all times (similar size to a credit card) – this will have an emergency contact number on it in case you should need it and details of the study number and product name.

**Table 1: Study Visit Schedule**

Study Month	Visits Occur
Screening	1 time
Day 1	1 time
Month 1 to 12	Every month
Month 12 plus 10 days	1 time
Month 15	1 time
Month 18	1 time
Month 21	1 time
Month 24	1 time
Follow-up visits	As needed if additional follow-up is needed for your safety

**b. What types of tests or procedures will be involved with this study?**

If you decide to participate in the study, some tests will be done to see if you are eligible for this study. This is called “screening”. If the test results show that you meet the study requirements, then you will be able to start the study. Some tests may be repeated to see if you meet the study requirements the second time. If the test results show that you do not meet the study requirements, you will not be able to start the study. The study doctor will discuss other options with you and/or refer you back to your regular doctor.

As part of your participation in this study, you will have tests or procedures done at each visit as shown in table 2 below.

**Table 2: Study Procedures and Their Timing**

Test or Procedure	Pre-study	During Study: study start (Day 1) to Month 18	End of Study
Medical, Fracture, and Medication History Check	1 time	---	---
Instructions for daily vitamin D and calcium intake	1 time	1 time: 12 months after study start	---
Medical Examination	1 time	1 time: 12 months after study start	1 time
Blood pressure, Temperature, Pulse	1 time	4 times: 1, 6, 12, and 18 months after study start	1 time
Height and Weight	1 time	3 times: 6, 12, and 18 months after study start	1 time
Blood Sample Collection	1 time	11 times: at study start and at the following time points thereafter: 1, 3, 6, 9, 11, and 12 months, 12 months plus 10 days, and 15, 18, 21 months	1 time
Periodontitis (gum disease) questionnaire	---	1 time: at study start	---
Spine x-ray	1 time	3 times: 6, 12, and 18 months after study start	1 time
DXA of the spine	---	2 times: at study start and 12 months after study start	1 time
DXA of the hip	1 time	1 time: 12 months after study start	1 time
Reporting of any fractures that occur	---	15 times; 1 <sup>st</sup> year: at every monthly visit; 2 <sup>nd</sup> year: 15, 18, and 21 months after study start	1 time
Questionnaires <ul style="list-style-type: none"> <li>• For all study participants</li> <li>• For study participants who fracture during the 1<sup>st</sup> year</li> </ul>	---	4 times: at study start and 6, 12, and 18 months thereafter 4 times: at the visit where the fracture is reported, and at the next 3 visits	1 time ---
Fracture healing follow-up (if a fracture occurs)	---	3 times: approximately 3, 6, and 12 months after the fracture occurred	---
Tooth count	---	2 times: at study start and 12 months thereafter	1 time
Information gathering about health issues and medications you are taking	1 time	16 times; 1 <sup>st</sup> year: at study start and at every monthly visit; 2 <sup>nd</sup> year: 15, 18, and 21 months after study start	1 time
Vitamin D starting dose	---	1 time, at study start	---
Investigational Product injection	---	14 times; 1 <sup>st</sup> year: AMG 785 - at study start and at every monthly visit; 2 <sup>nd</sup> year: denosumab - month 12 and month 18 after study start	---

Spine x-rays are used to detect any fractures of the spine you may have experienced before the study or you may experience while you are participating in

the study. The DXA test is a type of x-ray that measures the density of the bone in your spine and in your hip.

Information about your general health-related quality of life will be collected using questionnaires called Patient Reported Outcomes [PRO] questionnaires. You will be asked to fill in these questionnaires on your own so that they reflect your personal opinion.

At any study visit, about half a teaspoon (or 2.5 mL) to three teaspoons (or 15 mL) of blood may be collected from you. If you complete the entire study, the total amount of blood collected from you will be approximately five and a half tablespoons (or 82 mL). More blood may be collected from you if additional follow-up is needed for your safety. These blood samples will be used to monitor your health and safety.

All of your samples will be labeled with a special code. Only the study doctor and his/her study staff will be able to link your samples to you. All information obtained from your samples will be kept confidential as stated in the *CONFIDENTIALITY* section of this form.

