VENABLE LLP

575 7th Street, NW
Washington, DC 20004-1601

Telephone 202-344-4000
Facsimile 202-344-8300

www.venable.com

TO:
US PTO
Attn: Kathleen K. Fonda
M/S: HATCH-WAXMAN PTE

FAX NUMBER:
(571) 273-7754

PHONE NUMBER:
(571) 272-7754

SENDER:
Michael A. Gollin

SENDER'S FAX NUMBER:
(202) 344-8300

SENDER'S PHONE NUMBER:
(202) 344-4072

SENDER'S ASSISTANT:
Shana G. Stiles

ASSISTANT'S PHONE NUMBER:
(202) 344-4834

DATE:
5/3/2007

CLIENT/MATTER NUMBER:
32286-203599

PAGES, INCLUDING COVER: 8

MESSAGE:

Re: U.S. Patent No. 5,716,981
Issued: 10 February 1998
Application No. 08/478,203
Filed: 7 June 1995
For: *ANTI-ANGIOGENIC COMPOSITIONS AND METHODS OF USE*
Applicant(s): Hunter et al.
Our Reference: 32286-203599

32286-203599
PATENT/OFFICIAL

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Hunter et al.

Patent No.: 5,716,981
Issued: 10 FEB 1998

Application No.: 08/478,203
Filed: 7 June 1995

For: ANTI-ANGIOGENIC COMPOSITIONS AND METHODS OF USE

Legal Advisor: Kathleen Kahler Fonda
FAX # 571.273.7754

Atty. Docket No. 32286-203599

Customer No.
26694
26694
PATENT TRADEMARK OFFICE

REQUEST FOR RECONSIDERATION OF FINAL DETERMINATION

Commissioner for Patents
M/S HATCH-WAXMAN PTE
P.O. Box 1450
Alexandria, VA 22313-1450

Sir/Madam:

Applicants hereby request reconsideration of the Final Determination of Patent Term Extension under 35 U.S.C. § 156 dated April 3, 2007 for the referenced U.S. patent.

This PTE determination appears to be based in part on an interpretation of the patent laws that is contrary to the plain meaning of the statute and, further, contrary to implementing regulations promulgated by the PTO. The interpretation is expressed in a regulation promulgated by the Food and Drug Administration (FDA) governing the determination of the testing phase of the regulatory review period. Although FDA, as the delegate of the Secretary of HHS, is given the statutory duty to determine the review period for the PTO's issuance of the PTE, it is appropriate for the PTO to consider and to determine with FDA whether the statute was applied in a manner that is contrary to its plain meaning and that is contrary to the interpretation expressed by the PTO.

1. **The Patent Laws Appear to have Been Misapplied.**

It appears that, in determining the regulatory review period for Applicant's PTE, FDA interpreted the applicable provision of the patent laws, 35 U.S.C. 156(g)(3)(B)(i), to determine the commencement of the testing phase of the regulatory review period based on the effective date of the product's IDE rather than on the date of the first clinical study involving the product. This application of the statute is contrary to its plain meaning.

Applicant stated in its Application for Patent Term Extension (Application) that there was an IDE for the product, which was required for a Phase III study in the U.S. The Application also stated, however, that the first clinical study on the product was a Phase I study conducted in Germany commenced almost a year earlier than the submission of the U.S. IDE for the Phase III study. Although Applicant proposed in the Application that the regulatory review period should be determined based on the commencement date of the Phase I study in Germany, FDA rejected this proposal and determined the regulatory review period based on the effective date of the IDE for the Phase III study.

The apparent basis for this determination is the agency's regulation governing calculation of the regulatory review period. Although the statute mandates that the regulatory review period be deemed to commence "on the date a clinical investigation on humans involving the device was begun." 35 U.S.C. 156(g)(3)(B)(i), FDA's regulation imposes additional criteria. The regulation requires that testing phase of the regulatory review period be determined based on (1) the effective date of an IDE or (2) the commencement of a clinical investigation that was not subject to an IDE approval requirement and was "to be filed with FDA to secure premarket approval of the device." 21 C.F.R. 60.23(c)(1).

This application of the statute is contrary to the plain meaning of 35 U.S.C. 156(g)(3)(B)(i). The statute directs that the PTE be based an a regulatory review period commencing "on the date a clinical investigation on humans involving the device was begun" with no additional requirement. The imposition of additional statutory requirements is contrary to the plain meaning of the statute. *See, e.g., Friends of the Earth, Inc., v. EPA*, 446 F.3d 140 (D.C. Cir. 2006). As such it violates the rule of *Chevron U.S.A., Inc., v. Natural Res. Def. Council, Inc.*, 467 U.S. 837 (1984).

Moreover, Congress made clear in the broader context of the PTE provisions that it intended to distinguish the testing phase of the review period based on the commencement of a clinical investigation from a review period based on the effective date of a statutory investigational exemption under the FDCA. The PTE provisions provide specific criteria for the determination of the regulatory review periods for drugs, biologicals, devices, and other FDA-regulated products. In the case of drugs and biologicals, the statute provides expressly that the testing phase of the regulatory review period is deemed to commence "on the date of an exemption under subsection (i) of

section 505 [of the FDCA, 21 U.S.C. 355(i)]." This would be the date an IND would become effective.

Congress was aware, of course, of the IDE provisions under which a statutory exemption is provided for a U.S. investigation of a device. *See* 21 U.S.C. 360j(g). Congress clearly intended in the PTE provisions to address the regulatory review period for devices differently from the regulatory review period for drugs and biologicals, and to determine the review period for devices based on the commencement of "a clinical investigation in humans involving the device" – without regard to whether the investigation was conducted under an IDE and with no other restriction. This transparent congressional intent precludes the PTO from granting a PTE based on an FDA regulation that imposes an *ultra vires* requirement. As the United States Court of Appeals for the District of Columbia has held, "a regulation which operates to create a rule out of harmony with the statute is a mere nullity."[1]

2. Reconsideration Is Appropriate.

Where it is clear that the terms of a PTE determination are contrary to the patent laws, the PTO should reconsider the determination. Although, as noted above, Congress directed that FDA determine the review period for the PTO, it is appropriate for the PTO to consider and to determine – *with FDA* –whether the terms of the PTE were established on extra-statutory, and unlawful, criteria.

Although FDA, as the delegate of the Secretary of HHS, is given the statutory duty to determine the testing period for the PTO, it is appropriate for the PTO to consider with FDA whether criteria used in determining the testing phase of the regulatory review period, and relied upon by the PTO in issuing the PTE, were contrary to the governing patent law. Such a joint inquiry by the PTO and FDA is consistent with Congress' mandate that the PTO issue the PTE – a mandate that obligates the PTO to ensure that the PTE meets the requirements of the governing statute, including the requirement that FDA determine the regulatory review period under the applicable statutory provisions.

Moreover, the PTO's regulations may either involve the PTO in this erroneous application of the statute or reflect a different interpretation of the statute. The PTO regulations setting forth the content of a PTE application for a device require that the application provide:

> (A) The effective date of the investigational device exemption (IDE) and the IDE number, if applicable, *or the date on which the applicant began the first clinical investigation involving the device, if no IDE was submitted,* and any available substantiation of that date.

---

[1] *Social Sec. Admin., Baltimore, MD. v. Fed. Labor Relations Auth.*, 201 F.3d 465, 471 (D.C. Cir. 2000) (citing *Manhattan Gen. Equip. Co. v. Comm'r of Internal Revenue*, 297 U.S. 129, 134 (1936)). *See also Caldera v. J.S. Alberici Constr. Co.*, 153 F.3d 1381, 1383 n.** (Fed. Cir. 1998) ("Statutes trump conflicting regulations").

37 C.F.R. 1.740(v)(A) (emphasis added). It is not clear whether this regulation contemplates a determination of the regulatory review period based on the commencement of an clinical investigation without regard to a subsequently issued IDE (contrary to FDA's interpretation) or is meant to endorse FDA's interpretation. In either event, it is important for the PTO and FDA to assess whether their interpretations of the statute are consistent and are permitted by the statute.

In reconsidering the terms of the PTE, the PTO and FDA should also consider whether, even under FDA's regulation, the Application warranted a different determination of the regulatory review period. The Application makes clear that the first Phase I investigation was conducted in Germany, and thus did not require a U.S. IDE. The Application also makes clear that the Phase I study in Germany conducted in late 2000 was the linchpin of the clinical development program supporting that included a Phase III study to be conducted the next year in the U.S. under an IDE.[2]

Finally, the PTO and FDA should reconsider whether the submission of a PMA module begins the regulatory review as the date on which the application for premarket approval is "initially submitted." The submission of the module begins FDA's actual regulatory review of the PMA.

Applicant therefore requests that the PTO reconsider, in conjunction with FDA, the terms of the PTE and their consistency with the governing statute.[3]

Please charge any necessary fees that are not included herewith or credit any overpayment to deposit account no. 22-0261.

Respectfully submitted,

Date: 5/3/2007

Michael A. Gollin
Reg. No. 31,957
VENABLE LLP
P.O. Box 34385
Washington, DC 20043-9998
TEL 202.344.4000
202.344.4072 (direct)
FAX 202.344.8300

DC2/856050

[2] *See* Angiotech Pharmaceuticals: Boston Scientific Enrolls First Patient in International Drug-Eluting Stent Clinical Trial (July 10, 2001) (attached).

[3] The PTO indicated the period of extension to be 488 days. Applicants calculated a period of 807 days based on the appropriate interpretation of the law.

