Radius Health, Inc.
Form 8-K/A
July 20, 2011

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 8-K/A

(Amendment No. 1)

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the

Securities Exchange Act of 1934

Date of Report (date of earliest event reported): **May 17, 2011**

RADIUS HEALTH, INC.

(Exact name of registrant as specified in its charter)

Delaware	**000-53173**	**80-0145732**
(State of Incorporation)	(Commission File Number)	(IRS Employer Identification Number)

201 Broadway, 6th Floor

Cambridge, MA 02139

(Address of principal executive offices) (Zip Code)

(617) 551-4700

(Registrant s telephone number, including area code)

MPM ACQUISITION CORP.

c/o MPM Asset Management LLC, 200 Clarendon Street, 54th Floor, Boston, MA 02116

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 1.01. Entry into a Material Definitive Agreement.

The disclosures set forth under Item 2.01 hereof are hereby incorporated by reference in this Item 1.01.

Item 2.01. Completion of Acquisition or Disposition of Assets.

Pursuant to an Agreement and Plan of Merger dated April 25, 2011 (the **Merger Agreement**), by and among MPM Acquisition Corp. (referred to herein as the **Company** , **Radius** or the **Registrant**), RHI Merger Corp., a Delaware corporation and wholly owned subsidiary of the Company (**MergerCo**), and Radius Health, Inc., a Delaware corporation (**Target**), MergerCo merged with and into Target, with Target remaining as the surviving entity and a wholly-owned operating subsidiary of the Company. This transaction is referred to throughout this report as the Merger. The Merger was effective as of May 17, 2011, upon the filing of a certificate of merger with the Delaware Secretary of State.

At the effective time of the Merger (the Effective Time), the legal existence of MergerCo ceased and all of the shares of Target s common stock, par value $.01 per share (the **Target Common Stock**), and shares of Target s preferred stock, par value $.01 per share (the **Target Preferred Stock**), that were outstanding immediately prior to the Merger were cancelled and each outstanding share of Target Common Stock outstanding immediately prior to the Effective Time was automatically converted into the right to receive one share of the Company s Common Stock and each outstanding share of Target Preferred Stock outstanding immediately prior to the Effective Time was automatically converted into the right to receive one-tenth of one share of the Company s Preferred Stock from the Company as consideration for the Merger. More specifically, each share of Series A-1 Convertible Preferred Stock of Target outstanding immediately prior to the Effective Time was converted into the right to receive 0.1 shares of Series A-1 Convertible Preferred stock of the Company; each share of Series A-2 Convertible Preferred Stock of Target outstanding immediately prior to the Effective Time was converted into the right to receive 0.1 shares of Series A-2 Convertible Preferred stock of the Company; each share of Series A-3 Convertible Preferred Stock of Target outstanding immediately prior to the Effective Time was converted into the right to receive 0.1 shares of Series A-3 Convertible Preferred stock of the Company; each share of Series A-4 Convertible Preferred Stock of Target outstanding immediately prior to the Effective Time was converted into the right to receive 0.1 shares of Series A-4 Convertible Preferred stock of the Company; each share of Series A-5 Convertible Preferred Stock of Target outstanding immediately prior to the Effective Time was converted into the right to receive 0.1 shares of Series A-5 Convertible Preferred stock of the Company; and each share of Series A-6 Convertible Preferred Stock of Target outstanding immediately prior to the Effective Time was converted into the right to receive 0.1 shares of Series A-6 Convertible Preferred stock of the Company. The Company assumed all options and warrants of Target outstanding immediately prior to the Effective Time, which shall become exercisable for shares of the Company s Common Stock or Preferred Stock, as the case may be. See the description of the material terms of the options and warrants assumed in the merger in sections herein entitled 2003 Long-Term Incentive Plan and Description of Securities Stock Purchase Warrants , respectively. Target and the Company agreed to indemnify each of their officers and directors for their actions relating to the consideration, approval or consummation of the Merger Agreement, in accordance with an indemnity agreement (the **Indemnity Agreement**) entered into by and between Target, the Company and their respective officers before the closing of the merger. The Company s entry into the Merger Agreement was disclosed on the Company s Current Report on Form 8-K filed with the Securities and Exchange Commission on April 29, 2011, which is hereby incorporated by reference, including the copy of the Merger Agreement filed as Exhibit 10.1 thereto.

Contemporaneously with the closing of the Merger, pursuant to the terms of a Redemption Agreement dated March 25, 2011 by and among the Company and its then-current stockholders, the Company completed the repurchase of 5,000,000 shares of Common Stock (the **Redemption**) from its former stockholders in consideration of an aggregate of $50,000. The 5,000,000 shares constituted all of the issued and outstanding shares of the Company s capital stock, on a fully-diluted basis, immediately prior to the Merger. The Company s entry into the Redemption Agreement was disclosed on the Company s Current Report on Form 8-K filed with the Securities and Exchange Commission on April 29, 2011, which is hereby incorporated by reference, including the copy of the Redemption Agreement filed as Exhibit 10.2 thereto. Also in connection with the Merger, the Company entered into Indemnification Agreements with each member of its board of directors, copies of which are filed here with as Exhibits 10.52 to and including Exhibit 10.62.

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Upon completion of the Merger and the Redemption, the former stockholders of Target held 100% of the outstanding shares of capital stock of the Company. Accordingly, the Merger represents a change in control of the Company. As of the date of this report, there are 555,594 shares of our Common Stock and 1,549,130 shares of our Preferred Stock outstanding.

Pursuant to the Merger, we assumed all of the Target s obligations under its existing contracts, including those filed herewith as material contracts. In particular, we have assumed the obligations of Target under that certain Series A-1 Convertible Preferred Stock Purchase Agreement (the Original Purchase Agreement) with certain investors listed therein (the Investors) pursuant to which, among other things, we are obligated to issue and sell to the Investors up to an aggregate of 789,553 shares of Series A-1 Convertible Preferred Stock, par value $.01 per share, to be completed in three closings (the initial closing, the Stage I Closing , the second closing, the Stage II Closing and the final closing, the Stage III Closing) (collectively, the Series A-1 Financing). The Original Purchase Agreement was subsequently amended by Amendment No. 1 thereto to eliminate all closing conditions previously provided for in the Original Purchase Agreement (as so amended, the Purchase Agreement). Upon notice from us, the Investors are obligated to purchase, and we are obligated to issue, 263,178 shares of our Series A-1 Convertible Preferred Closing at the Stage II Closing and 263,180 shares of our Series A-1 Convertible Preferred Stock at the Stage III Closing, each at a purchase price per share of $81.42. There are no conditions to funding if we notify the Investors of any such closing. A copy of the Purchase Agreement is attached hereto as Exhibit 10.26, and is incorporated herein by reference.

The Merger will be accounted for as a capital transaction. Upon effectiveness of the Merger, Target s business plan became our business plan.

The foregoing description of the Merger Agreement, the Redemption Agreement, Purchase Agreement and the transactions contemplated thereby do not purport to be complete and are qualified in their entireties by reference to the Merger Agreement and the Redemption Agreement, respectively.

Following the Merger on May 17, 2011, our Board of Directors approved a transaction pursuant to which Target merged with and into the Company, leaving the Company as the surviving corporation (the Short-Form Merger). In connection with the Short-Form Merger, the Company relinquished its corporate name and assumed in its place the name Radius Health, Inc. The Short-Form and name change became effective on May 17, 2011, upon the filing of a Certificate of Ownership an Merger with the Delaware Secretary of State. Our certificate of incorporation, The Certificate of Ownership and Merger is filed as Exhibit 3.2 hereto.

On May 23, 2011, the Company entered into a Loan and Security Agreement with General Electric Capital Corporation (GECC) as agent and a lender, and Oxford Finance LLC (Oxford and together with GECC, the Lenders) as a lender, pursuant to which the lenders agreed to make available to the Company $25,000,000 in the aggregate over three term loans. The initial term loan was made on May 23, 2011 in an aggregate principal amount equal to $6,250,000 (the Initial Term Loan) and is repayable over a term of 42 months, including a six month interest only period. The Initial Term Loan bears interest at 10%. Pursuant to the Agreement, the Company may request two (2) additional term loans, the first, which must be funded not later than November 23, 2011, in an aggregate principal amount equal to $6,250,000 (the Second Term Loan) and the second, which must be funded not later than May 23, 2012, in an aggregate principal amount equal to $12,500,000 (the Third Term Loan). In the event the Second Term Loan is not funded on or before November 23, 2011, the Lenders commitment to make the Second Term Loan shall be terminated and the total commitment shall be reduced by $6,250,000. In the event the Third Term Loan is not funded on or before May 23, 2012, the Lenders commitment to make the Third Term Loan shall be terminated and the total commitment shall be further reduced by $12,500,000. Pursunt to the agreement, the Company agreed to issue to the Lenders (or their respective affiliates or designees) stock purchase warrants (collectively, the Warrants) to purchase in the aggregate a number of shares of the Company s Series A-1 Preferred Stock equal to the quotient of (a) the product of (i) the amount of the applicable term loan multiplied by (ii) four percent (4%) divided by (b) the exercise price equal to $81.42 per share. The exercise period of each Warrant to be issued will expire ten (10) years from the date such Warrants are issued. On May 23, 2011, the Company issued a Warrant to each of GECC and Oxford for the purchase of 3,070 shares of Series A-1 Preferred stock.

DESCRIPTION OF THE BUSINESS OF RADIUS HEALTH, INC.

EXPLANATORY NOTE: *Unless otherwise provided in this current report, all references in the balance of this current report to we, us, our company, our, or the Company refer to the combined Radius Health, Inc. entity after giving effect to the Merger and the Short-Form Merger.*

Overview

Radius is a pharmaceutical company focused on acquiring and developing new therapeutics for the treatment of osteoporosis and other women s health conditions. Our lead product candidate is BA058 Injection, a daily subcutaneous injection of our novel synthetic peptide analog of human parathyroid hormone-related protein (hPTHrP) for the treatment of osteoporosis. In April 2011, we began dosing of patients in a pivotal Phase 3 clinical study and expect to report top-line data from this study by late 2013. Based on our clinical and preclinical results to date, we believe that BA058 stimulates the rapid formation of new high quality bone in patients suffering from osteoporosis and may restore bone mineral density in these patients into the normal reference range. In addition to BA058 Injection, we are developing BA058 Microneedle Patch, a short wear time, transdermal form of BA058 that is delivered using a microneedle technology from 3M Drug Delivery Systems (3M). BA058 Microneedle Patch is being studied in a Phase 1b clinical study which began in December 2010. The BA058 Microneedle Patch may eliminate the need for daily injections and lead to better treatment compliance for patients. We believe that development costs for the BA058 Microneedle Patch will be lower than the development costs for BA058 Injection as it will not be necessary to conduct an additional fracture study for

this follow-on product. As a result of the compressed pathway for the BA058 Microneedle Patch, we expect that marketing approval of the BA058 Microneedle Patch can occur soon after the BA058 Injection.

While there are a number of drugs that help to reduce the rate of bone loss in patients suffering from osteoporosis, there are few that are able to build bone. The only approved therapy in the United States that increases bone mineral density (BMD) into the normal reference range in these patients is Forteo®, a daily subcutaneous injection of recombinant human parathyroid hormone (rhPTH(1-34)). The product is marketed by Eli Lilly and had reported worldwide sales of $830 million in 2010. We believe that BA058 may offer a number of important advantages over Forteo®, including greater efficacy, a faster benefit, a shorter course of therapy, an improved safety profile and no need to refrigerate in use BA058 Injection. We believe, if approved, the BA058 Injection and the BA058 Microneedle Patch will offer an attractive bone anabolic treatment option for prescribing physicians and women with compelling advantages in safety, efficacy and delivery over Forteo®.

Based upon guidance we have received from the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA), we believe that a single pivotal placebo-controlled, comparative Phase 3 study will be sufficient to support registration of BA058 Injection for the treatment of osteoporosis in both the United States and the European Union. Our planned study will enroll a total of 2,400 patients to be randomized equally to receive daily doses of one of the following: 80 micrograms (µg) of BA058, a matching placebo, or the approved dose of 20 µg of Forteo® for 18 months. The study will be powered to show that BA058 is superior to (i) placebo for fracture and (ii) Forteo® for greater BMD improvement at major skeletal sites and for a lower occurrence of hypercalcemia, a condition in which the calcium level in a patient s blood is above normal. We believe that the study will also show that BMD gains for BA058 patients will be earlier than for Forteo® patients.

Market Opportunity for BA058

Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to an increase in fractures. The prevalence of osteoporosis is growing in developed nations with the aging of the populations. The National Osteoporosis Foundation (NOF) has estimated that (i) 10 million people in the United States, comprising eight million women and two million are men, already have osteoporosis and another 34 million have low bone mass placing them at increased risk for osteoporosis and (ii) osteoporosis was responsible for more than 2 million fractures in the United States in 2005 resulting in an estimated $19 billion in costs. The NOF expects that the number of fractures due to osteoporosis will rise to more than 3 million by 2025.

In 2011, Cowen and Company (Cowen), an investment banking firm, estimated that total worldwide sales of osteoporosis products was $7.6 billion in 2010. There are two main types of osteoporosis drugs now available in the United States: (i) anti-resorptive agents such as bisphosphonates including Actonel®, Boniva® or Reclast®, and Prolia® (a nuclear factor kB ligand (RANKL) inhibitor marketed by Amgen), as well as calcitonins and selective estrogen receptor modulators such as Evista® marketed by Lilly; and (ii) anabolic agents, with Forteo® being the only approved drug of this type. Anti-resorptive agents act to prevent further bone loss by inhibiting the breakdown of bone whereas anabolic agents stimulate bone formation to build high quality, new bone. The use of bisphosphonates have been associated with infrequent but serious adverse events such as osteonecrosis of the jaw, atrial fibrillation and anomalous fractures resulting from frozen bone that have created increasing concern with physicians and patients. Many physicians are seeking alternatives to current anti-resorptive therapies and we believe this will drive greater demand for bone anabolic agents in the future. We believe that there is a significant opportunity for a new anabolic agent such as BA058 that will increase bone mineral density to a greater degree and at a faster rate than Forteo® with added advantages in convenience and safety.

Our Strategy

We plan to build a pharmaceutical company focused on acquiring and developing new therapeutics for osteoporosis and women s health by:

- Completing the single, pivotal Phase 3 clinical trial of BA058 Injection for the treatment of osteoporosis by the end of 2013;
- Pursuing the clinical development of BA058 Microneedle Patch as a follow-on product for the treatment of osteoporosis;

- Obtaining regulatory approval of BA058 Injection and BA058 Microneedle Patch for the treatment of osteoporosis, initially in the United States and subsequently in the European Union;

- Collaborating with third parties for the worldwide commercialization of BA058; and

- Collaborating with third parties for the further development and commercialization of RAD1901 and RAD140 on a worldwide basis.

To execute on our strategy, we have built a strong management team and Board of Directors with significant pharmaceutical development, regulatory and commercial experience.

Our Solution:

In addition to BA058 Injection and BA058 Microneedle Patch, we are currently conducting one other clinical and one preclinical program. Our second clinical stage product candidate is RAD1901, a selective estrogen receptor modulator, or SERM, licensed from Eisai Co (Eisai) in 2006 which has completed an initial Phase 2 clinical study for the treatment of vasomotor symptoms (hot flashes) in women entering menopause. Our third product candidate, RAD140, is a pre-investigational new drug, or IND, discovery. RAD140 is a selective androgen receptor modular, or SARM, that is an orally-active androgen agonist on muscle and bone and is a potential treatment for age-related muscle loss, frailty, weight loss associated with cancer cachexia and osteoporosis.

The following table summarizes the target indications, dosage forms, and stages of development for our product candidates.

BA058

BA058 is a novel synthetic peptide analog of Parathyroid hormone-related peptide (hPTHrP) being developed by us as a bone anabolic treatment for osteoporosis. hPTHrP is a critical cytokine for the regulation of bone formation, able to rebuild bone with low associated risk of inducing hypercalcemia as a side-effect. We believe that BA058 is the most advanced hPTHrP analog in clinical development for the treatment of osteoporosis. We acquired and maintain exclusive worldwide rights (except Japan) to certain patents, data and technical information related to BA058 through a license agreement with Ipsen Pharma S.A.S (Ipsen) dated September 2005. Based on clinical and preclinical data to date, we believe that BA058 has the following important potential advantages over

Forteo® rhPTH(1-34), the only other approved anabolic agent for osteoporosis in the US:

- Greater efficacy,
- Faster benefit,
- Shorter treatment duration,
- Less hypercalcemia,
- No additional safety risks, and
- No refrigeration required in use.

BA058 Injection

In August 2009, we announced positive Phase 2 data that showed BA058 Injection produced faster and greater BMD increases at the spine and the hip after 6 months and 12 months of treatment than did Forteo®, which was a comparator in our study. Key findings were that the highest dose of BA058 tested of 80 µg increased mean lumbar spine BMD at 6 and 12 months by 6.7% and 12.9% compared to the increases seen with Forteo® trial arms of 5.5% and 8.6%, respectively. BA058 also produced increases in mean femoral neck BMD at the hip at 6 and 12 months of 3.1% and 4.1% compared to increases for Forteo® of 1.1% and 2.2%, respectively. We believe there to be a strong correlation between an increased level of BMD and a reduction in the risk of fracture for patients with osteoporosis. BA058 was generally safe and well tolerated in this study, with adverse events similar between the BA058, placebo and Forteo® groups. In addition, the occurrence of hypercalcemia as a side-effect was half that seen with Forteo® for the 80 µg dose of BA058.

In March 2011, we entered an agreement with Nordic Bioscience (Nordic) to manage the Phase 3 study of BA058 Injection. The study will be conducted in 8 countries at 11 centers operated by the Center for Clinical and Basic Research (CCBR). CCBR is a leading global clinical research organization (CRO) with extensive experience in global osteoporosis registration studies. We expect to report top-line data from the Phase 3 study of BA058 Injection by late 2013.

BA058 Microneedle Patch

In December 2010, we initiated a combined single and seven-day repeat-dose Phase 1 clinical study of the BA058 Microneedle Patch in healthy subjects with top-line data expected to be available by mid-2011. Following this Phase 1 study, we plan to select a dose range to conduct a Phase 2 clinical study comparing multiple daily doses of the BA058 Microneedle Patch to placebo and BA058 Injection using lumbar spine BMD at 6 months as the primary endpoint. We expect to begin the Phase 2 BA058 Microneedle Patch clinical study in mid 2012 with top-line data available in mid 2013. If the BA058 Injection product is already approved by the FDA, we believe that we will only need to conduct a single non-inferiority Phase 3 clinical study comparing the change in lumbar spine BMD at 12 months for patients dosed with the BA058 Microneedle Patch to patients dosed with the BA058 Injection. We believe that development costs for the BA058 Microneedle Patch will be lower than the injectable version as it will not be necessary to conduct an additional fracture study for this follow-on product. As a result of the compressed pathway, we expect that marketing approval of the BA058 Microneedle Patch can occur soon after the BA058 Injection.

Background on Osteoporosis

Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue, which can lead to an increase in fractures. On its website, www.nof.org, the National Osteoporosis Foundation (NOF) has estimated that 10 million people in the United States, comprising eight million women and two million men, already have osteoporosis and another 34 million have low bone mass placing them at increased risk for osteoporosis and broken bones. All bones become more fragile and susceptible to fracture as the disease progresses. People tend to be unaware that their bones are getting weaker, and a person with osteoporosis can fracture a bone from even a minor fall. Fractures due to osteoporosis are most likely to occur in the hip, spine and wrist. According to the NOF, osteoporosis was responsible for more than 2 million fractures in the United States in 2005 and is expected to rise to more than 3 million fractures by 2025. Vertebral (spinal) fractures may result in severe back pain, loss of height or spinal deformities. There were approximately 293,000 Americans age 45 and over admitted to hospitals in 2005 with a fracture of the femoral neck, a common type of hip fracture that is

associated with osteoporosis. A women s lifetime risk of a hip fracture is equal to her combined risk of breast, uterine and ovarian cancer. An average of 24 percent of hip fracture patients aged 50 and over dies in the year following their fracture. An additional 20 percent of patients who were ambulatory before their hip fracture require long-term care.

The debilitating effects of osteoporosis have substantial costs. Loss of mobility, admission to nursing homes and dependence on caregivers are all common consequences of osteoporosis. The NOF has estimated that osteoporosis-related fractures were responsible for $19 billion in costs in 2005.

The prevalence of osteoporosis is growing and, according to the NOF, is significantly under-recognized and under-treated in the population. While the aging of the population is a primary driver of an increase in cases, osteoporosis is also increasing from the use of drugs that induce bone loss, such as chronic use of glucocorticoids for asthma, aromatase inhibitors that are increasingly used for breast cancer and the hormone therapies used for prostate cancer.

The range of treatment and prevention options for osteoporosis has expanded in recent years from anti-resorptive drugs that act to prevent bone loss by blocking bone resorption and now includes bisphosphonates, selective estrogen receptor modulators, calcitonins, and most recently in 2010, a RANKL inhibitor. Bisphosphonates remain the current standard of care with 2010 world-wide total sales of approximately $4.2 billion according to Cowen and Company s report dated March 2011 and entitled Therapeutic Categories Outlook, led by Actonel®, Boniva®, and Fosamax®. Generic versions of Fosamax® (alendronate) became available in the US in 2008 and have now gained share from branded oral bisphosphonates.

The only anabolic (i.e., stimulating bone formation) drug approved in the U.S. for osteoporosis is Forteo®, which was approved by the FDA in December 2002. In 2011, the medical journal, *Osteoporosis International*, published results of a study indicating that patients preferences for osteoporosis medications are strongly influenced by the mode of administration. In particular, when given the choice of subcutaneously injected Forteo® versus other therapies, patients preferred the alternative drugs over Forteo, which requires once-daily, self-administered injections and must be refrigerated for storage in use. We believe that this research suggests that there is a substantial opportunity to optimize patient outcomes and expand the market by improved treatment compliance with a bone anabolic drug that offers an alternative to daily injection, is room-temperature-stable and requires a shorter treatment duration, such as the BA058 Microneedle Patch. Forteo® had world-wide sales of $615 million in 2008 and grew to $830 million in sales for 2010.

Clinical Development Program for BA058

Radius is developing BA058 for the prevention of fractures in postmenopausal women at risk of fracture from severe osteoporosis. Recognizing both the therapeutic potential of BA058 in this indication as well as the drawbacks inherent in self-injection therapies in this population, Radius is also developing the BA058 Microneedle Patch for transdermal administration of the product using a microneedle technology from 3M. We plan to develop and register BA058 Injection as our lead product, with the BA058 Microneedle Patch as a fast-following product that provides greater patient convenience. The ability of the Microneedle Patch to capitalize on the more extensive fracture study data of BA058 Injection will allow the patch product to be accelerated though later phase development without requiring its own fracture study.

Planned and Completed BA058 Studies

Planned Studies

BA058 Injection, Phase 3

The Phase 3 study for BA058 Injection (Study BA058-05-003) was submitted as a draft protocol to IND 73,176 on December 18, 2009, and was the subject of a Type B End of Phase 2 Meeting conducted with the Agency on January 21, 2010. The protocol was subsequently revised and submitted to the FDA on December 17, 2010. The study is planned to enroll 2,400 patients at 11 medical centers in 8 countries in Europe, Latin America and Asia.

Study Objectives

The primary objective of this study is to determine the safety and efficacy of BA058 Injection 80 µg when compared to a matching placebo for prevention of vertebral fracture in otherwise healthy ambulatory postmenopausal women at risk of fracture from severe osteoporosis. Patients, investigators and independent assessors will be blinded as to treatment for that outcome. The secondary objectives of this study are to determine the safety and efficacy of BA058 80 µg when compared to placebo for prevention of non-vertebral fractures and for change in vertical height. Additional key secondary efficacy outcomes include BMD of spine, hip and femoral neck and hypercalcemia when compared to Forteo®.

Study Population

The study will enroll otherwise healthy ambulatory postmenopausal (≥ 5 years) women from 50 to 85 years of age (inclusive) who meet the study entry criteria and have provided written informed consent. The women will have a BMD T-score ≤ -2.5 and > -5.0 at the lumbar spine or hip (femoral neck) by dual energy x-ray absorptiometry (DXA) and radiological evidence of two or more mild or one or more moderate lumbar or thoracic vertebral fractures, or history of low trauma forearm, humerus, sacral, pelvic, hip, femoral, or tibial fracture within the past 5 years. Postmenopausal women older than 65 who meet the above fracture criteria but have a T-score ≤ -2.0 and > -5.0 may be enrolled. Women older than 65 who do not meet the fracture criteria may also be enrolled if their T-score is ≤ -3.0 and > -5.0.

All patients are to be in good general health as determined by medical history, physical examination (including vital signs) and clinical laboratory testing.

Study Design

The planned 2,400 eligible patients will be randomized equally to receive one of the following: BA058 80 µg, a matching placebo, or Forteo® 20 µg for 18 months. Study drug will be blinded to patients and medical personnel until the randomization process is completed. Treatment with BA058 80 µg or placebo will remain blinded to all parties throughout the study. Forteo® comes as a proprietary prefilled drug and device combination that cannot be repackaged and therefore, its identity cannot be blinded to treating physicians and patients once use begins. Study medication will be self-administered daily by SC injection for a maximum of 18 months.

The dosages of study medications and the number of patients per group are shown in below.

Study BA058-05-003 Medication Doses and Number of Patients per Group

Treatment Regimen	Study Medication	Daily Dose (SC)	Duration	Number of Patients
1	BA058	80 µg	18 months	800
2	Placebo		18 months	800
3	Forteo®	20 µg	18 months	800
			Total	2,400

All enrolled patients will also receive Calcium and Vitamin D supplementation from the time of enrollment until the end of the Treatment Period; it will be recommended to patients that they also continue these supplements through the one month follow-up period.

Primary Efficacy Outcomes

The primary efficacy endpoint will be the number of BA058-treated patients showing new vertebral fractures at End-of-Treatment when compared to placebo as evaluated by a blinded assessor (radiologist) according to a standardized graded scale of severity of the vertebral deformity (Genant scale).

Secondary Efficacy Endpoints

Secondary efficacy parameters will also include reduction in the incidence of non-vertebral fractures (wrist, hip, rib, etc.) and reduction in moderate and severe vertebral fractures. Other secondary efficacy endpoints will include changes in BMD of the spine, hip, femoral neck and wrist from baseline to end-of-treatment as assessed by DXA.

Additional secondary endpoints will include change in standing height and changes in serum bone markers across treatment, such as N-terminal propeptide of type I procollagen PINP, osteocalcin and bone-specific alkaline phosphatase. The frequency of hypercalcemia across treatment groups will also be assessed.

Safety Outcomes

Safety evaluations to be performed will include physical examinations, vital signs, 12-lead ECGs, clinical laboratory tests and monitoring and recording of adverse events. Specific safety assessments will include post-dose (4 hours) determination of serum calcium, determination of creatinine clearance, post-dose ECG assessments at selected visits and assessments of postural hypotension (60 minutes post-dose) at selected clinic visits.

Bone biopsy of the iliac crest will be performed in a subset of patients receiving BA058 80 µg and Placebo (up to 100 per group) for assessment of quantitative bone histomorphometry and will be read blinded to treatment by an independent blinded assessor. Renal safety will be further evaluated in a subset of 100 patients in each treatment group by renal CT scan.

Overall study safety will be monitored by an independent Data Safety Monitoring Board.

BA058 Microneedle Patch Phase 2

We plan to conduct a Phase 2 randomized, placebo-controlled, parallel group dose-finding clinical trial in mid-2012. The study will evaluate the safety and efficacy of the daily BA058 Microneedle Patch in women with osteoporosis. We intend to enroll about 250 patients and the study will be similar in design to the Phase 2 study for BA058 Injection. The study will evaluate the effects of 3 doses of the BA058 Microneedle Patch, compared to placebo and BA058 Injection 80 µg on change in BMD and anabolic bone markers over 6 months of treatment. The study will be powered to detect clinically meaningful changes in these efficacy measures (BMD and bone biomarkers).

Safety will be assessed as changes in incidence of adverse events, changes in laboratory parameters - in particular serum calcium, change from baseline in vital signs and physical examination.

Study participation will be preceded by 4 weeks of pretreatment with Calcium and Vitamin D supplements and treatment conclusion will be followed by a one month period of safety observation.

Completed BA058 Studies

BA058 Injection, Phase 2

A Phase 2 dose-finding clinical trial (Study BA058-05-002) was conducted as a randomized, placebo-controlled, parallel group dose-finding study in the United States, Argentina, India and the United Kingdom. The purpose of the study was to evaluate the safety and efficacy of daily subcutaneous (SC) injections of BA058 Injection in women with osteoporosis. The study evaluated the effects of BA058 Injection at multiple doses (0, 20, 40 and 80 µg) on recovery of BMD, a marker of fracture risk, and on biomarkers of anabolic and resorptive activity in bone. The study also included a Forteo® treatment arm for reference. These efficacy measures (BMD and bone biomarkers) were powered for statistical significance. After the initial 24 weeks of treatment, eligible patients were

offered a second 24 weeks of their assigned treatment. Safety was assessed throughout the study and reported on at both 6 months and 12 months. BA058 Injection and BA058-placebo were self-administered using a prefilled cartridge in a pen-injector device. Forteo® was self-administered as the marketed product at the approved dose of 20 µg per day by SC injection. Four weeks prior to start of treatment, patients began taking Calcium and Vitamin D supplements that continued throughout the study.

A total of 270 patients (mean age: 65 years) entered the Pretreatment Period, 222 patients were randomized, and 221 patients received study treatment and were analyzed in the intent to-treat (ITT) population with 55 continuing into the Extension Period. A total of 155 patients were included in the Efficacy Population (Per Protocol) in the initial 24 weeks of treatment.

Initial 24 weeks of treatment

The efficacy results of Study BA058-05-002 confirm the preclinical and early clinical hypothesis that BA058 Injection induces a dose-dependent increase in BMD and in markers of bone remodeling measurable at both the 12-week and 24-week assessments.

At week 12, in the ITT population the mean percent change in total analyzable spine BMD increased with dose, Figure A. The mean gains in BMD (active treatment placebo) for the BA058 Injection 40 µg and 80 µg groups were statistically significant ($p = .0013$ and $p < 0.001$, respectively). The difference was not statistically significant in the BA058 20 µg group and just missed significance in the Forteo® group ($p = 0.055$).

At week 24, the percent change from baseline continued to increase and was statistically significantly proportional to dose ($p<0.001$), Figure A. Again, the mean gain in total analyzable spine BMD was statistically significant for the BA058 Injection 40 µg ($p = <0.001$) and 80 µg ($p < 0.001$) groups. The BMD gain at week 24 was also significant for the Forteo® group ($p < 0.001$), but not for the placebo group.

Figure A Mean Standard Error of the Mean (SEM) Percent Change from Baseline at weeks 12 and 24 in Total Analyzable Spine BMD

An even greater proportional response in BMD was elicited in the hip region. By week 24, mean percent changes in total analyzable hip BMD were 0.4%, 1.4%, 2.0% and 2.6% for the placebo, BA058 20 µg, BA058 40 µg, and BA058 80 µg groups, respectively; mean percent change in the Forteo® (0.5%) group was similar to placebo, Figure B. Total hip showed a clear dose response to BA058 and a more than five-fold benefit of BA058 80 µg over Forteo®. A similar relative benefit of BA058 80 µg over Forteo® was seen in all regions of the hip.

Figure B - Mean (SEM) Percent Change from Baseline at weeks 12 and 24 in Total Analyzable Hip BMD (ITT Population, N=221)

BA058 Injection also induced a dose-dependent rise in all markers of bone anabolic activity studied (N-terminal propeptide of type I procollagen PINP, bone specific alkaline phosphatase BSAP, and osteocalcin). The response to Forteo® was generally somewhat greater for all anabolic markers, but similar for bone resorption markers (C-telopeptides of type I collagen crosslinks [CTX] and N-telopeptides of type I collagen crosslinks [NTX]), consistent with published data on later attenuation of Forteo® BMD benefit.

BA058 Injection was well tolerated at all doses and safety events were consistent with usual medical events in a study population of this age and gender. The safety profile was also similar to that of Forteo® and there were no treatment-related SAEs; however, treatment-emergent adverse events (TEAEs) were reported by 74% of patients in the first 6 months of treatment, with a similar incidence across all treatment groups. The majority of TEAEs events were mild to moderate in severity and there were no deaths reported. Seven subjects discontinued due to adverse events,1in the BA058 20 µg group, 1 in the BA058 40 µg group, 3 in the BA058 80 µg group and 2 in the teriparatide group Eight patients (4%) experienced at least 1 severe AE and the incidence of such events was similar across treatment groups. Five TSAEs were reported in 3 patients,

all unrelated to study drug. Local tolerance at the injection site was similar across treatment groups and fewer than 20% of subjects reported any one symptom, such as redness, at the injection site across the many months of injections.

Serum calcium levels were monitored throughout the study and clinically significant elevated levels ($\geq$ 10.5 mg/dL) were observed in 40% of the Forteo® group while also observed in 4%, 12%, 19% and 18% of the placebo, BA058 Injection 20 µg, 40 µg and 80 µg groups. Most elevations were noted at the 4-hour post-injection time point. Clinically significant hypercalciuria (8%) and hypercalcemia (5%) were also more common in the Forteo® group.

Blood pressure was assessed throughout the study for postural change. Postural changes in blood pressure (predetermined level of change in systolic or diastolic from lying to standing) were reported in 7 patients, including 0%, 5%, 2%, 2% and 7% of patients in the placebo, BA058 Injection 20 µg, 40 µg, 80 µg and Forteo® groups, respectively. Pre-dose postural changes in blood pressure were similar across treatment groups. There were no clinically meaningful differences in ECG parameters between the placebo and active treatment groups.

Seventeen patients had low titer antibodies against BA058 after 6 months of treatment. Of these, 1 was in the placebo group, 2 were in the BA058 20 µg group, 8 were in the BA058 40 µg group and 6 were in the BA058 80 µg group. There were no associated safety events and no attenuation of treatment efficacy. One antibody-positive patient in the BA058 Injection 40 µg group was found to have evidence of neutralizing activity at 24 weeks without evidence of attenuation of drug efficacy, having a 9.3% gain in total analyzable spine BMD at the week 24 assessment.

Extended 24 weeks of treatment

Patients who completed the initial 24 weeks of treatment and continued to meet eligibility criteria were offered participation in the 24-week extension study in which they would continue their assigned treatment. On completion of the regulatory process to approve the study extension, 69 patients remained eligible and 55 participated, including 13, 10, 7, 11 and 14 patients in the BA058 Injection 20 µg, 40 µg, 80 µg, placebo and Forteo® groups, respectively. Forty-eight patients completed the extended treatment period.

BMD continued to increase during the extended 24 weeks of treatment, with the largest percent increases in total analyzable spine BMD, femoral neck BMD and total analyzable hip BMD observed in the BA058 Injection 80 µg group. By week 48, mean percent changes in spine BMD were 0.7%, 5.1%, 9.8% and 12.9% for the placebo, BA058 20 µg, BA058 40 µg and BA058 80 µg, groups, respectively, while mean percent change from baseline in the Forteo® group was 8.6%. At week 48, the mean femoral neck BMD in the BA058 Injection 80 µg group gained 4.1% compared to the mean of the Forteo® group at 2.2%. The respective results for total analyzable hip BMD were 0.7%, 2.2%, 2.1% and 2.7% for the placebo, BA058 20 µg, BA058 40 µg and BA058 80 µg groups, respectively; compared to 1.3% for the Forteo® group.

No treatment-related SAEs or deaths were reported during this time period. Two patients discontinued treatment, one for bilateral femoral hernias (BA058 Injection 80 µg) and one for moderate syncope (BA058 Injection 40 µg). TEAEs occurred in a similar proportion of patients in each treatment group across the 52-week study period and the majority of events were mild or moderate in severity. The profile of events was not different in the second 6 months of study treatment.

Local tolerance of study drug injections was also similar in the second 6 months of treatment. There were no safety signals observed in the evaluation of clinical laboratory parameters.

In conclusion, this study demonstrated that treatment with BA058 Injection induces a substantial positive change in BMD at both spine and hip in women with osteoporosis and achieves this benefit safely and with substantially less hypercalcemia effect than Forteo®.

BA058 Injection Phase 1 Trials

The First Phase 1 Trial

The first Phase 1 clinical trial was a single-dose study conducted as a randomized, double-blind, placebo-controlled, parallel-group dose escalation study of BA058 Injection in a vial formulation administered as a single SC dose to healthy male and female subjects (mean age: 61 years). The study administered single SC doses of 2, 5, 7.5, 10, 15, 20, 40, 60, 80, and 100 µg BA058 Injection or placebo. Sixteen subjects also received 2.5 µg BA058 Injection by the intravenous (IV) route and 15 µg SC in separate study periods. In total, 76 subjects received BA058 while 20 received a placebo. No elevation in serum calcium was observed at doses of 80 µg or lower and no clinically relevant effects of BA058 Injection on ECG or Holter monitor readings were observed. In summary, this study demonstrated that BA058 Injection is 100% bioavailable when administered by the SC route. BA058

Injection did not induce hypercalcemia and was well tolerated at doses up to 80 µg SC.

The Second Phase 1 Trial

The second Phase 1 clinical trial was a multi-dose study of BA058 Injection when administered as a single SC injection for 7 days. Thirty-nine healthy postmenopausal women (mean age: 60 years) received BA058 Injection (5, 20, 40 or 80 µg) or placebo administered SC. BA058 was well tolerated at all doses and there were no serious adverse events (AEs) and no discontinuations. All AEs were mild or moderate in intensity and did not appear to be dose-related.

BA058 was rapidly absorbed, reaching mean peak plasma concentration within 1 hour, had a rapid clearance and mean half-life values ranged from 1.05 to 2.59 hours. Following BA058 administration, serum PTH decreased and serum 1,25-dihydroxyvitamin D and serum P1NP rose in an apparent dose-dependent manner. Serum calcium showed a slight rise within the normal range following BA058 administration. Three BA058 and 2 placebo patients had isolated calcium values just above the normal range.

The Third Phase 1 Trial

The third Phase 1 clinical trial was a multi-dose study, with the same design as the Second Phase 1 Trial, but using a liquid prefilled multidose cartridge of BA058 and conducted at doses of 80, 100 and 120 µg. BA058 Injection or placebo was administered daily as a SC dose for 7 days to healthy postmenopausal women. Thirty healthy postmenopausal women (mean age: 61 years) were enrolled and 29 completed treatment.

BA058 Injection was well tolerated at doses of up to 100 µg but not at 120 µg which met criteria for termination of dose escalation. One patient in the 120 µg group was intolerant of study drug and was discontinued. All adverse events were mild or moderate in intensity. No study subject developed serum antibodies to BA058 following the 7 days of exposure. BA058 pharmacokinetics was again characterized by rapid absorption, reaching mean peak plasma concentration within approximately 0.5 hours; mean half-life values ranged from 1.13 to 1.65 hours. Similar responses in serum PTH, 1,25-dihydroxy Vitamin D and serum P1NP were observed. These higher doses of BA058 Injection were not associated with occurrence of hypercalcemia. In summary, BA058 Injection was well tolerated at up to 100 µg QD (or daily) for 7 days.

BA058 Microneedle Patch

First Phase 1 Trial

The objectives of the Phase 1 study were to determine the safety, pharmacokinetics and time course of delivery of BA058 Microneedle Patch in healthy postmenopausal women and to compare the PK profiles of BA058 Microneedle Patch delivered transdermally to BA058 Injection administered subcutaneously.

This study was a randomized, double-blind, placebo-controlled, ascending single-dose study and enrolled 38 healthy postmenopausal women (mean age 57.6). Subjects underwent up to 3 single dose exposures to BA058 Microneedle Patch, Placebo Microneedle Patch or BA058 Injection 80 μg over the course of 3 Study Periods.

Pharmacokinetic Results

BA058 Microneedle Patch was characterized by a rapid absorption and elimination. The Cmax and half-life times were shorter than for BA058 Injection administration.

Safety Results

The BA058 Microneedle Patch was well tolerated. Safety events were similar between the BA058 Microneedle Patch and BA058 Injection, with the majority of AEs being mild (99%) and, of these, most were reactions at the application site. There was no clinically notable difference in laboratory or cardiac safety parameters across doses of BA058 or routes of administration.

In conclusion, this Phase 1 study of the BA058 Microneedle Patch demonstrated that BA058 can safely be delivered by this route of administration.

Second Phase 1 Trial

A second Phase 1 single and multiple (7-day) application study of the BA058 Microneedle Patch is currently being conducted in the United States using an optimized Microneedle Patch system. The study is designed as a safety, dose-ranging and time-course pharmacokinetic and pharmacodynamic study. This Phase 1 study will investigate optimal dose, wear time and application site for transdermal delivery of BA058 using an optimized microneedle array.

The study will use a matrix design and will first establish optimal wear time before exploring the impact of application site in the range of doses chosen for evaluation. The results obtained using the BA058 Microneedle Patch will be referenced to those of BA058 Injection 80 µg.

Preclinical Pharmacology

In pharmacology studies conducted with BA058, the following has been shown:

- BA058 is a potent selective agonist of the human PTHR 1 receptor;

- In models of calcium mobilization, BA058 has significantly less calcium mobilizing activity at higher doses than the native hPTHrP(1-34), and less activity than hPTH(1-34);

- BA058 Injection stimulates the formation of normal, well-organized bone and restores BMD in ovariectomized, osteopenic rats and primates. BA058 exhibited the majority of its effects through the growth of trabecular bone without compromising cortical bone. Similar studies in rats with BA058 Microneedle Patch show comparable restoration of bone;

- BA058 Injection was well tolerated over a wide range of doses in two species, rats and primates, for up to 6 months and 9 months, respectively;

- Safety pharmacology studies demonstrated no respiratory, gastroenterologic, hematologic, renal or CNS effects. Tachycardia and hypotension were observed in dogs following both intravenous and subcutaneous administration, however such effects were not observed in other species;

- The No Observed Adverse Effect Level (NOAEL) was 15, 25 and 25 µg/kg/day in rats in the 4-, 13 and 26-week studies, respectively, and 100, 50 and < 10 µg/kg/day in monkeys in the 4-, 13- and 39-week studies, respectively; and

- Repeat SC dose studies in both rats and cynomolgus monkeys at doses up to 300 and 450 µg/kg/day, respectively, revealed a relatively fast absorption (Tmax from 0.083 to 1.0 hr); peak serum concentration (Cmax) and Area under the Curve (AUC), a measure of drug exposure, increased as the dose increased.

These preclinical studies suggest that compared to hPTH(1-34), BA058 Injection can potentially be used to restore lost BMD with a reduced risk of hypercalcemia and loss of cortical bone.

Planned and Active Preclinical Safety Studies

A two-year subcutaneous injection carcinogenicity study of BA058 in Fischer 344 albino rats is currently on-going and will assess the carcinogenic potential of BA058. The study is being conducted according to the provisions set forth in Guidance ICH-S1A, ICH-S1B, and ICH-S1C(R2), and the design was accepted by FDA on 15 July 2009. This study will evaluate 3 BA058 dose levels, and the doses were selected based upon findings and tolerance in completed long-term rat toxicology studies and the anticipated tolerance over a 2-year dosing period and, furthermore, represents a good exposure multiple over maximum clinical doses. An active comparator arm is also included; a cohort of rats will be dosed with hPTH (1-34), because it is anticipated that osteosarcoma will be observed over time. The active comparator will allow confirmation of the sensitivity of the model. This study will be

conducted in parallel to the Phase 3 clinical program.

Two preclinical bone quality studies will also be conducted, one in ovariectomized (OVX) rats for up to 12 months of daily BA058 subcutaneous injection, the second study in adult OVX monkeys for up to 18 months. The primary objective of these studies is to demonstrate that long-term treatment with BA058 Injection will not lead to deleterious effects on bone quality by determining BA058 s effect on the mass, architecture and strength of bones. These studies will be conducted in parallel to the Phase 3 clinical program and, in both studies, BA058 will be compared to placebo. The 12-month rat study is being performed in OVX skeletally mature Sprague-Dawley rats, an appropriate species for osteoporosis studies as a result of the cancellous bone changes and bone strength changes similarly noted in humans. In this study, a 13-week bone depletion period will occur after ovariectomy/sham surgery and prior to initiation of daily SC injection dosing with vehicle or three different dose levels of BA058.