803 F.Supp.2d 409
United States District Court,
E.D. Virginia,
Norfolk Division.

PFIZER INC., Pfizer Ltd., and Pfizer Ireland Pharmaceuticals Unlimited Liability Co., Plaintiffs and Counterclaim Defendants,
v.
TEVA PHARMACEUTICALS USA, INC., Defendant and Counterclaim Plaintiff.

Civil No. 2:10cv128. | Aug. 12, 2011.

Synopsis

Background: Holder of patent claiming use of certain chemical compounds as method of treating erectile dysfunction brought action against competitor, alleging imminent infringement. Competitor counterclaimed, seeking declaration that competitor's planned drug would not infringe patent and that patent claims were invalid.

Holdings: Following bench trial, the District Court, Rebecca Beach Smith, J., held that:

[1] patent assignee had standing to sue for infringement of patent;

[2] licensee lacked standing to sue competitor for infringement;

[3] amendment to competitor's complaint during trial to include inequitable conduct claim would prejudice counsel and patent holder;

[4] patent was not invalid based on obviousness;

[5] patent was not invalid for obviousness-type double patenting; and

[6] attorney's failure to produce statement of claim to Patent and Trademark Office (PTO) did not constitute inequitable conduct.

Ordered accordingly.

Attorneys and Law Firms

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OPINION AND FINAL ORDER

REBECCA BEACH SMITH, District Judge.

On March 24, 2010, Pfizer, Inc., Pfizer, Ltd., and Pfizer Ireland Pharmaceuticals Partnership [1] (collectively "Pfizer") [2] filed ***414** suit in this court against Teva Pharmaceuticals USA, Inc. ("Teva") [3] alleging imminent infringement of Pfizer's United States Patent No. 6,469,012 ("the '012 patent"), entitled "Pyrazolopyrimidinones for the Treatment of Impotence." United States Patent No. 6,469,012 (filed May 13, 1994) (issued Oct. 22, 2002), Plaintiff's Exhibit (hereinafter referred to as "PTX") 0001. The '012 patent claims the use of certain chemical compounds as a method of treating erectile dysfunction ("ED"). Only Claims 25 and 26 of the '012 patent are in dispute in this case. *See Pfizer, Inc. v. Teva Pharms. USA, Inc.*, No. 2:10cv128, 803 F.Supp.2d 459, 463–64, 2011 WL 3610654 (E.D.Va. Jan. 18, 2011) (noting that only these claims are at issue in this case), Docket # 77. [4]

One of the especially preferred compounds of the '012 patent is sildenafil, the active ingredient in the ED drug Viagra. [5] On October 25, 2004, Teva filed an Abbreviated New Drug Application with the Food and Drug Administration ("FDA") seeking approval to market a generic equivalent of Viagra containing sildenafil citrate. *See* PTX 238. On April 24, 2007, the FDA granted Teva tentative approval to do so. [6] Pfizer alleges in its Amended Complaint that Teva's planned generic drug will infringe the '012 patent, and seeks a declaration from the court to that effect.

On April 29, 2010, Teva answered the Complaint and filed a Counterclaim against Pfizer seeking a declaration that Teva's planned drug will not infringe the '012 patent and that the claims of the '012 patent are invalid. Teva subsequently sought, and was granted, leave of the court to file an Amended Answer and Counterclaim, which amendment added an allegation that the '012 patent is invalid because of inequitable conduct committed during its prosecution before the Patent and Trademark Office ("PTO"). [7] On December 13, 2010, this court held a hearing pursuant to *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 372, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996), and issued an opinion on March 17, 2011, construing the disputed terms of the patent. *See* ***415** *Pfizer, Inc. v. Teva Pharms. USA, Inc.*, 803 F.Supp.2d 397, 2011 WL 996794 (E.D.Va.2011).

A bench trial in this case commenced on June 15, 2011, lasting for twelve days. At trial, Teva stipulated to infringement, and therefore this issue is not before the court. *See* Docket # 330. On July 17, 2011, after final arguments had concluded, this court took all outstanding issues under advisement. This Opinion and Final Order addresses and resolves all remaining motions and merits determinations.

I. Factual Overview

The patent in suit in this case is the '012 patent, and in particular Claims 25 and 26, which claim:

> **25.** A method of treating erectile dysfunction in a male human, comprising orally administering to a male human in need of such treatment an effective amount of a compound selected from:
>
> [listing nine different chemical compounds]
>
> or a pharmaceutically acceptable salt thereof;
>
> or a pharmaceutical composition containing either entity.
>
> **26.** A method as defined in claim 25, wherein said compound is [listing a chemical compound] or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity.

'012 patent col. 10, lines 1–39, PTX 0001. [8] Thus, these claims of the patent teach the oral administration of sildenafil and other compounds for the treatment of ED. [9] The '012 patent will expire on October 22, 2019. *See* Final Pretrial Order ¶ 9, Docket # 267. [10]

As the patent in suit concerns the treatment of ED, bringing with it a host of technical terminology and a background of underlying knowledge, this court will first review the biology and physiology of erections [11] and then will move to a description of the invention and patents concerned.

A. [12]

The penis of a male human contains erectile tissue called the corpus cavernosum, consisting of two corpora cavernosa that run its length. The corpus cavernosum is smooth muscle tissue that is spongy and composed of cavernosal spaces which ***416** can expand and fill with blood to produce an erection. The corpus cavernosum is surrounded by fibrous tissue known as the tunica albuginea. When the penis is in a flaccid state, the corpus cavernosum is contracted. An erection is produced when the corpus cavernosum relaxes so that it expands and fills with blood. As the corpus cavernosum relaxes, the tunica albuginea compresses the veins that drain blood from the penis, thus preventing blood from flowing out and raising pressure inside the penis, producing an erection. Detumescence of the penis occurs when the corpus cavernosum contracts and bloods flows out of the penis.

An erection is controlled by the nervous system. There are three neurotransmission pathways in the human body: the adrenergic nerves; the cholinergic nerves; and the non-adrenergic, non-cholinergic ("NANC") nerves. The NANC nerves control erectile function. When a male human reacts to sexual stimuli, the NANC nerves send a signal to the penis. The neurotransmitter in this case is nitric oxide ("NO"). [13] Thus, when the NANC nerves send a signal to the penis, they synthesize NO from L-arginine in the endothelial cells of the vascular system. The NO travels into the smooth muscle cells of the corpus cavernosum where it activates an enzyme known as guanylate cyclase. Guanylate cyclase synthesizes another enzyme, cyclic guanosine monophosphate ("cGMP") by interacting with guanosine triphosphate. cGMP is the signaling enzyme that cues smooth muscle tissue, in this case the corpus cavernosum, to relax. [14] This entire process is known as the L-arginine-nitric oxide-cyclic GMP pathway.

cGMP is a cyclic nucleotide, a form of enzyme. Enzymes, as is evident from cGMP's function in the smooth muscle

described above, are proteins that catalyze chemical reactions in the body. cGMP is degraded by cGMP phosphodiesterase ("PDE"), another enzyme, which binds to cGMP and breaks it down into GMP. GMP does not have the same signaling effect in smooth muscle as cGMP. At the time the '012 patent was filed, there were five known types of PDEs: PDE1, PDE2, PDE3, PDE4, and PDE5. PDE1 and PDE5 both degrade cGMP and, thus, are termed cGMP PDEs. [15]

cGMP PDE can be inhibited by cGMP PDE inhibitors. An inhibitor functions in the same was that cGMP PDE itself functions with cGMP, by binding to it to block or decrease the activity of the enzyme. In other words, cGMP PDE inhibitors bind to cGMP PDE so that it, in turn, cannot bind to cGMP. The effectiveness of a PDE inhibitor is measured in terms of its potency, the amount of the inhibitor required to effectively inhibit the PDE, [16] and its selectivity, i.e., the ratio at which the inhibitor prefers one PDE over another. [17]

***417 B.**

Beginning in 1985, Pfizer researchers in Sandwich, England were working on the creation of cGMP PDE inhibitor drugs to treat cardiovascular diseases such as hypertension and angina. Dr. Peter Ellis was the head of the team of biologists on the project, while Dr. Nicholas Terrett led the chemists. Pfizer hoped that cGMP PDE inhibitors would be able to treat these cardiovascular diseases by-causing relaxation of the smooth muscle tissue in the arteries, thereby lessening stress on the cardiovascular system. In particular, Pfizer aimed to create compounds that would inhibit cGMP PDEs, thereby enhancing the action of cGMP within smooth muscle and causing smooth muscle relaxation.

