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UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

NUVASIVE, INC. and
OSIRIS THERAPEUTICS, INC.,

Plaintiffs,

v.

ORTHOFIX INTERNATIONAL N.V., ORTHOFIX, INC., ORTHOFIX HOLDINGS, INC., ORTHOFIX BIOLOGICS, ORTHOFIX SPINAL IMPLANTS, and MUSCULOSKELETAL TRANSPLANT FOUNDATION,

Defendants.

Civil Action No. _____

Hon. _____

COMPLAINT FOR PATENT INFRINGEMENT AND DEMAND FOR JURY TRIAL

Plaintiffs NuVasive, Inc. and Osiris Therapeutics, Inc. (collectively, "Plaintiffs"), by their undersigned attorneys, bring this action against Defendants Orthofix International N.V., Orthofix, Inc., Orthofix Holdings, Inc., Orthofix Spinal Implants, Orthofix Biologics (collectively "Orthofix") and the Musculoskeletal Transplant Foundation (collectively, "Defendants"), and hereby allege as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement arising under the patent laws of the United States, Title 35, United States Code, regarding infringement of U.S. Patent No. 6,355,239 ("the '239 Patent"). A copy of the '239 Patent is attached hereto as Exhibit A.

2. Osiris Therapeutics, Inc. ("Osiris") is the rightful owner and assignee of the '239 Patent. NuVasive, Inc. ("NuVasive") is a rightful licensee under the '239 Patent and, by contract, has the right to enforce the patent against Defendants.

3. Osiris invested millions of dollars and many years in researching and developing allogeneic mesenchymal stem cell-based ("MSCs") products for use in various therapies, including repairing defective connective tissues, such as bone. In 2008, NuVasive purchased from Osiris, for $85 million, one such allogeneic MSC-based product line designed to repair defective bone, which purchase included receiving a license under the '239 Patent and a right to enforce the same. This product line was known as OsteoCel®.

4. Before NuVasive purchased this product line, Defendants, through their affiliate Blackstone Medical Inc. ("Blackstone"), were authorized by Osiris to distribute OsteoCel®. Defendants' distributed the product line under the trade name "Trinity®." However, as described below, after Osiris sold its OsteoCel® product line to NuVasive,

Defendants lost their right to continue to distribute this product line in an authorized manner - but not before hastily filing a lawsuit (later dismissed) to enjoin the sale of the product line to NuVasive.

5. Undeterred, and rather than give up the economic benefits associated with selling the "Trinity®" product line, Defendants partnered with the Musculoskeletal Transplant Foundation ("MTF") to deliberately make, offer for sale and sell a rival MSC-based product line that infringes the '239 patent and competes with NuVasive's licensed product line.

6. By this lawsuit, Plaintiffs seek to enjoin, and collect damages for, Defendants' infringement of the '239 Patent, which improperly undermines NuVasive's market position.

THE PARTIES

7. NuVasive is incorporated under the laws of the State of Delaware with its principal place of business at 7475 Lusk Boulevard, San Diego, California 92121. NuVasive is a medical device company focused on the design, development, and marketing of state-of-the-art products for the surgical treatment of spine disorders.

8. Osiris is incorporated under the laws of the State of Delaware with its principal place of business at 7015 Albert Einstein Drive, Columbia, Maryland 21046. Osiris is a leading stem cell company focused on developing and marketing products to treat medical conditions in the inflammatory, orthopedic and cardiovascular areas.

9. Defendant Orthofix International N.V. is incorporated under the laws of the Netherlands Antilles with United States corporate headquarters at 800 Boylston Street, Boston, Massachusetts 02199. On information and belief, Defendant Orthofix International

N.V. has carried out business in this District, has induced and/or contributed to infringement of the '239 Patent in this District, and will continue to engage in such acts of infringement in this District.

10. Defendant Orthofix, Inc. is incorporated under the laws of the State of Minnesota with a principal place of business at 1720 Bray Central Drive, McKinney, Texas 75069. On information and belief, Defendant Orthofix, Inc. has carried out business in this District, has induced and/or contributed to infringement of the '239 Patent in this District, and will continue to engage in such acts of infringement in this District.

11. Defendant Orthofix Holdings, Inc. is incorporated under the laws of the State of Delaware with a principal place of business at 2711 Centerville Road, