NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

HOFFMANN-LA ROCHE INC. et al., Plaintiffs, v. APOTEX INC. and APOTEX CORP., Defendants.	Civil Action No. 07-4417 (SRC) (MAS) Civil Action No. 08-3065 (SRC) (MAS) Civil Action No. 08-4053 (SRC) (MAS) Civil Action No. 10-6241 (SRC) (MAS) (consolidated with 07-4417 for all purposes) **OPINION**
HOFFMANN-LA ROCHE INC. et al., Plaintiffs, v. DR. REDDY'S LABORATORIES, LTD. and DR. REDDY'S LABORATORIES, INC., Defendants.	Civil Action No. 07-4516 (SRC) (MAS) Civil Action No. 08-3607 (SRC) (MAS) Civil Action No. 08-4055 (SRC) (MAS) Civil Action No. 10-5623 (SRC) (MAS) (consolidated with 07-4516 for all purposes)
HOFFMANN-LA ROCHE INC. et al., Plaintiffs, v. WATSON LABORATORIES, INC., WATSON PHARMACEUTICALS, INC., WATSON PHARMA, INC., COBALT PHARMACEUTICALS INC., and COBALT LABORATORIES, INC., Defendants.	Civil Action No. 07-4539 (SRC) (MAS) Civil Action No. 07-4540 (SRC) (MAS) Civil Action No. 08-4054 (SRC) (MAS) Civil Action No. 10-6206 (SRC) (MAS) (consolidated with 07-4539 for all purposes)

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HOFFMANN-LA ROCHE INC. et al., Plaintiffs, v. ORCHID CHEMICALS & PHARMACEUTICALS LTD., ORCHID HEALTHCARE, ORCHID PHARMACEUTICALS INC., and ORGENUS PHARMA INC., Defendants.	Civil Action No. 07-4582 (SRC) (MAS) Civil Action No. 08-4051 (SRC) (MAS) Civil Action No. 10-4050 (SRC) (MAS) (consolidated with 07-4582 for all purposes)
HOFFMANN-LA ROCHE INC. et al., Plaintiffs, v. MYLAN INC., MYLAN PHARMACEUTICALS INC., GENPHARM ULC and GENPHARM, L.P., Defendants.	Civil Action No. 07-4661 (SRC) (MAS) Civil Action No. 08-4052 (SRC) (MAS) Civil Action No. 11-0579 (SRC) (MAS) (consolidated with 07-4661 for all purposes)

CHESLER, U.S.D.J.

This matter comes before the Court on the motion for summary judgment, pursuant to Federal Rule of Civil Procedure 56, by Defendants Watson Pharmaceuticals, Inc., Watson Laboratories, Inc., Watson Pharma, Inc., Cobalt Pharmaceuticals Inc. and Cobalt Laboratories, Inc., Apotex Inc. and Apotex Corp., Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc., Orchid Chemicals & Pharmaceuticals Ltd., Orchid Healthcare, Orchid Pharmaceuticals Inc., Orgenus Pharma Inc., Mylan Inc., Mylan Pharmaceuticals Inc., Genpharm

ULC and Genpharm, L.P. (collectively, "Defendants") that claims 1-8 of U.S Patent No. 7,718,634 (the "'634 patent) are invalid based on obviousness. The Court held oral argument on the motion on April 30, 2012. For the reasons stated below, the motion will be granted.

BACKGROUND

This matter involves several Hatch-Waxman actions for patent infringement. The cases have been consolidated for pretrial purposes and arise from the following facts. Briefly, Plaintiff Hoffman-La Roche Inc. ("Roche") owns the '634 patent, which is directed to compounds and treatment methods associated with Roche's osteoporosis drug Boniva®. Defendants are generic pharmaceutical manufacturers who have filed Abbreviated New Drug Applications seeking FDA approval to engage in the manufacture and sale of generic versions of Boniva® prior to the expiration of the Roche patents.

On March 14, 2012, this Court issued an Opinion denying Roche's application for a preliminary injunction, finding, *inter alia*, that Defendants had raised a substantial question about whether the '634 patent was invalid due to obviousness. Pending at that time was the instant motion for summary judgment. Roche has since appealed the denial of its preliminary injunction application to the United States Court of Appeals for the Federal Circuit.

APPLICABLE LEGAL STANDARDS

I. Summary Judgment

Summary judgment is appropriate under FED. R. CIV. P. 56(a) when the moving party demonstrates that there is no genuine issue of material fact and the evidence establishes the moving party's entitlement to judgment as a matter of law. Celotex Corp. v. Catrett, 477 U.S. 317, 322-23 (1986). A factual dispute is genuine if a reasonable jury could return a verdict for

the non-movant, and it is material if, under the substantive law, it would affect the outcome of the suit. Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248 (1986). "In considering a motion for summary judgment, a district court may not make credibility determinations or engage in any weighing of the evidence; instead, the non-moving party's evidence 'is to be believed and all justifiable inferences are to be drawn in his favor.'" Marino v. Indus. Crating Co., 358 F.3d 241, 247 (3d Cir. 2004) (quoting Anderson, 477 U.S. at 255).

"When the moving party has the burden of proof at trial, that party must show affirmatively the absence of a genuine issue of material fact: it must show that, on all the essential elements of its case on which it bears the burden of proof at trial, no reasonable jury could find for the non-moving party." In re Bressman, 327 F.3d 229, 238 (3d Cir. 2003) (quoting United States v. Four Parcels of Real Property, 941 F.2d 1428, 1438 (11th Cir. 1991)). "[W]ith respect to an issue on which the nonmoving party bears the burden of proof . . . the burden on the moving party may be discharged by 'showing' – that is, pointing out to the district court – that there is an absence of evidence to support the nonmoving party's case." Celotex, 477 U.S. at 325.

Once the moving party has satisfied its initial burden, the party opposing the motion must establish that a genuine issue as to a material fact exists. Jersey Cent. Power & Light Co. v. Lacey Township, 772 F.2d 1103, 1109 (3d Cir. 1985). The party opposing the motion for summary judgment cannot rest on mere allegations and instead must present actual evidence that creates a genuine issue as to a material fact for trial. Anderson, 477 U.S. at 248; Siegel Transfer, Inc. v. Carrier Express, Inc., 54 F.3d 1125, 1130-31 (3d Cir. 1995). "[U]nsupported allegations . . . and pleadings are insufficient to repel summary judgment." Schoch v. First Fid.

Bancorporation, 912 F.2d 654, 657 (3d Cir. 1990). "A nonmoving party has created a genuine issue of material fact if it has provided sufficient evidence to allow a jury to find in its favor at trial." Gleason v. Norwest Mortg., Inc., 243 F.3d 130, 138 (3d Cir. 2001).

If the nonmoving party has failed "to make a showing sufficient to establish the existence of an element essential to that party's case, and on which that party will bear the burden of proof at trial, . . . there can be 'no genuine issue of material fact,' since a complete failure of proof concerning an essential element of the nonmoving party's case necessarily renders all other facts immaterial." Katz v. Aetna Cas. & Sur. Co., 972 F.2d 53, 55 (3d Cir. 1992) (quoting Celotex, 477 U.S. at 322-23).

II. Patent invalidity due to obviousness

"A patent is presumed to be valid, 35 U.S.C. § 282, and this presumption can only be overcome by clear and convincing evidence to the contrary." Bristol-Myers Squibb Co. v. Ben Venue Labs., 246 F.3d 1368, 1374 (Fed. Cir. 2001) (citations omitted). The party asserting invalidity bears the burden of establishing it. 35 U.S.C. § 282. "This burden is especially difficult when . . . the infringer attempts to rely on prior art that was before the patent examiner during prosecution." Glaxo Group Ltd. v. Apotex, Inc., 376 F.3d 1339, 1348 (Fed. Cir. 2004) (quotation omitted).

To patent an invention, the subject matter must be non-obvious:

> A patent may not be obtained . . . if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

35 U.S.C. § 103(a).

The Federal Circuit has set forth these basic principles to guide the determination of obviousness:

> Obviousness is ultimately a question of law, based on underlying factual determinations. The factual determinations that form the basis of the legal conclusion of obviousness include (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) evidence of secondary factors, known as objective indicia of non-obviousness.

Altana Pharma AG v. Teva Pharms. USA, Inc., 566 F.3d 999, 1007 (Fed. Cir. 2009) (citations omitted).

ANALYSIS

I. Defendants' motion for summary judgment

The '634 patent contains 10 claims. Only claims 1-8 are at issue in the instant litigation, as they are directed to treatment methods involving the active ingredient in Boniva®. Claims 9 and 10 are directed to treatment methods involving a different pharmaceutical compound, risedronic acid. Claims 1-8 are:

> 1. A method for treating or inhibiting postmenopausal osteoporosis in a postmenopausal woman in need of treatment or inhibition of postmenopausal osteoporosis by administration of a pharmaceutically acceptable salt of ibandronic acid, comprising: (a) commencing the administration of the pharmaceutically acceptable salt of ibandronic acid by orally administering to the postmenopausal woman, on a single day, a first dose in the form of a tablet, wherein the tablet comprises an amount of the pharmaceutically acceptable salt of ibandronic acid that is equivalent to about 150 mg of ibandronic acid; and (b) continuing the administration by orally administering, once monthly on a single day, a tablet comprising an amount of the pharmaceutically acceptable salt of ibandronic acid that is equivalent to about 150 mg of ibandronic acid.
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> 2. The method of claim 1, wherein the pharmaceutically acceptable salt is a sodium salt of ibandronic acid.