You will have a tooth count performed three times during the study. The tooth count will be performed by the study doctor (or a member of his/her staff) and should not cause you any pain or discomfort. The purpose of the tooth count is to check for any signs of a condition called osteonecrosis of the jaw (ONJ). ONJ is a potentially serious condition that can present as a sore in the mouth. Additional information about signs and symptoms of ONJ is provided in Section 3 (Safety – potential risks and discomforts).

Your signature on the consent form at the end of this participant information sheet, means that you allow the study doctor and his/her study staff to complete the set plan of study procedures (called a study protocol), including the collection of samples. Your signature also allows Amgen and its authorized representatives to use these samples for tests outlined in the study protocol or for tests necessary to ensure your safety. If you stop participating in this study, Amgen and its authorized representatives may continue to use the samples collected during your participation in the study for tests and procedures described in this section.

You can ask the study doctor or his/her study staff about the tests listed in the study protocol. The study doctor may ask you to come back for additional safety tests after the end of the study.

Your regular medical care may include some of the study tests and procedures. The study doctor and his/her study staff can answer any questions you may have about which tests and procedures are not part of your regular medical care.

#### Optional Sub-studies

In addition to the main study, there are some optional sub-studies being performed. These are OPTIONAL (you can choose not to participate, even if you choose to take part in the main study). The information about these sub-studies is contained within separate sub-study consent forms that your study doctor will provide you if they consider that you may be suitable for participation. If you agree to take part in any of these sub-studies you will be asked to read and sign the separate sub-study consent forms.

**c. Use of Samples for Future Research**

Any samples remaining from the tests listed in Table 12 and from any sub-studies you may decide to participate in, including blood samples and samples for biomarker development, may be used for future research. These samples will be used to learn more about bone diseases, and/or mechanism of action, and to better understand the effects of AMG 785 or identify patients who are most likely to be helped by AMG 785.

No additional risks are expected because the sample(s) are already being collected.

These samples may be stored for up to 20 years after all the participants have finished the study. Amgen and its authorized representatives will make sure your samples are destroyed at the end of the storage period. At any time, you may ask that your samples not be used for this future research by contacting the study doctor. If you ask for this, your samples will be destroyed once all protocol-defined procedures are completed. However, any information collected from your samples before your request to destroy them will be kept by Amgen.

If you decide to stop participating in the study, but do not request that your samples be destroyed, Amgen and its authorized representatives may continue to use your samples for future research until the end of the storage period.

This testing will not benefit you directly or change how your disease is treated. Therefore, the results will not be added to your medical record and will not be made available to you, members of your family, your personal doctor (GP) or other third parties, except as stated in the *CONFIDENTIALITY* section of this form.

**3. SAFETY – POTENTIAL RISKS AND DISCOMFORTS**

**a. Are there any risks from taking part in this study?**

There may be risks to being in this study from the investigational product or from some of the procedures or tests done in this study. Also, your condition may get better but it could stay the same or even get worse.

If you participate in this study, you or your family members should tell the study doctor or his/her study staff immediately if you have any unusual health problems, injuries or side effects, even if you do not think these problems are caused by the study or by the investigational product(s).

If you experience any side effects, you will be monitored by the study doctor and/or his staff until the event is fully resolved. Depending on the side effect, the study doctor may contact your local doctor (GP) to arrange for you to receive alternative treatment. This may result in you needing to be withdrawn from the study treatment.

If there is any new important safety information or other information that could affect your willingness to participate in this study, the study doctor will let you know.

If you have medical insurance or life insurance, you should notify your insurers of your participation in this study as this could affect your cover.

**b. What are the likely risks with AMG 785 and what are the likely risks with denosumab?**

**For the first year of the study, you will be taking AMG 785 or placebo. The risks associated with AMG 785 are as follows:**

AMG 785 may cause all, some, or none of the side effects listed below. These side effects can be mild but could also be serious or even result in death. There may also be unknown side effects from taking AMG 785 alone or with other medications you may be taking.

As of 30 June 2011, approximately 858 people have been exposed to AMG 785 in research studies.

Side effects other people have had in research studies that are thought to have been caused by AMG 785 are:

- **Very Common side effects  $\geq 10\%$**  (which may affect more than 1 person in 10): common cold, joint pain, pain in arms or legs, back pain
- **Common side effects  $\geq 5\%$  to  $<10\%$**  (which may affect between 5 and 10 people in every 100): stomach flu, cough, constipation, bronchitis, injection site pain, urinary tract infection, feeling tired, muscle and bone pain, swelling in the legs or feet.