NEWS RELEASE TRANSMITTED BY CCNMatthews

ANGIOTECH Pharmaceuticals

FOR: **ANGIOTECH PHARMACEUTICALS INC.**

TSE SYMBOL: ANP
NASDAQ SYMBOL: ANPI

JULY 10, 2001 - 10:24 EDT

Angiotech Pharmaceuticals: Boston Scientific Enrolls First Patients In International Drug-Eluting Stent Clinical Trial

NATICK, MASSACHUSETTS--

Boston Scientific's third paclitaxel drug-eluting stent clinical trial is underway

Trial to support European CE mark application

Angiotech Pharmaceuticals (NASDAQ:ANPI; TSE:ANP) was notified today by Boston Scientific Corporation (NYSE: BSX) that it has begun enrollment in its international TAXUS II drug-eluting stent clinical trial led by principal investigator, Dr. Antonio Colombo, EMO Centro Cuore Colombus, Milan, Italy.

The TAXUS program is a series of studies aimed at collecting clinical information on Boston Scientific's proprietary paclitaxel drug-eluting stent technology for reducing coronary restenosis, the regrowth of vascular tissue within an artery after angioplasty and stenting. Paclitaxel, the active component of the popular chemotherapeutic agent Taxol(R), has demonstrated promising results in pre-clinical studies for reducing the processes leading to restenosis. Boston Scientific's paclitaxel-eluting stent technology is designed to provide direct delivery of paclitaxel through a polymer on a stent at the desired location with a very predictable and controlled release to prevent restenosis.

TAXUS II is a 532-patient, multi-center, international study where patients are randomized to receive either a paclitaxel-eluting stent or a bare, stainless steel control stent. In addition to monitoring clinical outcomes, intravascular ultrasound (IVUS) will be used to study safety and performance of two separate dose releases of paclitaxel. The trial is designed to collect critical information for proof of principle and to support regulatory filings for product commercialization in several markets around the world, including a CE Mark in Europe.

"The initiation of our third drug-eluting stent clinical trial

marks a pivotal point in our development program," said Jim Tobin, President and Chief Executive Officer of Boston Scientific. "The foundation was set by long-term animal studies that have identified dose ranges that minimize restenosis and promote vascular healing. We are beginning to gain clinical experience with these doses in larger patient populations and are a step closer to providing physicians with a promising treatment option for restenosis."

Commenting on the TAXUS II trial, Dr. Colombo, the Principal Investigator, said, "The entire interventional cardiology community looks forward to rapid completion of this study which will add important clinical data in the battle to prevent restenosis."

Boston Scientific is gaining comprehensive clinical experience with drug-eluting stents. The TAXUS I trial is a 61-patient, randomized safety study evaluating slow dose release formulation. It completed enrollment in February. Thirty-day MACE (major adverse cardiac events) evaluation has been completed in all patients with no adverse events. Six-month angiographic and IVUS follow-up is expected to be complete by the fall.

TAXUS III is a 30-patient registry study examining the feasibility of paclitaxel-eluting stent technology for treatment of in-stent restenosis. This group represents patients with more complex vascular disease who tend to have an increased probability of restenosis. To date, TAXUS III has enrolled 22 patients. Enrollment is expected to be complete by the end of the summer.

The fourth trial in the TAXUS program, TAXUS IV, is a pivotal study to be based in the U.S. to collect key data to support regulatory filings for U.S. product commercialization. The company expects to begin enrolling patients in a U.S. clinical trial before the end of the year. The comprehensive TAXUS program positions Boston Scientific to launch paclitaxel-eluting stents in Europe in 2002 and in the U.S. in 2003.

Boston Scientific has acquired worldwide co-exclusive rights from Angiotech to use paclitaxel to coat its coronary stent products and other vascular and non-vascular products. Angiotech Pharmaceuticals is a Canadian pharmaceutical company dedicated to the development of medical coatings and treatments for chronic inflammatory diseases through reformulation of the anti-cancer drug, paclitaxel.

Boston Scientific is a worldwide developer, manufacturer and marketer of medical devices whose products are used in a broad range of interventional medical specialties.

Statements contained herein that are not based on historical fact, including without limitation statements containing the words "believes," "may," "will," "estimate," "continue," "anticipates," intends," " expects" and words of similar import, constitute "forward-looking statements" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause the actual results, events or developments to be materially different from any future results, events or developments expressed or implied by such forward-looking statements. Such factors include, among others, the following: general economic and business conditions, both national and in the regions in which the Company operates;

technology changes; competition; changes in business strategy or development plans; the ability to attract and retain qualified personnel; existing governmental regulations and changes in, or the failure to comply with, governmental regulations; liability and other claims asserted against the Company; and other factors referenced in the Company's filings with the securities and Exchange Commission. Given these uncertainties, readers are cautioned not to place undue reliance on such forward-looking statements. The Company disclaims any obligation to update any such factors or to publicly announce the result of any revisions to any of the forward-looking statement contained herein to reflect future result, events or developments.

-30-

FOR FURTHER INFORMATION PLEASE CONTACT:
Boston Scientific Corporation
Milan Kofol
Investor Relations
(508) 650-8569
or
Boston Scientific Corporation
Paul Donovan
Media Relations
(508) 650-8541
or
Angiotech Pharmaceuticals Inc.
Cindy Yu
Corporate Communications
(604) 221-7676
Website: www.angiotech.com

Other Recent News

Hot Company Links | Stock Quote | Stock Chart