3. The method of claim 2 wherein the pharmaceutically acceptable sodium salt is a monosodium salt of ibandronic acid.

4. The method of claim 3 wherein the pharmaceutically acceptable monosodium salt of ibandronic acid is a monohydrate.

5. A method for treating or inhibiting postmenopausal osteoporosis in a postmenopausal woman in need of treatment or inhibition of postmenopausal osteoporosis by administration of a pharmaceutically acceptable salt of ibandronic acid, consisting essentially of orally administering to the postmenopausal woman, once monthly on a single day, a tablet comprising an amount of the pharmaceutically acceptable salt of ibandronic acid that is equivalent to about 150 mg of ibandronic acid.

6. The method of claim 5, wherein the pharmaceutically acceptable salt is a sodium salt of ibandronic acid.

7. The method of claim 6 wherein the pharmaceutically acceptable sodium salt is a monosodium salt of ibandronic acid.

8. The method of claim 7 wherein the pharmaceutically acceptable monosodium salt of ibandronic acid is a monohydrate.

Defendants have moved for summary judgment on their affirmative defense to infringement that claims 1-8 of the '634 patent are invalid due to obviousness.[1] In brief, Defendants argue that a group of prior art references, viewed together, render the subject matter of the '634 patent obvious to the skilled artisan. Defendants contend that this evidence is sufficient to justify the legal conclusion that the '634 patent is obvious in view of the prior art, and that it is sufficient to show that "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject

[1] For convenience, this Opinion may at times refer to the questions of invalidity or obviousness of the '634 patent, without including a qualifying phrase that specifies claims 1-8. It should be understood that only the validity of claims 1-8 is presently before this Court in this litigation. No statements in this Opinion should be understood to involve claims 9 and 10.

matter pertains." 35 U.S.C. § 103(a).

Defendants point to, *inter alia*, the following prior art references: Lunar News Spring 1999, Ravn 1996, United States Patent No. 6,432,932 ("Daifotis '932"), United States Patent No. 6,143,326 ("Möckel '326"), Riis 2001, United States Patent Application No. 2003/0118634 ("Schofield"), U.S. Patent 6,468,559 ("Chen '559"), Krause 2001, and U.S. Patent No. 5,616,560 ("Geddes '560"). This Court will begin by describing and making preliminary observations about these references, and then turn to the parties' arguments.

Defendants point to the article titled "Update: Bisphosphonates" in the Spring 1999 issue of "Lunar News" ("Lunar News Spring 1999"). A paragraph in the article begins: "Researchers are seeking solutions for better compliance. . ." and describes one dosing regimen using alendronate. (PI-2-APP-09654.) The article then states:

> Another approach is to use bisphosphonates with high potency yet low irritability, such as zolendronate (Novartis) and ibandronate (Roche) [29, 30]. Oral agents could be given intermittently (once/month, for example) and still be quite potent. The projected mode for ibandronate is injection once every three months. . .

(Id.) Roche posits a reading of these sentences that is distorted and implausible, essentially ignoring the sentence about oral agents being given once per month. Roche contends that, as to ibandronate, the reference discloses only a treatment in which it is injected once every three months. This interpretation might make sense if zolendronate was an oral agent and ibandronate was administered only by injection, but this does not appear to be the case: the '814 patent on ibandronate, issued in 1990, discloses both therapeutic use for the treatment of osteoporosis as well as oral administration in tablet form. '814 patent col.1 ll.30-35, col.6 ll.12-16. Roche does not argue that the skilled artisan in 1999 would not have understood that ibandronate could be

used as an oral agent. Roche's attempt to deny that the "Lunar News" reference disclosed oral administration of ibandronate on a once-monthly basis is unpersuasive. Furthermore, the article teaches that this monthly dosing regimen, despite its intermittent nature, could be potent.

The "Lunar News" article teaches the combination of two of the three key elements of the treatment method presently at issue: 1) oral administration of ibandronate[2] 2) once monthly, for the treatment of osteoporosis. The only key element of the patented methods that is not disclosed in this reference is the 150 mg dose.

Defendants also point to the 1996 research report by Ravn et al. in the journal, "Bone" ("Ravn 1996"). (PI-2-APP-10007-13.) The article describes a "dose finding study" of the effect of ibandronate on women with postmenopausal osteoporosis. (PI-2-APP-10007.) In the experimental groups, patients were administered daily doses in a range of .25 through 5 mg for twelve months. (PI-2-APP-10008.) The study concluded that the 2.5 mg daily dose was the most effective, but that positive outcomes were found in both the 2.5 mg and 5 mg groups. (PI-2-APP-10007, -10012.)

Defendants point as well to the research report by Riis et al. published in 2001 in the "Journal of Bone and Mineral Research," entitled, "Ibandronate: A Comparison of Oral Daily Dosing Versus Intermittent Dosing in Postmenopausal Osteoporosis" ("Riis 2001"). (PI-2-APP-10026-10033). The discussion section in this reference states: "preclinical data with ibandronate provided evidence that a total dose administered over a defined period provides equivalent

[2] No party has asserted that the chemical differences between the various descriptions of the form of ibandronate administered – ibandronate, ibandronate sodium, ibandronic acid, or salt of ibandronic acid – are material to this dispute, nor that the skilled artisan would find such differences material in terms of the issues at hand.

results irrespective of the dosing schedule, providing that the dose used is efficacious."[3] (PI-2-APP-10030). The study concluded that "intermittent ibandronate is as effective as the continuous treatment . . ." (PI-2-APP-10032).

Defendants observe that combining the teaching of the total dose concept from Riis 2001 with the findings of Ravn 1996 leads to two answers to the question of what would be an effective dose for once-monthly administration of oral ibandronate: multiplying the two daily doses found to be effective in the Ravn study by 30 yields monthly doses of 75 mg and 150 mg. Defendants also point to United States Patent No. 6,432,932 ("Daifotis '932"), applied for in 1999, directed to inhibiting bone resorption in mammals by oral treatment with a bisphosphonate using dosing regimens of once every week or once every two weeks. Daifotis '932 col.1 ll.16-24. The patent teaches that certain bisphosphonates, including ibandronate, have "high potency as inhibitors of osteoclastic bone resorption." Id. at col.1 l.60. The patent discloses that bisphosphonates are known for causing adverse gastrointestinal side effects, associated particularly with treatment methods using daily dosing. Id. at col.2 ll.24-26, 65-67. The patent teaches that other treatment methods utilize "a cyclic regimen of treatment and rest periods." Id. at col.2 ll.59-60. It further states:

> In the present invention, it is found that the adverse gastrointestinal effects that can be associated with daily or cyclic dosing regimens can be minimized by administering the bisphosphonate at a relatively high unit dosage according to a continuous schedule having a dosing interval selected from the group consisting of once-weekly dosing, twice-weekly dosing, biweekly dosing, and twice-monthly dosing. In other words, it is found that the administration of a bisphosphonate at a high relative dosage at a low relative dosing frequency causes less adverse gastrointestinal effects, particularly esophageal effects, compared to the administration of a low relative dosage at a high relative dosing frequency. This

[3] This is referred to as the "total dose concept."

> result is surprising in view of the teachings suggesting that adverse gastrointestinal effects would be expected to increase as a function of increasing bisphosphonate dosage.

Id. at col.3 l.58-col.4 l.6. The patent also teaches a treatment method involving weekly dosing of ibandronate:

> For once-weekly dosing, an oral unit dosage comprises from about 7 mg to about 100 mg of the ibandronate compound, on an ibandronic acid active weight basis, i.e. calculated on the basis of the corresponding acid. Examples of weekly oral dosages include a unit dosage which is useful for inhibiting bone resorption, and treating and preventing osteoporosis selected from the group consisting of 35 mg, 40 mg, 45 mg, or 50 mg.

Id. at col.13 ll.39-46. Thus, Daifotis '932 teaches that a once-weekly dose of ibandronate in the amount of 35 mg, 40 mg, 45 mg, or 50 mg is useful for inhibiting bone resorption. The skilled artisan would likely observe that 35 mg per week corresponds to 5 mg per day, which coincides with Ravn's finding that 5 mg/day was an effective dose. Applying the total dose concept, this points to a once-monthly dose of 150 mg. Applying the total dose concept, the other weekly doses recommended by Daifotis would be equivalent to once-monthly doses of approximately 171 mg, 193 mg, and 214 mg.

Defendants also point to United States Patent No. 6,143,326 ("Möckel '326"), issued on November 7, 2000, which discloses the use of oral ibandronate to treat osteoporosis, and teaches that a single dose of ibandronate should be in the range of .1 mg to 250 mg. Möckel '326 col.1 ll.10-21, col.5 ll.7-11.

Defendants also point to the United States Patent Application No. 2003/0118634 ("Schofield"), descended from a provisional application filed on December 21, 2001. The Schofield reference teaches a method of treating osteoporosis consisting of administering a

loading dose of a bisphosphonate, followed by a maintenance dose. (PI-2-APP-09645 at ¶ 0018.) The application states that, during the maintenance period, "a bisphosphonate must be given at least once every three months." (Id. at ¶ 0023.) The reference lists possible dosing frequencies, including once monthly. (Id.) It teaches that ibandronate is a preferred bisposphonate. (Id. at ¶ 0029.) Significantly, Schofield states:

> The oral unit dosage forms of the bone-active phosphonate for the maintenance dose preferably contains from about 2.5 to about 15 mg per day from about 5 to about 10.[4] . . . Equivalent doses can be given every other day, twice a week, weekly, biweekly or monthly.

(Id. at ¶ 0037.) Like Riis 2001, this expresses the total dose concept: one may treat osteoporosis by administering a particular amount of bisphosphonate as a daily dose, or one may administer the proportionately equivalent amount intermittently (monthly, for instance).[5]

The parties do not dispute that the Schofield reference – like all of these references – was before the examiner during prosecution of both patents, nor that the patentee overcame an obviousness rejection in view of Schofield during the prosecution of U.S. Patent No. 7,410,957, a sibling patent to the patent in suit. The rejection was overcome by amending the claim language to exclude use of a loading dose. Despite the fact that the patentee was able to

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[4] The wording of this sentence in the patent application is confusing. From the surrounding sentences, it appears likely that the word "preferably" was omitted, and that the sentence was intended to express a preference for a range of about 5 mg to about 10 mg per day.

[5] At oral argument, Roche argued that this Court had erred in its analysis of Schofield in the preliminary injunction Opinion of March 14, 2012. Roche contended that there was no evidence that the skilled artisan would have understood Schofield to teach specific ibandronate dosages. The Court acknowledges the ambiguity in Schofield that provides the opening for this argument. Whether or not Roche is correct on this point, Schofield clearly teaches the total dose concept for bisphosphonates, and it clearly teaches maintenance treatment of osteoporosis using once monthly oral doses of ibandronate.

overcome the obviousness rejection, it seems to this Court that Schofield's treatment method for the maintenance period is very, very close to the treatment method at issue. Schofield discloses that one can maintain osteoporosis treatment by administering once-monthly doses of ibandronate which are equivalent to daily doses in the range of 5 mg to 10 mg.[6] As noted above, the 150 mg once-monthly dose is equivalent to a daily dose of 5 mg.

The Chen '559 patent is directed to an oral dosage form of bisphosphonates useful in the treatment of, *inter alia*, osteoporosis. Chen '559 abstract. The specification discloses that one example of such a bisphosphonate is ibandronic acid (Chen '559 col.6 l.66), and that the invention has the following utility:

> It should be emphasized, however, that because the present dosage forms provide for substantially improved drug absorption relative to conventional formulations, it may not be necessary to administer the drug more than once every two to twelve weeks. Thus, in a preferred embodiment, a dosage form of the invention is administered to a patient every two weeks, preferably once a month, more preferably once every six weeks, most preferably every two months, and optimally every twelve weeks.

Chen '559 col.21 ll.42-50. Chen '559 thus discloses the use of oral administration of ibandronic acid, once monthly, to treat osteoporosis.

Krause 2001 is an article from the December 17, 2001 issue of the periodical "Chemical Market Reporter." Discussing new developments in the marketing of bisphosphonates for the treatment of osteoporosis, the article states:

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[6] As noted in the preceding footnote, Roche contends that this reading of Schofield is incorrect. Even if Roche is right, it does not affect this Court's decision, which relies primarily on the specific dosage teachings of Ravn 1996 and Daifotis '932, along with the total dose concept from Riis 2001. These references by themselves are sufficient to render obvious the choice of a 150 mg dose for a once-monthly ibandronate regimen for the treatment of osteoporosis. One could drop Schofield from consideration entirely and arrive at the same conclusion.

> Roche is expected to file ibandronate in a once-daily formulation . . . say analysts. More competitive formulations, an oral once-monthly and a quarterly IV, may be filed in 2003, with a 2004 launch.

(PI-2-APP-09650.) Krause 2001 thus discloses the use of oral administration of ibandronate, once monthly, to treat osteoporosis.

The Geddes '560 patent is directed to a method of treating osteoporosis which has a parathyroid hormone administration component and a bisphosphonate administration component. Geddes '560 abstract. As to the bisphosphonate component, the patent teaches that the bisphosphonate must be administered on at least one day out of every thirty-day treatment period. Id.

As the moving party with the burden of proof at trial of the affirmative defense to infringement of patent invalidity due to obviousness, Defendants have carried their initial summary judgment burden. Defendants have pointed to prior art that supports the conclusion that "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. § 103(a). The burden then shifts to Plaintiffs, who must show that a genuine issue as to a material fact exists, precluding the entry of judgment as a matter of law.

A. The Graham factual inquiries: the scope and content of the prior art

Plaintiffs first contend that "a threshold fact in dispute is whether a POSA on May 10, 2002 would have even looked to ibandronate at all in devising any osteoporosis therapy." (Pls.' Opp. Br. 10.) Plaintiffs assert that "[b]efore May 10, 2002, the art reported that ibandronate used in the treatment of postmenopausal osteoporosis was a failure." (CSOF ¶ 208.) The evidence

Plaintiffs point to in support of this statement, however, shows that it is inaccurate. In support of this assertion, Roche offers four expert reports and a citation to one prior art study, Schnitzer 2001.

Roche's own experts paint a far more nuanced picture of the art's view of ibandronate as of the critical date. The report of Roche's own expert, Dr. Bilezekian, gives this assessment of the prior art as of May 10, 2002:

> 120. Prior to May 10, 2002, the only antifracture data that was published for ibandronate (Recker) showed that ibandronate failed to reduce incidence of fracture. There was no published data on antifracture efficacy of any oral ibandronate regimen prior to May 10, 2002.
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> 121. Published data for ibandronate prior to May 10, 2002 showed increases in bone mineral density (BMD) for both oral and IV administrations. See Ravn 1996, Thiebaud 1997, Recker 2000, and Riis 2001. However, the failed IV study by Recker taught that ibandronate was not as potent as had previously been thought. As I explained at my deposition, the thinking in the art was that the IV ibandronate study failed because (1) the dose was too low, or (2) the dose-free interval was too long, or (3) the drug ibandronate was not going to work at all.

(Bilezekian Resp. Rpt.) Dr. Daifotis confirms Dr. Bilezekian's view of how the art viewed the results of the Recker study. (Daifotis Supp. Rpt. ¶ 155.) Dr. Daifotis concedes that the Recker study showed that intravenous ibandronate was effective in increasing bone mineral density. (Id.) The cited report statements by Drs. Harris and Russell add nothing new or conflicting. (Harris Resp. Rpt. ¶ 90, Russell Resp. Rpt. ¶ 102.)

Roche's experts provide a consistent picture of what published research studies on ibandronate had shown as of the critical date. Studies had found that both oral and intravenous ibandronate were effective in increasing bone mineral density. One large study – Recker 2000 – showed that intravenous ibandronate did not produce statistically significant antifracture effects,

despite being effective in increasing bone mineral density.[7] This does not support Roche's claim that ibandronate was known in the art to be a failure for the treatment of osteoporosis. The most that can be said is that ibandronate at that time had not shown statistically significant antifracture efficacy, and that a major study of intravenous treatment had not shown statistically significant antifracture efficacy.

Roche does not explain – nor does this Court perceive – how or why the failure to demonstrate statistically significant antifracture efficacy is relevant to the present motion. The claims of the '634 patent say nothing about fractures or antifracture efficacy. The claims are

[7] It is worth noting that the abstract of the Recker study originally published in "Osteoporosis" was titled "Quarterly injections of ibandronate reduce the risk of fractures in women with postmenopausal osteoporosis." (Harris Decl. Ex. J.) The abstract does not otherwise disclose the results of the study. A detailed presentation of the study was published in 2004 with the title, "Insufficiently dosed intravenous ibandronate injections are associated with suboptimal antifracture efficacy in postmenopausal osteoporosis." (Harris Decl. Ex. XX.) The article reports that the intravenous ibandronate treatment did reduce the incidence of fractures, though not to the point that the reduction achieved statistical significance. (Id.) Rather than admitting failure or defeat, the article concluded that the doses used had been too low, and that use of the same method but with higher doses would result in success in terms of antifracture efficacy. (Id.) In 2001, Black reported that Recker presented his research results at the World Congress on Osteoporosis in Chicago in 2000, and Black described the major points Recker presented there. (Hinchen Decl. Ex. 27.) Reporting on Recker's study, Black states: "the reduction in vertebral fractures (about 25%) was not statistically significant. It has been speculated that a higher dose might have suppressed bone remodeling for a longer time and might have been more effective in reducing fracture risk." (Id. at OR 017849.) This provides a basis to believe that Recker's study results would not, as Roche contends, have discouraged investigation into using ibandronate to treat osteoporosis. This report by Black in 2001, based on Recker's conference presentation in 2000, suggests that the skilled artisan would not have viewed the antifracture results of the Recker study as a failure of intermittent ibandronate dosing to produce antifracture effects. Rather, Black appears to have viewed the study as demonstrating some antifracture efficacy, with the expectation that increasing the dose – not shortening the dosing interval – would have improved such efficacy. Because this Court concludes that the issue of antifracture efficacy is not material to the instant obviousness inquiry, these factual questions do not preclude the entry of judgment as a matter of law.

directed to a method for treating or inhibiting postmenopausal osteoporosis.[8] The specification does discuss antifracture efficacy, stating:

> Prior to the completion of the ibandronate clinical development program, no bisphosphonate had prospectively demonstrated fracture reduction efficacy with a drug-free interval beyond daily administration. In summary, it is quite unexpected that fracture reduction benefit can be derived from a monthly administration of an oral bisphosphonate with a single or multiple tablet administration scheme.

'634 patent col.2 l.63-col.3 l.3. The patent does not otherwise refer to antifracture efficacy. In view of the fact that the applicants did not claim antifracture efficacy as a component of their invention, the evidence as to the content of the prior art regarding the antifracture efficacy of ibandronate is not material to this inquiry.[9] Indeed, at oral argument, Roche conceded that one did not need to demonstrate FDA approvability – which, Roche has argued, hinged on proof of antifracture efficacy – to demonstrate the enablement of the invention.

Plaintiffs contend that Schnitzer 2001 teaches away from the claimed invention. There are a number of problems with Plaintiffs' position. First, Schnitzer 2001 deals with a study of alendronate, not ibandronate.[10] (PI-2-APP-09668.) More significantly, however, Plaintiffs

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[8] The Court conducted claim construction on claims 1 and 5, and no issues regarding antifracture efficacy were raised. (See Joint Claim Construction and Prehearing Statement Under L.Pat.R.4.3.)

[9] Thus, even if it is true that the FDA published guidelines requiring evidence of antifracture efficacy for approval of any treatment of postmenopausal osteoporosis, the patent does not claim compliance with FDA requirements and they are not relevant to this inquiry.

[10] Plaintiffs' position on the use of references dealing with other bisphosphonates is inconsistent. On page 5 of the opposition brief, Plaintiffs rely on the Schnitzer 2001 study of alendronate, arguing that it teaches away from once-monthly ibandronate dosing. But on page 29 of the opposition brief, Plaintiffs object to Defendants' reliance on the Schnitzer 2000 study of alendronate, and state: "one cannot generalize from one specific example to what might hold true for other doses at other dosing intervals of other specific bisphosphonates." Plaintiffs do not explain why this objection is not equally valid with regard to Schnitzer 2001.

mischaracterize what Schnitzer 2001 teaches in regard to once-monthly dosing. The reference discusses the research results that show that intravenous administration of alendronate once every three months produces increases in bone mineral density, and that similar results have been obtained with other bisphosphonates. (PI-2-APP-09668.) The article states:

> While these studies show that dosing less frequently than daily can produce increases in BMD, there is evidence that the desired reductions in bone turnover are not maintained if dosing intervals are longer than 1 or 2 weeks. . . This may partly explain why no decrease in fracture risk was seen in a trial of intermittent ibandronate, despite a modest increase in BMD.
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> . . .
>
> A trial of intermittent closing with iv. ibandronate failed to demonstrate a significant reduction in fracture risk despite modest increases in BMD. Levels of biochemical markers of bone turnover tended to rise between ibandronate doses, which were given once every 3 months. These findings suggest that continuous suppression of bone turnover may be necessary to reduce fracture risk. Thus, it appears that alendronate should be given at least about once a week to maintain beneficial suppression of bone turnover and optimal increases in bone density.

(PI-2-APP-09669, 09671.) A citation indicates that the trial referenced here is Recker's study of quarterly intravenous dosing with ibandronate. Schnitzer 2001 appears to accurately and fairly portray the scientific evidence at the time: intravenous quarterly dosing with both alendronate and ibandronate produced increases in bone mineral density, but the Recker study of intravenous ibandronate did not show statistically significant antifracture efficacy.

This Court takes judicial notice of the fact that Schnitzer 2001 was published in September of 2001[11] and that Riis 2001 was published on October 1, 2001.[12] Thus, to whatever

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[11] See "Expert Opinion on Pharmacotherapy: Volume 2, Number 9 (September 2001)," http://informahealthcare.com/toc/eop/2/9 (last visited May 2, 2012).

[12] See "Journal of Bone and Mineral Research: Volume 16 Issue 10 (October 2001)," http://www.jbmr.org/details/issue/503657/Volume_16_Issue_10_October_2001.html?page=2

extent the skilled artisan might have read Schnitzer 2001 as teaching away from the invention at issue, on October 1, 2001, with the publication of Riis 2001, the game changed. As stated by Dr. Bauss, the applicant from whom the "Bauss patent" gets its name, Riis's study was a highly influential "breakthrough:"

> Q: So after Riis would show that the interval could extend to 9 weeks, the drug-free interval could extend to 9 weeks, was the concern over the lifespan of the osteoclast being 2 weeks, was that a concern anymore when it came to intermittent dosing schedules?
>
> A: To my knowledge, it was the first time it has been proven. It was a success, a breakthrough in bone metabolism. It was the basis of my invention, but a lot of other things have to be considered.
>
> . . .
>
> Q: If someone was trying to come up with a dosing regimen for a bisphosphonate with an intermittent dosing regimen, would they have had any reason to be concerned about the 2-week osteoclast lifespan after Riis?
>
> A: For the osteoclast, not.

(Hinchen Dec. II Ex. 81 41:15-42:4, 43:2-10.) Dr. Bauss himself thus makes absolutely clear that Riis 2001 persuasively refuted the osteoclast life cycle theory, and openly states that he based his work on the discovery by Riis. Dr. Bauss thus clearly states that Riis 2001 was a breakthrough that led him to reject the idea that dosing must be biweekly or more frequently. The skilled artisan would have understood Riis 2001 to have superceded the views about intermittent dosing with ibandronate expressed in Schnitzer 2001. See Graham v. John Deere Co. of Kan. City, 383 U.S. 1, 36 (1966) (following publication of a critical piece of prior art, "unsuccessful attempts to reach a solution . . . made before that time became wholly irrelevant.")

(last visited May 2, 2012).

It is on this basis that this Court rejects Roche's argument that the claimed invention is nonobvious because Schnitzer 2001 taught away it.[13]

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[13] Although this Court concludes that Dr. Bauss's testimony about Riis 2001 is sufficient to defeat Roche's argument that the claimed invention is nonobvious because of the teaching away of Schnitzer 2001, it offers the following analysis as an alternative approach. Plaintiffs' contention that Schnitzer 2001 teaches away from the claimed invention must be viewed in the context of Federal Circuit law, which does not support Plaintiffs' understanding of teaching away:

> A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. A reference does not teach away, however, if it merely expresses a general preference for an alternative invention but does not criticize, discredit, or otherwise discourage investigation into the invention claimed.

Depuy Spine, Inc. v. Medtronic Sofamor Danek, Inc., 567 F.3d 1314, 1327 (Fed. Cir. 2009) (citations omitted). Schnitzer 2001 clearly expresses a preference for weekly oral dosing with alendronate and views it as superior. It also states that intravenous quarterly administration of ibandronate increases bone mineral density but does not reduce fracture risk, and it speculates that dosing intervals may need to be two weeks or less.

The closest Schnitzer comes to discouraging once-monthly oral dosing is the statement that "there is evidence that the desired reductions in bone turnover are not maintained if dosing intervals are longer than 1 or 2 weeks." (PI-2-APP-09669.) This has been termed the "osteoclast life cycle theory," because it relies on the idea that the life cycle of an osteoclast is about 2 weeks. Schnitzer 2001 is the one reference offered by Plaintiffs that might, at first glance, appear to teach away from the subject matter of the '634 patent. Careful examination does not support this initial impression because, rather than teach away from a once-monthly 150 mg dose, Schnitzer 2001 asserts the inferiority of a combination already in the prior art. There are two aspects of this to discuss: 1) the question of the combination at issue; and 2) statements of inferiority.

The first point is that, to the extent that Schnitzer criticizes something related to the patent at issue, what it criticizes specifically is a prior art combination that existed as of the critical date: quarterly intravenous dosing with ibandronate. The broadest view of the criticism in Schnitzer 2001 is, as Plaintiffs contend, that it criticizes intermittent bisphosphonate dosing at intervals beyond two weeks. It is quite clear that this combination is in the prior art, since Schnitzer expressly discusses Recker's study of quarterly intravenous dosing with ibandronate. Schnitzer 2001 says nothing about the dosage amount to be used in a regimen of intermittent bisphosphonate dosing at intervals of two weeks or longer.

This Court's overall obviousness analysis holds that the combination of prior art references that would produce the subject matter of the invention at issue can be summarized as follows, using an algebraic metaphor:

> [treatment of osteoporosis via monthly oral dosing with ibandronate, Lunar News Spring 1999] + [150 mg once-monthly dosage] = [subject matter of claims of '634 patent at issue]
>
> [therapeutic efficacy of 2.5 mg and 5 mg daily ibandronate doses, Ravn 1996] + [total dose concept, Riis 2001] = [75mg, 150 mg once-monthly dosages]

The point of this analysis is that, viewing the criticism in Schnitzer 2001 in the broadest way, it does not target either of these combinations that could have produced the subject matter at issue. Rather, it targets a combination that already existed in the art. What the patentees in this case did is that they took an existing "device" – treatment of osteoporosis via monthly oral dosing with ibandronate – and they improved it. They improved it by finding a dosage that gave superior results. Schnitzer 2001 merely observes the inferiority of the existing device. Certainly, it could be argued that Schnitzer speculates that the device cannot be improved, but the reference does not deal at all with the specific combinations, represented above, that could result in the subject matter at issue. Had Schnitzer, for example, discredited the Ravn 1996 study, or attacked the total dose concept, those criticisms might have been germane to the combinations that resulted in the improvement. Schnitzer 2001 cannot be understood to make such criticisms, criticisms that would truly teach away from finding what the patentees found that was new: the 150 mg once-monthly dose.

The second point is that, to the extent that Schnitzer makes criticisms, they are statements of the inferiority of the prior art. The key case to distinguish statements of inferiority from statements which teach away is In re Fulton, 391 F.3d 1195, 1200 (Fed. Cir. 2004), which states:

> Appellants first argue that the Board's finding of a motivation to combine lacks substantial evidence because the Board failed to demonstrate that the characteristics disclosed in Pope, hexagonal surfaces in a facing orientation, are preferred over other alternatives disclosed in the prior art. This argument fails because our case law does not require that a particular combination must be the preferred, or the most desirable, combination described in the prior art in order to provide motivation for the current invention. "The question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination," not whether there is something in the prior art as a whole to suggest that the combination is the most desirable combination available. *See In re Beattie*, 974 F.2d at 1311 (internal quotation omitted; emphasis added.) A case on point is *In re Gurley*, 27 F.3d 551, 552-53 (Fed. Cir. 1994), in which we upheld the Board's decision to reject, on

> obviousness grounds, the claims of a patent application directed to one of two alternative resins disclosed in a prior art reference, even though the reference described the resin claimed by Gurley as "inferior." Far from requiring that a disclosed combination be preferred in the prior art in order to be motivating, this court has held that "[a] known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use" and the reference "teaches that epoxy is usable and has been used for Gurley's purpose." *Id.* Thus, a finding that the prior art as a whole suggests the desirability of a particular combination need not be supported by a finding that the prior art suggests that the combination claimed by the patent applicant is the preferred, or most desirable, combination.

Fulton's discussion of In re Gurley is entirely on point, especially the quote from Gurley that a "known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994). This accurately applies to Plaintiffs' contention about Schnitzer 2001: Plaintiffs' position is tantamount to the argument that the prior art combination of a once-monthly oral ibandronate treatment of osteoporosis became patentable simply because Schnitzer described it as somewhat inferior for treating osteoporosis to a weekly alendronate regimen. In both Gurley and Fulton, the Federal Circuit firmly rejected that argument.

The facts of Gurley are quite analogous to those in the instant case. Gurley sought to patent an epoxy-based printed circuit board, but the Yamaguchi reference taught that epoxy was an inferior material for making printed circuit boards. The Federal Circuit held that Yamaguchi did not teach away from subject matter of the patent at issue:

> The facts in Gurley's record are that this use of epoxy was known, the structure of these circuit boards was known, and epoxy had been used for Gurley's purpose. We share Gurley's view that a person seeking to improve the art of flexible circuit boards, on learning from Yamaguchi that epoxy was inferior to polyester-imide resins, might well be led to search beyond epoxy for improved products. However, Yamaguchi also teaches that epoxy is usable and has been used for Gurley's purpose. The Board recognized Yamaguchi's teaching of the deficiencies of epoxy-impregnated material, but observed that Gurley did not distinguish his epoxy product from the product described by Yamaguchi. On the facts of this case, Gurley's "teaching away" argument was insufficient to establish patentability. Gurley did not offer specific epoxies, or improved properties, and we are not presented with the question of whether any such products might meet the requirements of patent-ability.

Gurley, 27 F.3d at 553. The same reasoning applies to the analogous facts of the instant case, the Schnitzer reference's implication that a once-monthly dosing interval would likely be inferior to

a weekly one.

A key distinction that appears in the Federal Circuit's jurisprudence on teaching away concerns a combination which is inferior versus one that is inoperative. See In re Icon Health & Fitness, Inc., 496 F.3d 1374, 1382 (Fed. Cir. 2007); see also Syntex (U.S.A.) LLC v. Apotex, Inc., 407 F.3d 1371, 1380 (Fed. Cir. 2005) (citing Gurley in holding: "Under the proper legal standard, a reference will teach away when it suggests that the developments flowing from its disclosures are unlikely to produce the objective of the applicant's invention.") The prior art showed that the intravenous quarterly ibandronate regimen was inferior as a treatment (compared to weekly oral alendronate, for example), but not that it was inoperative for the purpose of treating osteoporosis. Thus, Schnitzer can be read as having disclosed the expectation, based on the osteoclast life cycle theory, that regimens with intervals longer than two weeks would be similarly inferior – but not inoperative.

"Stated another way, the prior art as a whole must 'suggest the desirability' of the combination." Fulton, 391 F.3d at 1200. The prior art does not have to suggest that "the combination claimed by the patent applicant is the preferred, or most desirable, combination." Id. The prior art, as a whole, does suggest the desirability of once-monthly ibandronate treatment for osteoporosis. It need not suggest that it is the most desirable regimen.

The Federal Circuit has held: "in general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." Gurley, 27 F.3d at 553. The intrinsic evidence shows that the applicants sought the result of treating bone resorption disorder, specifically osteoporosis. The applicants described their invention as "a method of treating disorder characterized by pathologically increased bone resorption," as stated in the '634 abstract, or as a "method for treating or inhibiting postmenopausal osteoporosis in a postmenopausal woman in need of treatment or inhibition of postmenopausal osteoporosis," as stated in independent claims 1 and 5. The evidence thus supports only the inference that the result sought by the applicants for the '634 patent was the treatment or inhibition of osteoporosis. The prior art did not suggest that once-monthly oral ibandronate treatment would not produce this result – but, rather, that it might not do it as well as some regimens with shorter dosing intervals.

The criticisms of the prior art in Schnitzer 2001 do not fall within the scope of the Federal Circuit's definition of statements which teach away from the subject matter of the patent in suit. This provides an alternative basis to reject Roche's position that the claimed invention is nonobvious because Schnitzer 2001 taught away from it.

This review of the prior art demonstrates that, contrary to Roche's claim that the prior art study of ibandronate to treat osteoporosis as of the critical date showed failure, the evidence is quite clear that the prior art showed ibandronate in general, and oral ibandronate in particular, to be effective in increasing bone mineral density and useful for treating osteoporosis.

B. The Graham factual inquiries: the level of ordinary skill in the art

The parties do not dispute the level of ordinary skill in the art.

C. The Graham factual inquiries: the differences between the claimed invention and the prior art

Plaintiffs first argue that Defendants' prior art citations to monthly dosing neither teach nor suggest the claimed methods. Plaintiffs discuss Chen '559, Lunar News Spring 1999, Krause 2001, and Culverwell 2002.

Plaintiffs contend that Chen '559 teaches away from using tablets. This position borders on frivolous. The notion that Chen '559 should be understood to persuade the skilled artisans in the pharmaceutical industry in 2002 to stop believing that pharmaceuticals can be usefully administered in tablet form is outlandish, and the notion that the breakthrough invention of the '634 patent was a tablet is not credible. Nor does the text of the Chen '559 patent support Plaintiffs' characterization of it. The specification states:

> Although the bisphosphonic acids are therapeutically effective, oral administration of the drugs is problematic, primarily because of adverse gastrointestinal effects, particularly irritation of the esophagus. . .
>
> Although efforts have been made to reduce the adverse gastrointestinal effects of bisphosphonic acids, there is a continuing need for dosage forms containing these active agents wherein undesirable side effects are minimized and patient compliance and thus therapeutic efficacy are improved.

Chen '559 col.1 l.65-col.2 l.16. This does not teach away from using tablets. It simply states

what was well-known: the bisphosphonates tend to produce adverse gastrointestinal effects, which should be minimized to increase patient compliance with treatment.

Chen '559 "does not criticize, discredit, or otherwise discourage investigation into the invention claimed." Depuy Spine, 567 F.3d at 1327. The most that might be reasonably said about Chen '559 is that it expresses a preference for the alternative invention (an enterically coated capsule housing a nonsolid composition of a bisphosphonate), but does not discourage investigation into tablet forms. Plaintiffs have pointed to no part of Chen that criticizes or discredits tablets. Chen '559 does not teach away from tablets. No reasonable trier of fact could read this reference and conclude that Plaintiffs' reading is correct.

This Court has already rejected Plaintiffs' distorted and implausible reading of the Lunar News Spring 1999 reference. Lunar News Spring 1999 does not teach away from oral administration of ibandronate: it advocates it. (PI-2-APP-09654.) No reasonable trier of fact could conclude otherwise.

Plaintiffs attempt to create a factual dispute about Krause 2001, but fail for a number of reasons. The first is that Krause 2001 is not essential to Defendants' case: it is cumulative of Lunar News Spring 1999, disclosing once-monthly oral dosing of ibandronate to treat osteoporosis. Second, Plaintiffs' position depends on introducing a corroboration element into the law of prior art: Plaintiffs argue that "Krause 2001's uncorroborated statements would not have led a POSA to pursue monthly dosing." (Pls.' Opp. Br. 14.) The Supreme Court has distilled the obviousness inquiry as follows: the Court must "determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue." KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 1741 (2007.) The Supreme Court did not require

a solid reason, nor a substantial one, nor a corroborated reason – only an "apparent" one. The apparent reason to combine the elements as disclosed in Krause 2001 is that rumor had it that a major pharmaceutical company might be planning to market a treatment based on the combination. That sounds both apparent and good enough to meet the KSR test.

Culverwell 2002 is unnecessary to Defendants' obviousness case, and so this Court need not reach the dispute over whether this reference was publically accessible before the critical date.

Plaintiffs next argue that combining Daifotis '932 and Lunar News Spring 1999 does not render the claims at issue obvious, on two grounds: 1) Daifotis '932 teaches away from monthly dosing; and 2) the two cannot be combined as their teachings are incompatible. Neither argument is persuasive.

Plaintiffs contend that Daifotis '932 teaches away from monthly dosing "by repeatedly explaining that one cannot dose bisphosphonates with a dose-free interval beyond about 14-16 days." (Pls.' Opp. Br. 18.) There is just one problem: Plaintiffs do not identify where Daifotis '932 explains this, and this Court cannot find such an explanation in that reference. Plaintiffs' brief cites to paragraph 335 in their counter-statement of facts, which repeats the assertion and cites to several statements in reports by experts Daifotis and Bilezikian. Conspicuously absent is any citation to any particular statement in the Daifotis '932 reference itself – by anyone. The cited report statements of Dr. Daifotis do no more than point out the obvious: Daifotis '932 does not teach monthly dosing. (Daifotis Supp. Rpt. ¶¶ 94, 167-169.) Dr. Daifotis does indeed invoke the osteoclast life cycle theory in her report, but does not point to any part of the Daifotis '932 reference which discloses that theory. (Daifotis Supp. Rpt. ¶¶ 167, 169.) The cited statements by

Dr. Bilezekian echo Plaintiffs' assertion of teaching away but do not identify any specific statement in any reference in support. (Bilezikian Resp. Rpt. ¶ 227.)

The Daifotis '932 reference itself is a patent on a method for treating osteoporosis using risedronate in intermittent dosing regimens essentially involving one dose every week or two weeks. Daifotis '932 claim 1. As Plaintiffs state, the patent does not disclose monthly dosing. It does not, however, "criticize, discredit, or otherwise discourage investigation into" monthly dosing. Depuy Spine, 567 F.3d at 1327. Under Federal Circuit law, then, Daifotis '932 does not teach away from monthly dosing.[14] Nor have Plaintiffs shown any genuine factual dispute over the content of this prior art reference.

Plaintiffs next argue that the teachings of Daifotis '932 and Lunar News Spring 1999 are in such conflict that the teachings of the two references could not be combined. This argument rests entirely on Plaintiffs' distorted reading of the two references. Plaintiffs have failed to identify disclosures in the two references which conflict.

Plaintiffs next address a number of other prior art references cited by Defendants, contending that they would not have motivated the skilled artisan to develop monthly oral administration of ibandronate. At the outset, even if Plaintiffs are correct – and they are not –, it is of no moment, since this Court has determined that Lunar News Spring 1999 discloses monthly oral administration of ibandronate. Plaintiffs discuss Schofield, Riis 2001, and Möckel '326.

As to the Schofield reference, Plaintiffs first assert a factual dispute over whether a

[14] If anything, it appears that Daifotis '932 contains teaching which could point toward monthly dosing, as it discusses the osteoporosis treatment method in U.S. Patent No. 5,366,965, which "requires nontreatment periods from 20 to 120 days." Daifotis '932 col.3 ll.44-45.

skilled artisan would believe that the loading dose was optional. There is no dispute that Schofield requires a loading dose. In support, Plaintiffs cite statements made by their expert, Dr. Harris, which observe this fact and make the conclusory assertion, unsupported by analysis, that Schofield would not have motivated any skilled artisan to make any modification of its claimed treatment method. (Harris Resp. Rpt. ¶¶ 146, 155; Harris 2009 Rpt. ¶¶ 263-264.) "Conclusory expert assertions cannot raise triable issues of material fact on summary judgment." Sitrick v. Dreamworks, LLC, 516 F.3d 993, 1001 (Fed. Cir. 2008).

Plaintiffs have failed to show any genuine and material factual dispute over Schofield. The facts are these: 1) Schofield requires a loading dose, and does not teach that the maintenance period may be used without the loading dose; and 2) aside from the dosage amount, there is no meaningful difference between the patented treatment methods at issue and the method employed in Schofield's maintenance period. There are no disputes over these facts. There are disputes over how the Court should use these facts in arriving at its legal conclusion of obviousness, but that is a matter of law.

Furthermore, Plaintiffs concede that "Schofield is silent as to any dosage of ibandronate and is silent as to any dosing absent a loading dose." (Pls.' Opp. Br. 22.) If Schofield is silent about dosing absent a loading dose, it cannot "criticize, discredit, or otherwise discourage investigation into" using the maintenance regimen without the loading dose. Depuy Spine, 567 F.3d at 1327.

Plaintiffs argue that "[a]ny combination with Schofield eviscerates the basic premise of Schofield's loading dose method." (Pls.' Opp. Br. 22.) In support, Plaintiffs cite In re Fritch, 972 F.2d 1260, 1266 n.12 (Fed. Cir. 1992), which states: "This court has previously found a

proposed modification inappropriate for an obviousness inquiry when the modification rendered the prior art reference inoperable for its intended purpose." This is a surprising thing to assert, given that once-monthly Boniva® could never have achieved commercial success had dropping the loading dose rendered the Schofield method inoperable for treating osteoporosis.

Plaintiffs next raise the Riis 2001 reference, but their arguments about Riis 2001 entirely overlook the significance of two key teachings in it. First, it taught the total dose concept: "a total dose administered over a defined period provides equivalent results irrespective of the dosing schedule." (PI-2-APP-10030.) There can no dispute that Riis 2001 teaches this: it is a direct quote. Second, it taught that a daily regimen and an intermittent regimen with a 9-week rest period were equally effective in increasing bone mineral density. As discussed above, Dr. Bauss himself described Riis 2001 as "a breakthrough in bone metabolism" and the basis for his work – which is quite inconsistent with the position that Riis 2001 taught away from what Plaintiffs say Dr. Bauss invented. (Hinchen Dec. II Ex. 81 42:2.) The only evidence offered by Plaintiffs in support of their argument that Riis 2001 teaches away from the methods at issue is unfounded, conclusory assertions by their expert, Dr. Harris. (Harris Dec. Ex.CC 25:24-29:15, 33:14-34:21, 44:7-45:20.)[15] This Court finds no material factual disputes over the content of Riis 2001.

Lastly, Plaintiffs address Möckel '326. Plaintiffs again attempt to find factual disputes

[15] Dr. Harris's observation that Riis 2001 shows that oral ibandronate treatment is associated with diarrhea is consistent with the well-known fact that oral treatment with bisphosphonates causes adverse gastrointestinal effects. Dr. Harris may have had his qualms, but he does not cite any place that Riis 2001 makes statements which "criticize, discredit, or otherwise discourage investigation into" administration of oral ibandronate. Depuy Spine, 567 F.3d at 1327. Rather, it would appear likely that it is because oral administration of ibandronate may cause diarrhea that once-monthly administration improves patient compliance.

over the reference, again based only on the conclusory assertions of their expert, Dr. Harris. Harris 2009 Rpt. ¶¶ 211, 212. The Möckel '326 reference says that a single dose of ibandronate should be in the range of .1 mg to 250 mg. Möckel '326 col.5 ll.7-11. Again, there can no dispute that Möckel '326 teaches this. This Court find no material factual disputes over the content of Möckel '326.

Plaintiffs next argue that Defendants' reliance on the "total dose concept" is misplaced. Plaintiffs contend that dose efficacy says nothing about dose safety, which appears to be correct, but Defendants use the total dose concept only to argue that the amount of a once-monthly dose effective for the treatment of osteoporosis is obvious in view of the prior art. Plaintiffs then object that the total dose concept conflicts with their understanding of human biology. That may be but, nonetheless, there can be no dispute that, as discussed above, Riis 2001 taught the total dose concept. The significance of this concept is that it implies that an effective monthly dose would be an amount that is 30 or 31 times an effective daily dose. There is no dispute that Ravn 1996 teaches that administration of 2.5 mg and 5 mg oral daily ibandronate doses effectively treats osteoporosis. Defendants argue that a skilled artisan, facing the problem the art was facing – how to treat osteoporosis while minimizing gastrointestinal side effects and maximizing patient compliance – would have considered intermittent treatment regimens with bisphosphonates, an approach that was common in the art in 2002. Lunar News Spring 1999 would have suggested treating osteoporosis with a regimen of once-monthly oral administration of ibandronate. The only thing missing, then, is what the once-monthly dose should be. Defendants contend that combining the total dose concept teaching of Riis 2001 with the teaching of Ravn 1996 yields two possible once-monthly doses to try: 75 mg and 150 mg. Plaintiffs object that the fact that

Ravn 1996 found a higher incidence of gastrointestinal side effects with the higher daily dose would have dissuaded the skilled artisan from trying the higher once-monthly dose.

It does seem likely that the skilled artisan would have considered the frequency of gastrointestinal side effects in solving the problem of the amount of the once-monthly oral dose of ibandronate. Yet this fact alone does not suffice to derail Defendants' obviousness case, for two reasons. First, as just noted, combining the findings of Ravn with the other teachings in the art results in only two options to try.

In KSR, 550 U.S. at 416, the Supreme Court held: "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results."[16] In KSR, the Supreme Court changed the law of "obvious to try:"

> The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was '[o]bvious to try.' When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

Id. at 421 (citations omitted). Following KSR, it is possible to prove obviousness by showing that a combination was obvious to try.

In Bayer Schering Pharma AG v. Barr Labs., Inc., 575 F.3d 1341, 1347 (Fed. Cir. 2009), the Federal Circuit clarified the law of "obvious to try:"

> *O'Farrell* observed that most inventions that are obvious were also obvious to try, but found two classes where that rule of thumb did not obtain.

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[16] Similarly, the Court stated: "If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability." Id. at 417.

> First, an invention would not have been obvious to try when the inventor would have had to try all possibilities in a field unreduced by direction of the prior art. When what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful an invention would not have been obvious. This is another way to express the *KSR* prong requiring the field of search to be among a "finite number of identified" solutions. It is also consistent with our interpretation that *KSR* requires the number of options to be "small or easily traversed."
>
> Second, an invention is not obvious to try where vague prior art does not guide an inventor toward a particular solution. A finding of obviousness would not obtain where what was 'obvious to try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. This expresses the same idea as the *KSR* requirement that the identified solutions be 'predictable.'

Id. (citations omitted).

Applying KSR to the instant case leads to the conclusion that demonstrating that it was obvious to try once-monthly oral administration of ibandronate at doses of 75 mg and 150 mg is legally sufficient to prove obviousness. There is no dispute that, in 2002, there was market pressure to solve the problem of finding an osteoporosis treatment with reduced gastrointestinal side effects and improved patient compliance. Based on the reasoning explained above, the combination of Ravn 1996, Lunar News Spring 1996, and Riis 2001 suggests two possible treatments: once-monthly oral administration of ibandronate at doses of 75 mg and 150 mg. The set of these two options contains a finite number of identified solutions.

Furthermore, Daifotis '932 can be viewed as encouraging the use of the higher dosage. The specification states:

> For once-weekly dosing, an oral unit dosage comprises from about 7 mg to about 100 mg of the ibandronate compound, on an ibandronic acid active weight basis,

> i.e. calculated on the basis of the corresponding acid. Examples of weekly oral dosages include a unit dosage which is useful for inhibiting bone resorption, and treating and preventing osteoporosis selected from the group consisting of 35 mg, 40 mg, 45 mg, or 50 mg.

Daifotis '932 col.13 ll.39-46. These weekly doses, using the total dose concept, are the equivalent of daily doses in the range of 5 mg to roughly 7 mg. Thus, of the two daily doses found effective by Ravn 1996, Daifotis '932 encourages the artisan to select the 5 mg daily dose, the equivalent of the 35 mg weekly dose. The prior art gives some direction to the skilled artisan to assist in picking one from the set of two options.

The only remaining question is whether these two options were predictable solutions. The law does not require absolute predictability; "[f]or obviousness under § 103, all that is required is a reasonable expectation of success." In re O'Farrell, 853 F.2d 894, 904 (Fed. Cir. 1988). The question to be answered, then, is whether the skilled artisan, faced with the problem of what dose to choose for an osteoporosis treatment consisting of once-monthly administration of ibandronate, would have a reasonable expectation of success with the 75 mg and 150 mg doses. The evidence shows that there was good reason to expect success[17] with these two

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[17] As Defendants pointed out at oral argument, as to the 150 mg dose, Roche's expert Dr. Harris admitted this when testifying at the preliminary injunction hearing:

> Q. And as of May 6, 2002, without the '957 or the '634 patents but in view of all the other references that came before, would a person of ordinary skill in the art have had a reasonable expectation that a 150 mg dose of ibandronate taken orally would inhibit bone resorption to some degree in postmenopausal women?
>
> A. One would have an expectation for some degree of inhibition for some period of time.

(3/8/12 Hrg. Tr. 113:12-19.)

solutions, because they are straightforward applications of the total dose concept proven by Riis to the research findings of Ravn, and the selection of a once-monthly dose equivalent to the 5 mg daily dose is supported by the recommendation of a 35 mg weekly dose in Daifotis '932. The options of 75 mg and 150 mg doses are not shots in the dark. They are the products of the application of reasoning to empirical research. Applying the standard of a reasonable expectation of success, they are predictable solutions. Thus, pursuant to KSR, the development of the 150 mg once-monthly dose appears to be the product of ordinary skill and common sense, not innovation.

In Bayer, the Federal Circuit explained that predictability, as used in KSR, can be understood in terms of the guidance provided by the prior art toward a particular solution. 575 F.3d at 1347. In the instant case, the prior art provided a substantial amount of guidance toward the 75 mg and 150 mg doses. This provides additional support for the conclusion that these two solutions were predictable, and thus that the patented treatment method was obvious.

Plaintiffs' brief argues that Defendants mislead in asserting that dose-finding is a routine process in pharmaceutical development – but the brief ends up only attempting to confuse the issues. Plaintiffs point to failures in trials with other bisphosphonates – pamidronate and tiludronate – as well as the failure to achieve statistically significant antifracture efficacy with intravenous ibandronate, discussed at length above. Yet Plaintiffs ignore the Federal Circuit's oft-repeated quote: "all that is required is a reasonable expectation of success." O'Farrell, 853 F.2d at 904. Arguments that the skilled artisan would not have been absolutely confident of success with a 150 mg once-monthly dose are fruitless, since the law requires only a reasonable expectation. Pointing to the alleged necessity of proving antifracture efficacy to obtain FDA

approval is also fruitless, since the patent does not expressly claim antifracture efficacy, nor have Plaintiffs even argued that such efficacy is implicit.

The same holds true with regard to Plaintiffs' arguments about safety. Again: all that is required is a reasonable expectation of success, and this applies to finding a safe dose. Möckel '326 teaches that a single dose of ibandronate should be in a range up to 250 mg. Möckel '326 col.5 ll.7-11. Daifotis '932 teaches that, for "human oral compositions," the range of a typical unit dosage goes up to 200 mg. Daifotis '932 col.13 ll.1-6. Schofield teaches that a loading dose of any of a group of bisphosphonates, which includes ibandronate, may be as much as 20 times the maintenance dose, which may be as high as 15 mg per day, yielding a maximum loading dose of 300 mg per day. (PI-2-APP-09645 at ¶¶ 0021, 0037.) These are sufficient to give the skilled artisan a reasonable expectation of safety with a 150 mg dose. They also provide substantial evidence that the art knew of the safety of the 150 mg unit dose in 2002, and Plaintiffs have pointed to no evidence that says otherwise. Plaintiffs point to Dr. Bilezekian's testimony that his institutional review board would never have approved a research study using a 150 mg dose because of safety concerns, but Plaintiffs have confused hypothetical institutional standards with what is required under Federal Circuit law. (Harris. Dec. Ex. Z 335:8-22.) It is quite understandable that Dr. Bilezekian would speculate that his review board might demand a greater guarantee of safety but, again, that is an entirely different matter from what the law requires for obviousness: a reasonable expectation of success. Such evidence does not raise any material factual dispute. The material facts here are that Möckel '326, Daifotis '932, and Schofield all taught that a 150 mg dose of ibandronate could be used to treat osteoporosis in humans. Dr. Bilezekian's qualms appear to be unsupported by evidence of record and, because they are purely

conclusory and unsupported, they do not suffice to raise a factual dispute over whether the skilled artisan would have had a reasonable expectation that the 150 mg dose would be safe for humans.

The prior art disclosed treatment of osteoporosis through once-monthly oral administration of ibandronate. The prior art also pointed to two possible once-monthly dosages, and it predicted that successful results would be obtained with them, which the applicants "merely had to verify through routine testing." Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1367 (Fed. Cir. 2007). While such verification is scientifically valuable, the results are not patentable under the law.

D. The Graham factual inquiries: objective considerations

Plaintiffs first point to evidence that Boniva® has been commercially successful, which is undisputed: Dr. Vellturo stated that Roche realized $169.7 million in net sales in the first six months of 2011. (Vellturo Resp. Rpt. ¶ 12.) Plaintiffs argue that Boniva® has been a commercial success because of, *inter alia*, the 150 mg once-monthly dosing regimen covered by the patent at issue. In this case, however, this Court does not find this commercial success to have much value as an indicator of nonobviousness.

The Federal Circuit has held commercial success to be of "minimal probative value on the issue of obviousness" when a patent not at issue blocks people from competing with the patentee in the marketplace. Merck & Co. v. Teva Pharms. USA, Inc., 395 F.3d 1364, 1376 (Fed. Cir. 2005). On this matter, the facts of Merck are on all fours with this case. The patent at issue in that case disclosed a method of treating osteoporosis by weekly dosing with the bisphosphonate, alendronate. Id. at 1366. The patentee held another patent on the use of alendronate to treat osteoporosis (and was also protected by a grant of exclusivity pursuant to 21

U.S.C. 355). Id. at 1377. The Federal Circuit found the two patent claims at issue to be obvious in view of two "Lunar News" articles, and held that the district court had erred both in the way that it had differentiated the subject matter of the invention from the prior art references, and in how it had weighed the secondary consideration evidence of commercial success. Id. at 1375-77. The Federal Circuit held:

> Although commercial success might generally support a conclusion that Merck's claimed invention was non-obvious in relation to what came before in the marketplace, the question at bar is narrower. It is whether the claimed invention is non-obvious in relation to the ideas set forth in the Lunar News articles. Financial success is not significantly probative of that question in this case because others were legally barred from commercially testing the Lunar News ideas. . .
>
> In this case Merck had a right to exclude others from practicing the weekly-dosing of alendronate specified in claims 23 and 37, given (1) another patent covering the administration of alendronate sodium to treat osteoporosis, U.S. Pat. No. 4,621,077 (issued Nov. 4, 1986); and (2) its exclusive statutory right, in conjunction with FDA marketing approvals, to offer Fosamax at any dosage for the next five years. 21 U.S.C. § 355(c)(3)(D)(ii) (2000). Because market entry by others was precluded on those bases, the inference of non-obviousness of weekly-dosing, from evidence of commercial success, is weak. Although commercial success may have probative value for finding non-obviousness of Merck's weekly-dosing regimen in some context, it is not enough to show the claims at bar are patentably distinct from the weekly-dosing ideas in the Lunar News articles.

Id. at 1377.

This reasoning applies in the instant case, since Roche owned the '814 patent on ibandronate sodium, which prevented anyone from commercially testing any methods which used ibandronate to treat osteoporosis. As such, the inference of non-obviousness of monthly dosing, from evidence of commercial success, is weak. As in Merck, Roche's commercial success with monthly dosing of ibandronate is not enough to show that the claims at bar are patentably distinct from the monthly dosing ideas in the prior art references.

Roche next asserts, as an objective consideration, long-felt but unresolved need and skepticism. Roche's single paragraph on this issue in its opposition brief cites no evidence beyond the conclusory assertions of its experts, and merely asserts the point as a conclusion, with no supporting analysis. "Evidence is particularly probative of obviousness when it demonstrates both that a demand existed for the patented invention, and that others tried but failed to satisfy that demand." Eurand, Inc. v. Mylan Pharms., Inc. (In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.), 2012 U.S. App. LEXIS 7571, *53-*54 (Fed. Cir. Apr. 16, 2012). The evidence of record amply supports the idea that, in 2002, the field of intermittent bisphosphonate treatments for osteoporosis was busy with researchers trying out various bisphosphonate treatments using various regimens; moreover, Merck was already marketing the bisphosphonate Fosamax®.[18] Any claim that Roche's once-monthly ibandronate treatment filled a long-felt but unresolved need must be grounded in a careful analysis of the many alternatives in development and in the marketplace – an analysis which Roche has not yet offered. The evidence of record suggests not that others tried and failed to satisfy the demand, but that it was Merck, with Fosamax®, that appears to have satisfied an unmet need, not Roche. The evidence does not support finding that, in practicing the '634 patent, Roche met a long-felt but unresolved need.

[18] Roche's expert Vellturo states that competitor Merck introduced once-weekly Fosamax® in October of 2000, and that Fosamax® "has been the most frequently prescribed osteoporosis drug by a substantial margin." (Vellturo Resp. Rpt. 2009 ¶¶ 23, 25.) Given that Roche concedes that Fosamax® has been more frequently prescribed than Boniva® – by a factor of ten, according to Vellturo –, this casts doubt on Roche's assertions that the treatment method of the '634 patent resolved a long-felt and previously unresolved need. Roche does not explain, for example, how Boniva® met a need that weekly Fosamax® had failed to resolve – if in fact it takes that position.