A short-term decrease in blood calcium levels below normal has been observed in some people receiving AMG 785 who were not taking supplemental calcium. Symptoms of decreased blood levels of calcium may include a tingling sensation, muscle cramping or an abnormal heart rate. During the study, if you experience any of these symptoms you should notify your doctor immediately. Your study doctor may administer calcium intravenously to treat these symptoms. Taking calcium supplements as directed by the protocol may lower the risk that your calcium level will drop below normal.

You may have an allergic reaction to AMG 785. Symptoms of an allergic reaction may include headache, rash, flushing, swelling, shortness of breath, nausea and sometimes vomiting. Severe allergic reactions can cause dizziness, difficulty breathing or swallowing, a decrease in blood pressure, and could be life threatening. If you have symptoms of an allergic reaction, you should contact the study doctor or his/her study staff immediately.

After you start taking AMG 785, it is possible that your body may make antibodies (proteins that can cause AMG 785 not to work). In people treated with AMG 785, there have been reports of people developing this type of antibodies. Blood tests will be used to check for antibodies during the study. In studies conducted with AMG 785 there have been no ill effects in people who have developed antibodies to AMG 785. If any antibodies are identified during this study, blood tests will continue to be performed until there are no further signs of antibodies.

Reactions at or near the area of the injection have been seen in other people taking AMG 785. Symptoms may include redness, tenderness or pain, bruising, warmth, swelling, itching and/or infection at the injection site. If you have any of these symptoms, you should contact the study doctor or his/her study staff immediately.



AMG 785 is expected to increase bone density. The risks associated with excessive increases in bone density are not known at this time. Bone density measurements will be monitored throughout the clinical study.

AMG 785 is expected to increase bone growth. In animal studies, where AMG 785 was given at higher doses than you will be receiving, excessive bone growth was observed. A potential consequence of bone overgrowth is nerve compression, which may include facial drooping, numbness or changes in hearing or vision. Human subjects receiving AMG 785 in clinical studies have not reported symptoms of excessive bone growth.

**For the second year of the study, you will be taking denosumab. The risks associated with denosumab are as follows:**

Denosumab may cause all, some or none of the side effects listed below. These side effects can be mild but could also be serious or even result in death. There may also be unknown side effects from taking denosumab alone or with other medications you may be taking.

As of November 29, 2010, approximately 15,900 people have received denosumab in research studies.

Side effects that other people have had in research studies that are thought to have been caused by denosumab are:

- **Very Common side effects** (which may affect more than 1 person in 10): joint pain, pain in extremity, shortness of breath, decreased phosphorus in the blood
- **Common side effects** (which may affect between 1 and 10 people in every 100): reports of high cholesterol, muscle and bone pain, dizziness, cough, osteoarthritis, cataracts, eczema, muscle pain, difficulty emptying the bladder and decreased skin sensation

**Eczema.** In some studies comparing denosumab with placebo, more patients receiving denosumab developed eczema (itchiness and redness on the skin.) Eczema was observed commonly in patients receiving denosumab. If you have any of these symptoms, please notify your doctor.

**Skin infections such as cellulitis.** Although denosumab does not appear to increase the occurrence of infection when compared to placebo, in one large study, skin infections that required hospitalization were observed more in patients treated with denosumab than in placebo. Skin infections leading to hospitalization were observed uncommonly in patients receiving denosumab. Symptoms of skin infection include development of a swollen, red area of skin, most commonly in the lower leg, that may feel hot and tender, and may be accompanied by symptoms of fever. If you have any of these symptoms, please notify your doctor.

**Low blood calcium.** Temporary lowering of blood calcium levels below normal have been observed in people treated with denosumab. Low levels of calcium in the blood were common (between one and ten people in 100) in people treated with denosumab 60 mg every six months. Low levels of calcium in the blood were very common (more than one person in 10) in people treated with denosumab 120mg dose every 4 weeks. The risk of this happening may be higher in people with severe kidney disease. You may not have any symptoms of low blood calcium;

however, with very low levels of calcium, symptoms may occur such as a tingling sensation, muscle cramping, abnormal heart rate, or seizures. Your study doctor may ask you to take calcium tablets by mouth to correct the low blood calcium or in rare cases, the doctor might decide to give the calcium through the veins. During the study, if you experience any of these symptoms you should notify your doctor immediately. Taking calcium and vitamin D supplements as directed by your study doctor will lower the risk that your calcium level will drop below normal.