The project first started with the chemistry team creating compounds. Such compounds were based off other compounds known to inhibit cGMP PDE, and the chemistry team worked to make such compounds more selective, in terms of which enzyme they inhibited, and more potent in their inhibitory capability. [18] Once the compounds were made, the biology team tested the compounds in assays it designed to determine their selectivity and potency for cGMP PDE. The chemistry team then received feedback and modified the compounds further, if necessary, to improve their biological activity. The chemistry team also ran tests to assess the safety of the compounds, while the pharmacokinetic team studied the compounds to determine their absorption, distribution, metabolism, and excretion in the human body.

The chemistry team first synthesized sildenafil in 1989, and it quickly became a "lead compound," after the biology and pharmacokinetic tests had been run. [19] The results were so encouraging that the team working on the project recommended that Pfizer begin clinical development of sildenafil for the treatment of angina. *See* PTX 354. A year later, in July 1991, Pfizer began its first clinical trial using sildenafil, Study 201. Trial Tr. 695:21–697:14. As this clinical trial was a Phase I study, the subjects were healthy volunteers, in this case males, and the goal was to assess the safety of the drug and further determine its pharmacokinetic properties. This initial study, and several others after it, all tested single doses of sildenafil.

In 1992, Pfizer began a multiple dose study of sildenafil, again using healthy male volunteers, Study 207. Trial Tr. 697:21–699:9. The volunteers were administered three doses of sildenafil or a placebo daily for ten days. At the conclusion of the study, volunteers reported several side effects; the most common were myalgia, [20] headaches, and spontaneous erections. The Early Candidate Management Team ("ECMT"), the team charged with the initial testing and development of sildenafil that included Dr. Ellis, was surprised to hear that a common side effect was spontaneous erections, as such a side effect had never been previously reported in Pfizer clinical trials. As a result of this report from the volunteers, the ECMT decided to run a clinical trial with sildenafil directed toward the treatment of ED.

The first Phase II clinical study with sildenafil, Study 350, began on July 28, 1993, and concluded on November 15, 1993. *See* PTX 471. As it was a Phase II ***418** study, its volunteers were males with the targeted disease, i.e., men who suffered from ED. The volunteers were orally administered either sildenafil or a placebo three times a day for seven days. They recorded any erectile activity experienced during the first six days. On the seventh day, while each volunteer was provided sexual stimulation by watching an erotic video, rigidity and circumference of his penis was measured using a Rigiscan. [21] The results showed that sildenafil significantly improved erections for those men in the test with ED.

Pfizer then commenced a single dose Phase II study, Study 351, on February 24, 1994, concluding May 30, 1994. Trial Tr. 706:21–707:20. In this study, male volunteers with ED were given a single dose of sildenafil on one occasion, and

a Rigiscan was administered. The same volunteers were then given sildenafil once a day for seven days, and they made note of their erectile activity. The results were encouraging and showed a correlation between the administration of sildenafil and improved erectile function for men with ED.

Based on the results of the studies described, Pfizer applied to the FDA for approval of Viagra, sildenafil citrate. Viagra was approved by the FDA in 1998 in New Drug Application No. 20–895 as a drug to treat ED. Viagra works, as the '012 patent states, because it is a PDE5 inhibitor that prevents PDE5 from binding to cGMP and rendering cGMP inactive in the L-arginine-nitric oxide-cyclic GMP pathway, thus increasing the level of cGMP in the corpus cavernosum. Viagra's introduction on the market in 1998 generated a flurry of publicity and interest from scientists and consumers alike. Experts from both parties admitted that Viagra revolutionized the treatment of ED, making the treatment both more effective and accessible. Since its introduction in 1998, Viagra has generated cumulative sales of over $10 billion.

C.

After successfully creating sildenafil and other related compounds, Pfizer filed a series of applications for patents. [22] Initially, Pfizer filed several compound patents. The first was European Patent Number 0463756A1 ("EP '756") entitled "Pyrazolopyrimidinone Antianginal Agents," filed June 7, 1991, and published February 1, 1992. PTX 0352. EP '756 first disclosed sildenafil, among other compounds, and claimed such compounds as selective cGMP PDE inhibitors [23] which elevate the levels of cGMP. *See* EP '756, 3:5–7, PTX 0352. The specification of the patent discloses:

> [T]he compounds have utility in the treatment of a number of disorders, including stable, unstable and variant (Prinzmetal) angina, hypertension, congestive heart failure, atherosclerosis, conditions of reduced blood vessel patency e.g. postpercutaneous transluminal coronary angioplasty (post-PTCA), peripheral vascular disease, stroke, bronchitis, chronic asthma, allergic asthma, allergic rhinitis, glaucoma, and diseases ***419** characterized by disorders of gut motility, e.g. irritable bowel syndrome (IBS).

EP '756, 3:9–14, PTX 0352. Of the compounds in Claims 25 and 26 of the patent in suit, EP '756 disclosed five, including sildenafil. [24]

Pfizer next filed European Patent Number 0526004A1 ("EP #004"), also entitled "Pyrazolopyrimidinone Antianginal Agents," on February 7, 1992. EP '004 was published on March 2, 1993. PTX 0066. EP '004 claimed additional potent and selective cGMP PDE inhibitors useful in the treatment of:

> [S]table, unstable and variant (Prinzmetal) angina, hypertension, pulmonary hypertension, congestive heart failure, atherosclerosis, conditions of reduced blood vessel patency e.g. postpercutaneous transluminal coronary angioplasty (post-PTCA), peripheral vascular disease, stroke, bronchitis, chronic asthma, allergic asthma, allergic rhinitis, glaucoma, and diseases characterized by disorders of gut motility, e.g. irritable bowel syndrome (IBS).

EP '004, 2:10–14, PTX 0066. EP '004 disclosed four of the compounds in Claim 25 of the '012 patent. [25]

Finally, Pfizer filed United States Patent Number 5,250,534 ("the '534 patent") on May 14, 1992. PTX 0002. The '534 patent is the U.S. equivalent of EP '756 and, thus, is also entitled "Pyrazolopyrimidinone Antianginal Agents" and shares the same specification and characteristics of EP '756 described above, including the diseases the compounds were believed to be useful in treating. The '534 patent likewise covers five of the compounds listed in Claims 25 and 26 of the '012 patent, including sildenafil. The '534 patent issued on October 5, 1993. [26] Each of these compound patents —EP '756, EP '004, and the '534 patent—disclosed oral administration of the relevant compounds.

After Pfizer had filed the compound patents for sildenafil and the other cGMP PDE inhibitors, it filed the patent in suit directed to a method of treating ED using some of the compounds from EP '756 and EP '004. Claims 25 and 26 specifically claim oral treatment of ED, and the specification of the patent states that oral administration is the preferred route. '012 patent, col. 5, lines, 62–65, PTX 0001. [27] In the specification of the patent, Pfizer discloses that the compounds of the '012 patent have been found to be potent and selective inhibitors of PDE5 such that they enhance cGMP levels in the corpus cavernosum. *Id.* col. 5,

lines 33–35, 39–44, PTX 0001.[28] The '012 patent issued, after overcoming numerous rejections, on October 22, 2002.

With the pertinent factual underpinnings of the case set out, this court turns to the substantive issues remaining before it.

II. Teva's Motion to Dismiss for Lack of Standing

During trial on July 6, 2011, Teva filed a Motion to Dismiss for Lack of Standing. ***420** *See* Docket # 412. Teva argues that Pfizer has failed to carry its burden to demonstrate that each plaintiff has standing to sue for infringement of the patent in suit because it has failed to prove that any plaintiff has sufficient interest in the patent to sue for infringement. Per a briefing schedule set by the court, Pfizer responded in opposition on July 15, 2011, *see* Docket # 435, and Teva replied on July 20, 2011, *see* Docket # 451. The motion is now ripe for decision.

A.

The issue of standing in this case is bound up with the evidence on the issue of ownership,[29] and thus the court reviews the evidence as to both presented at trial.[30] Looking first to the patent in suit itself, Pfizer, Inc. is named as the owner-assignee on the face of the '012 patent. PTX 0001. Pfizer, Inc. received the assignment of rights to the patent from the patent's inventors, Drs. Nicholas Terrett and Peter Ellis, on October 10, 1995. PTX 0363. In the assignment, Drs. Terrett and Ellis agreed to:

> [S]ell, assign, and transfer unto PFIZER, INC .... the entire right, title, and interest in and to our application for Letters Patent of the United States ... entitled PYRAZOLOPYRIMIDINONES FOR THE TREATMENT OF IMPOTENCE and our entire right, title, and interest in the United States in and to all our inventions, whether joint or sole, disclosed in said application for Letters Patent, and in all and to all United States patents granted on the foregoing inventions.

Id. at 1. On the same day, Pfizer, Ltd., whose employment of Drs. Terrett and Ellis entitled it to claim full rights to the patentable inventions, consented to the assignment, noting that "PFIZER LIMITED desires that PFIZER INC. receive the full benefits of the foregoing assignment by its aforesaid employee(s)." *Id.* at 3.

Previously on August 9, 1993, Pfizer, Inc. and Pfizer, Ltd. entered into a Patent Filing Agreement. PTX 0322. The Patent Filing Agreement memorialized "the procedures to be applied in respect of the filing of patent applications resulting from research carried out under the Cost Sharing Agreement [between Pfizer, Inc. and Pfizer, Ltd.] and the procedure applicable to patent applications resulting from other research carried on by LIMITED." *Id.* at 2. Specifically:

> LIMITED Property patent applications will be filed by PFIZER [INC.] in the USA.... In filing such applications, PFIZER [INC.] will act as agent for LIMITED, so that such applications and any patents issued thereon shall be held ***421** by PFIZER [INC.] in trust for LIMITED, as the beneficial owner thereof.

Id. at 3–4. In addition, to effectuate the filing of patents, Pfizer, Ltd. agreed that it would be "deemed to assign PFIZER [INC.] ... all rights necessary ... to file patent applications hereunder." *Id.* at 5. In consideration for its filing of the patent applications, Pfizer, Inc. could receive from Pfizer, Ltd. "a non-exclusive license ... with respect to any such LIMITED Property in the USA." *Id.* at 6.

After the application for the '012 patent was filed, but before it was issued by the PTO, Pfizer, Ltd. executed a license agreement with Pfizer Pharmaceuticals Production Corporation, effective as of January 1, 1997. PTX 0324. The license agreement concerned patents for sildenafil, either issued or currently pending, including both the '534 patent and the '012 patent. *Id.* at 13. Therein, Pfizer, Ltd. granted to Pfizer Pharmaceuticals Production Corporation "(1) an exclusive license under the U.S. Patent Rights to make, use, sell, and offer for sale Licensed Product in the Commercial Territory, and to import Licensed Product into the Commercial Territory and (2) an exclusive license to use the Technical Information in the Commercial territory in connection with the activities referred to [above]." *Id.* at 4. "Commercial Territory" was defined as the United States of America, *id.* at 2, and "Licensed Product" was defined as "any drug for human use containing the Compound, [sildenafil]." *Id.* at 3. Thus, Pfizer Pharmaceuticals Production Corporation received, in essence, an exclusive license to manufacture and sell sildenafil in the United States. This exclusive license was subject to Pfizer, Ltd.'s retained "Conversion Right," the right

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