Roche next asserts, as an objective consideration, the failure of others to develop "greater-than-daily dosing." (Pl.'s Opp. Br. 35.) Roche has failed to frame the issue correctly. Not every development failure in the osteoporosis treatment field is relevant as an indicator of nonobviousness of the claims at issue. As Defendants point out, since once-monthly oral administration of ibandronate was known in the prior art, and what was unknown was the 150 mg dose, what might be relevant here is evidence that others tried to find an effective dose for once-monthly oral treatment with ibandronate and failed. Instead, Roche points to Reginster's work with tiludronate, Ryan's work with pamidronate, and the studies of intravenous administration of ibandronate. None of these is relevant evidence of a failure of others to find an effective dose for once-monthly oral treatment with ibandronate.

Roche next offers three sentences asserting, as an objective consideration, the evidence that it has licensed the '938 patent. Roche's brief is coy and disingenuous, if not actually misleading, on this subject. Roche contends that its licensing to P&G for Actonel® indicates nonobviousness, but never actually asserts that it has licensed the claims at issue in the '634 patent. Since it appears that the active ingredient in Actonel® is risedronate, and the claims at issue on this motion are directed to the use of ibandronate, Roche's suggestion that the license is meaningful evidence appears disingenuous. Roche does not explain how the licensing of a patent not the subject of the instant motion is relevant. "Licenses taken under the patent in suit may constitute evidence of nonobviousness; however, only little weight can be attributed to such evidence if the patentee does not demonstrate a nexus between the merits of the invention and the licenses of record." In re GPAC Inc., 57 F.3d 1573, 1580 (Fed. Cir. 1995). Roche has offered evidence about the licensing of a different patent, and has not demonstrated a nexus between the

merits of the patent at issue and the license offered.

Roche next asserts copying as an objective consideration, and points to the fact that Defendants seek to copy Roche's invention. If this could be substantial evidence of nonobviousness, no patent in Hatch-Waxman litigation would ever be found obvious, because these cases always involve claims of copying.

Lastly, Roche asserts unexpected results as an objective consideration. Plaintiffs have not, however, offered evidence that is sufficient under Federal Circuit law:

> One way for a patent applicant to rebut a prima facie case of obviousness is to make a showing of unexpected results, i.e., to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected.

In re Soni, 54 F.3d 746, 750 (Fed. Cir. 1995). Plaintiffs have pointed to no evidence in support of their claim that the skilled artisan would have been surprised that the 150 mg once-monthly dose was superior to the 2.5 mg daily dose. As Defendants observe, the finding that a higher dose of a medication is more effective than a lower one is not surprising.[19] At oral argument, Roche raised the contention that the non-linear bioavailability of ibandronate was an unexpected result. This theory was not raised in Roche's opposition brief and the new argument will not be considered.

While secondary considerations such as commercial success require factual determinations, the Court weighs the totality of the evidence, including secondary considerations, as a matter of law. This Court thus holds, as a matter of law, that Roche's evidence as to

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[19] Curiously, while the patent specification asserts that the antifracture efficacy of the claimed ibandronate method was an unexpected result, Plaintiffs did not make that argument in briefing this motion. '634 patent col.2 l.63-col.3 l.3.

objective indicia is insufficient to outweigh the evidence of obviousness. Roche's evidence regarding objective indicia of nonobviousness is fairly characterized as meager. Roche has certainly failed to persuade this Court that the objective evidence indicates nonobviousness. Rather, given that Roche's expert Vellturo states that Merck's Fosamax®, which predates Boniva®, has been substantially more successful than Boniva®, this Court has great difficulty seeing Roche's claims of success, long-felt and unresolved need, failure of others, and copying as meritorious. Vellturo computed total prescriptions for the different bisphosphonate treatments during the years 2000 through 2009, finding a total of about 162 million prescriptions for various forms of Fosamax®, and about 16 million total prescriptions for Boniva®. (PI-2-APP-7586.) Given this evidence – and given Roche's failure to offer in its opposition brief any analysis that explains how the relatively small success of Boniva® supports finding that the claims at issue are nonobvious – this Court finds that Roche's evidence as to objective indicia of nonobviousness does not outweigh the evidence of obviousness already discussed.

Furthermore, when considering a motion for summary judgment, this Court applies the "mere scintilla" standard; as the Supreme Court has held, "[t]he mere existence of a scintilla of evidence in support of the plaintiff's position will be insufficient" to defeat a motion for summary judgment. Anderson, 477 U.S. at 252. Roche's objective considerations evidence does not rise to the level of a mere scintilla, and it is not sufficient to defeat the motion for summary judgment.

Having examined all of the evidence offered by the parties, this Court finds that Defendants have met the requirements of Federal Rule of Civil Procedure 56(a) and have shown "that there is no genuine dispute as to any material fact and the movant is entitled to judgment as

a matter of law." While the conclusion of invalidity based on obviousness rests on factual determinations, and this Court has examined a substantial number of facts in deciding this motion, this motion is nonetheless amenable to resolution on summary judgment. As the Supreme Court has held:

> Where, as here, the content of the prior art, the scope of the patent claim, and the level of ordinary skill in the art are not in material dispute, and the obviousness of the claim is apparent in light of these factors, summary judgment is appropriate.

KSR, 550 U.S. at 427. This Court has found no dispute over any of the underlying material facts regarding the content of the prior art. The parties have not disputed on this motion the scope of the claims at issue or the level of ordinary skill in the art, and so summary judgment is appropriate. Although the Court finds Roche's evidence of nonobviousness based on objective considerations to be meager, it resolves any conflict between the strong evidence of obviousness provided by the primary considerations (the first three Graham factors) and the very weak evidence as to objective considerations as a matter of law. See Rogers v. Desa Int'l, Inc., 198 Fed. Appx. 918, 923 (Fed. Cir. 2006) (summary judgment of obviousness affirmed despite secondary considerations showing nonobviousness because the weighing of secondary considerations is an issue of law).

The instant case and motion resemble the situation in Chore-Time Equipment, Inc. v. Cumberland Corp., 713 F.2d 774, 778-779 (Fed. Cir. 1983), in which the Federal Circuit held:

> Though we approach the question, as we must, prepared to resolve all doubt respecting the presence or absence of material issues of fact in Chore-Time's favor, we discern no basis for doubting the absence of any such issue here. The mere incantation of the fact findings listed in *Graham* cannot establish the impropriety of issuing a summary judgment when there is no material issue of fact requiring a trial to resolve, and the facts of record require a holding of patent invalidity. Many, if not most, suits for patent infringement give rise to numerous

> and complex fact issues, rendering those suits inappropriate for summary disposition. Where no issue of material fact is present, however, courts should not hesitate to avoid an unnecessary trial by proceeding under Fed. R. Civ. P. 56 without regard to the particular type of suit involved.
>
> It is undisputed that the district court had before it all of the relevant prior patented art. The subject matter, i.e., the scope and content, of those patents being easily discernible from their drawings and written descriptions, no testimony, expert or otherwise, regarding their scope and content was necessary.

Such is the case here: this Court has before it the relevant prior art, and has found that its scope and content are discernible without the need for expert testimony. There is no need for trial.

Furthermore, this Court finds that, even considering the presumption of validity given to an issued patent, the heavy burden that falls on a challenger relying on art that was before the examiner during prosecution, and the statutory standard requiring the challenger to prove obviousness by clear and convincing evidence, this Court finds that the evidence of obviousness offered by Defendants is so strong that they are entitled to judgment as a matter of law. "[A] moving party seeking to invalidate a patent at summary judgment must submit such clear and convincing evidence of facts underlying invalidity that no reasonable jury could find otherwise." SRAM Corp. v. AD-II Eng'g, Inc., 465 F.3d 1351, 1357 (Fed. Cir. 2006). Defendants have done so, and have proven by clear and convincing evidence that, pursuant to 35 U.S.C. § 103(a), claims 1-8 of U.S Patent No. 7,718,634 are obvious and therefore invalid.

CONCLUSION

In summary, the Court views the obviousness analysis as follows. Prior to the critical date, May 10, 2002, it was well-known in the field that bisphosphonates, administered orally, were antiresorptive agents effective for the treatment of disorders of bone resorption such as osteoporosis, and that ibandronate was a powerful antiresorptive agent. It was also well-known

that oral administration tended to produce adverse gastrointestinal effects, which led to problems with patient compliance, and that a general solution to these problems lay in intermittent dosing regimens. One particular solution, once-monthly oral administration of ibandronate, was placed into the public domain by the Lunar News Spring 1999 reference, as well as the Krause 2001 reference. The skilled artisan, seeking to implement that solution, would only have needed to figure out what dosage to use, and then would have had in possession the subject matter of claims 1-8.

It is the answer to the question of what dosage to use that this Court holds would have been suggested by combining the prior art references of Ravn 1996 (daily oral ibandronate doses of 2.5 mg and 5 mg effectively treat osteoporosis) and Riis 2001 (the total dose concept), supported by Daifotis '932 (recommending weekly oral ibandronate doses of 35, 40, 45, and 50 mg). The differences between the subject matter which the applicants sought to patent in claims 1-8 of the '634 patent and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. The differences appear quite small and amenable to being bridged by the application of common sense and ordinary skill.

The evidence of obviousness provided by the prior art analysis is so clear and convincing that the objective considerations evidence, largely the modest commercial success of Boniva®, cannot overcome it.

For the reasons stated above, this Court finds that Defendants have met the requirements of Federal Rule of Civil Procedure 56(a) and have shown "that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Defendants' motion

for summary judgment is granted, and judgment on Defendant's affirmative defense of invalidity due to obviousness to the claim of infringement of the '634 patent is entered in favor of Defendants. Claims 1-8 of U.S Patent No. 7,718,634 are hereby declared invalid due to obviousness, pursuant to 35 U.S.C. § 103(a).

s/ Stanley R. Chesler
Stanley R. Chesler, U.S.D.J.

Dated: May 7, 2012