Denosumab has not been studied in newborns, children and adolescents; therefore, the effect on bones and teeth before normal bone growth is completed is not known. In studies of monkeys whose bones were still growing denosumab caused abnormalities in the bone where growth occurs (growth plate). As a result, this part of the bone may be more prone to injury and bone length may be reduced in people whose bones are still growing. An agent similar to denosumab administered to rats soon after birth also affected the growth plate resulting in bones not growing properly. This agent also prevented teeth from surfacing from the gums and caused the roots of the teeth to grow abnormally.

In one study of men with prostate cancer receiving denosumab or placebo and other drugs to lower testosterone levels, cataracts or cataract operations were reported commonly and more frequently with denosumab. It is not known at this time if denosumab can cause cataracts or make existing cataracts worse. In a larger study of postmenopausal women with osteoporosis in which cataracts were also reported commonly, more patients on the placebo arm were reported to have cataracts than those who received denosumab.

**Osteonecrosis of the jaw (ONJ)** is a potentially serious condition that can present as a sore in the mouth through which the jaw bone is sometimes visible. The gum tissue over the bone may heal slowly or not heal at all. How this happens is poorly understood. The symptoms of ONJ include pain or infection in the jaw bone and gums. If you develop any of these symptoms, your doctor should examine your mouth to determine if you have ONJ. The risk of developing ONJ is higher in patients who have had tooth removal.

In clinical trials in patients treated with denosumab, ONJ has been reported. In studies of patients in whom cancer has spread to bone who received up to 3.5 years of treatment, ONJ occurred with a similar frequency in denosumab (2.2%) (120 mg every 4 weeks) and zoledronic acid (1.6%) treatment groups. In patients with prostate cancer without bone involvement, who received treatment for up to 4 years, ONJ occurred with a greater frequency in denosumab (4.6%) (120 mg every 4 weeks) than in placebo (0%) treatment groups. ONJ has also been reported rarely (equal to or greater than 0.01% and less than 0.1%) in patients treated with denosumab (60 mg every 6 months) for osteoporosis.

It is important that you maintain good oral hygiene and avoid dental procedures immediately before and during your participation in the study, if possible.

Your study doctor and dentist should discuss the benefits and risks of any dental procedure. Tell your dentist that you are taking a medicine to strengthen your bones before a dental procedure is planned.

In a large study comparing denosumab to zoledronic acid in patients with a variety of cancers that had spread to bone, there were a similar number of deaths in each group. In a small group of patients within this study with the disease multiple myeloma, more patients in the denosumab treatment group died. The meaning of this finding is not clear and a larger multiple myeloma study is planned to compare these two products more completely.

The effect of denosumab on bone resorption appears fully reversible and discontinuing the drug can lead to reversal of the gains made in your bone density. To ensure these losses in bone density are not excessive, if you discontinue denosumab, you should be followed carefully. Alternative approaches to maintaining prior gains should also be discussed with your study doctor.

You may also develop antibodies (a protein made by the body to attack a foreign substance that the body thinks is harmful) to denosumab. These antibodies can cause denosumab not to work. The development of antibodies to denosumab in patients has been uncommon and has had no clinical effects and has not reduced the effect of denosumab on bones. Blood tests will be used to check antibodies during the study.

You may have an allergic reaction to denosumab. Drug hypersensitivity has been reported rarely in patients taking denosumab. Symptoms of an allergic reaction may include headache, rash, flushing, swelling, shortness of breath, nausea and sometimes vomiting. Severe allergic reactions can cause dizziness, difficulty breathing or swallowing, a decrease in blood pressure, and could be life threatening. If you have symptoms of an allergic reaction, you should contact the study doctor or his/her study staff immediately.

**c. What are the risks of using AMG 785 or denosumab in combination with other drugs?**

Tell the study doctor or his/her study staff about any **medications** you are taking, have recently taken or are planning to take, including drugs obtained without a prescription. The side effects of using AMG 785 or denosumab in combination with other **medications** are unknown at this time. Please discuss any concerns you may have with the study doctor.

**d. What are the risks of taking the other drugs required by this study?**

The following products are not being studied by Amgen, but you are required to take them as part of this study: vitamin D and calcium supplements. These products are often used to treat your condition. The study doctor will talk with you about the risks of taking these products.

**e. What are the risks associated with procedures done in this study?**

The known risks and side effects of study related tests or procedures (listed in Section 2b) are noted here.

**Blood Sample Collection**

You will have your blood taken during the study. Possible side effects of having blood taken are tenderness, pain, bruising, bleeding and/or infection where the needle goes into the skin and blood vein. Having your blood taken may also cause you to feel nauseated and/or lightheaded.

### **Lateral Spine X-ray and Dual Energy X-ray Absorptiometry (DXA)**

This study requires you to have lateral (from the side) chest and spine x-rays, and a range of DXA scans in the main and sub-studies. These are additional to the care you could receive if you do not take part in this study. This will expose you to a small amount of radiation, equivalent to about 7 months average natural background radiation. The Health Protection Agency Radiological Protection Division describes this as 'Very Low Risk' and so you are unlikely to identify any health detriment arising from these x-rays.

The doses that are used in x-rays carry a possible risk of causing cancer at a later date (as does your exposure to background radiation), but the risk is very low.

#### **f. Could AMG 785 or denosumab be harmful to an unborn or breastfed baby?**

For the first year of the study, you will be taking AMG 785 or placebo.

AMG 785 has been found to cause abnormal fetal development in animals. In a study where AMG 785 was given to pregnant rats in higher doses than you will be receiving, abnormal bone formation was seen.

If you have intercourse during this study, you should understand that even with the use of effective birth control there is still a small chance, should it still be possible for you to become pregnant, that a pregnancy could occur. Potential risks include loss of the pregnancy (a miscarriage) and birth defects.

For the second year of the study, you will be taking denosumab.

Denosumab has been found to cause abnormal fetal development in animals. In animals exposed to denosumab during pregnancy, increased stillbirths, abnormal fetal development, birth defects, and increased death of infants soon after birth have occurred.

#### **Females**

Pregnant women and women planning to become pregnant should not participate in this study. If you could become pregnant, you should let your sexual partner know you are in this study. While receiving AMG 785/placebo, you should use one highly effective method of birth control during the study and for another 3 months after the last dose of AMG 785/placebo. While receiving denosumab, you should use two highly effective methods of birth control during the study and for another 7 months after the last dose of denosumab.

Amgen has not tested whether AMG 785 or denosumab is present in breast milk nor assessed the effects of AMG 785 or denosumab in breast-fed infants. Women considering breast feeding while using AMG 785 or denosumab should talk to their healthcare providers to determine whether the benefits of breast feeding while using AMG 785 or denosumab outweigh the potential risks.

#### **Highly effective methods of birth control**

You and the study doctor should discuss and agree on how you will prevent pregnancy if it might be applicable to you. If you can become pregnant and plan to have vaginal sex during this study, you should understand that even with the use of highly effective birth control there is still a small chance that a pregnancy could occur. Potential risks include loss of the pregnancy (a miscarriage) and birth

defects. Highly effective forms of preventing pregnancy include not having sex (abstinence) or birth control methods that work at least 99% of the time when used the right way every time you have vaginal sex, and include:

- birth control pills, shots, implants (placed under the skin by a health care provider) or patches (placed on the skin)
- intrauterine devices (IUDs)
- sexual activity with a male partner who has had a vasectomy (surgery to become sterile)
- condom or occlusive cap (diaphragm or cervical/vault caps) used with spermicide

If you are abstinent (no vaginal sexual intercourse) or have had a sterilization procedure, you do not need to use a second method of birth control.

**g. What if you become pregnant during the study?**

If you become pregnant or think you are pregnant during this study, please tell the study doctor or his/her study staff right away. The use of the investigational product(s) may be stopped. The study doctor will notify Amgen of the pregnancy and ask for your consent to obtain information on the pregnancy outcome for you and the baby.

#### **4. BENEFITS OF PARTICIPATION**

**Are there any benefits to taking part in this study?**

No one knows if this study will help you. Your condition may get better but it could stay the same or even get worse. The information from this study might help to develop better treatments in the future for postmenopausal osteoporosis.

#### **5. ALTERNATIVES TO PARTICIPATION**

**a. Do you have any other choices?**

You can choose not to participate in this study. If you do not participate, your personal doctor (GP) can discuss other healthcare choices with you.

Other healthcare choices may include but are not limited to: bisphosphonates, selective estrogen receptor modulators, denosumab, teriparatide, calcitonin or strontium, if available from your healthcare provider.

The benefit of these therapies is that they have been shown to be effective in the treatment of postmenopausal osteoporosis. There may be risks associated with these other therapies that the study doctor or your personal doctor (GP) can discuss with you.

**b. Confirmation of understanding of disease condition and treatment options**

Your study doctor is required to provide you with information about postmenopausal osteoporosis. He/she will also explain your individual risk for fracture. In addition, the study doctor is required to explain which existing therapies may be a good option to treat your osteoporosis.

This completes Part 1. If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

**END OF PART 1**

## **PART 2**

### **6. POTENTIAL COSTS/REIMBURSEMENTS**

#### **a. What will this study cost me?**

You will not incur any additional costs if you participate in this study. You will receive study product AMG 785 or Placebo free of charge and there will be no charges for the visits, tests or procedures that are part of this study. You will be responsible for all costs not related to the study, including those related to the normal treatment of your disease such as prescription charges if they apply.

#### **b. Will I be paid for expenses that I have because of being in the study?**

You will be reimbursed for reasonable out of pocket expenses including your travel to the study site, such as the mileage rate for your own vehicle and any parking costs incurred because of the study.

#### **c. Will I be paid for my biologic samples (for example, blood or tissue) or medical information?**

No, you will not be paid for the use of your biologic samples or medical information or for the information or by-products obtained from these.

#### **d. Will the study doctor or the Hospital Trust be paid for the study?**

Your study doctor's organisation will be paid for including you in this study to cover all reasonable costs incurred by the hospital whilst you are on this study.

### **7. Who is organising and funding the study?**

The study is being funded and organised by Amgen.

### **8. CONFIDENTIALITY**

#### **a. How will my medical records and information be kept confidential?**

Your medical records will be kept confidential as allowed by the applicable laws. If results of the study are published, your identity will not appear. Your results and your samples which leave the hospital will have your name and address removed so that you cannot be recognised. Information about your participation in this study will be associated with you by only using a subject identification number, your date of birth, and your gender. Only the study doctor and their research staff will be able to link your identification number to you at all times. Therefore the information collected about you is 'pseudonymised', which means that the holder of the information cannot identify you. The study doctor or staff will label all of your samples with the identification number. All information obtained from the testing of your samples will be kept confidential. The information collected in this study will be used to help find out whether AMG 785 is beneficial for people with osteoporosis and may be used for research into other therapies. The Sponsor, companies within the Amgen group, and companies assisting Amgen in the study who will receive your information may be located in countries outside of Europe, such as the USA and countries in Latin America, India, Australia-New Zealand and Asia. The places receiving your information may be in countries where the laws don't protect your privacy to the

same extent as the law in the UK, but Amgen and companies assisting Amgen in the study will take all reasonable steps to protect your privacy.

You have a right of access to your information and a right to correct information which is not correct, but you cannot be given information about which study product you are receiving during the blinded part of the study (first year) and/ or the results from study procedures while the study is being conducted.

People outside of Amgen may need to see your pseudonymised information for this study. Some of the information collected from you, including X-rays, DXA scans and blood results, may contain confidential information. An outside company (central vendor) will analyze and interpret this information and report results back to Amgen, the companies assisting Amgen in the study, and/or the study doctor. The outside company will be bound by confidentiality obligations but will not be able to tell your identity from the information they receive.

**b. Who will have access to my medical records?**

Your participation in this study will be noted in your medical records. If your family doctor (GP) is different from the study doctor, he/she will also be notified.

If you take part in this study, your medical records and the information collected for the study will be looked at by Dr Hilary Shaw, Synexus Thames Valley Clinical Research Centre, by Amgen and companies assisting Amgen with the study, as well as possibly by regulatory authorities from your country or countries where the information is submitted (such as the European Medicines Agency- EMA or the US Food and Drug Administration- FDA). These people will be checking that the study has been performed correctly and they will see your name, other personal information such as date of birth and gender, and your medical information, but will be obliged to keep this information confidential.

**9. What if relevant new information becomes available?**

Your study doctor will discuss with you any important new findings that may develop during the study and affect your willingness to participate. If you decide to come off the study, your normal care will not be affected. If you decide to continue in the study you may be asked to sign an updated consent form.

**Also, on receiving new information, your study doctor might consider it to be in your best interests to take you off the study. He/she will explain the reasons why.**

**10. What will happen to the results of the study?**

It is likely that a report containing the results of this study will be written, presented at scientific meetings and published in scientific magazines following the end of the patient recruitment. Your identity will not be known in this document.



## **11. COMPENSATION FOR INJURY**

### **a. If I have an injury/illness related to my participation in the study, will I be compensated in any way?**

Compensation for any injury caused by taking part in this study will be in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI). Broadly speaking the ABPI guidelines recommend Amgen, without legal commitment, should compensate you without you having to prove that it is at fault. This applies in cases where it is likely that such injury results from giving any new drug or any other procedure carried out in accordance with the protocol for the study. Amgen will not compensate you where such injury results from any procedure carried out which is not in accordance with the protocol for the study. Your right at law to claim compensation for injury where you can prove negligence is not affected. Copies of these guidelines are available from your study doctor on request.

### **12. What if I have any concerns?**

If you have any concerns or other questions about this study or the way it has been carried out, you should contact your study doctor Dr Hilary Shaw on 0 118 987 4088, or you may contact the hospital or Dedicated Research Centre Synexus Thames Valley Clinical Research Centre complaints department on 01257 230 723.

Any complaints will be assessed on a case by case basis and will be dealt with or forwarded on to the relevant regulatory bodies as required. We recommend that you obtain a copy of your Hospital or Dedicated Research Centre complaints procedure or policy if you intend to make a complaint.

### **13. Who has reviewed the study?**

All research in the UK is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by NRES Committee London –Brent Research Ethics Committee. The study has also been reviewed by a Local Research Ethics Committee.

### **14. Contact for further information**

Now or during the course of the study, if you have any needs or questions concerning this study or your rights as a patient or in case of emergency, you should contact your study doctor Dr Hilary Shaw on 0118 987 4088 or nurse Christine Daniels on 0118 987 4088(24 hours). You will be given a copy of the information sheet and a signed consent form to keep.

We would like to thank you for considering taking part in this study.

Centre Number: 65003  
Study Number: 20070337  
Patient Identification Number for this trial:



**CONSENT FORM**  
**AMG 785/Placebo in Postmenopausal Women With Osteoporosis**

By signing your name below, you confirm the following: Please initial box

- 1. I confirm that I have read and understand the information sheet dated 20<sup>th</sup> April 2012, (version 1.1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
  - 2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my normal care or legal rights being affected. I also understand that if I withdraw from the study early, the data collected whilst I was on the study will be retained and used by Amgen for the tests described in the Participant Information Sheet.
  - 3. I understand that my medical records may be looked at by Amgen, companies assisting Amgen in the conduct of the study and regulatory authorities. I give permission for these individuals, who are obliged to keep my information confidential, to have access to my records.
  - 4. I understand that a commercial pharmaceutical or diagnostic product(s) may be developed through the use of my samples or medical information collected during this study. Amgen or other researchers may patent or sell discoveries that result from this research. Neither Amgen nor the researchers will compensate me if this happens and I do not have any rights to future inventions.
- I give my permission for the processing of my information and samples
- 5. I give my permission for access to my confidential information.
  - 6. I agree to my GP being informed about my participation in this study.
  - 7. I agree to take part in the above study.

\_\_\_\_\_  
PRINT patient's name                      Date<sup>1</sup>                      Patient's signature

\_\_\_\_\_  
PRINT name of the person taking consent                      Date<sup>1</sup>                      Signature of person taking consent

<sup>1</sup>Each person who signs the consent must personally enter the date for his/her signature.  
1 copy for participant; 1 copy for researcher site file; 1 (original) to be kept in medical notes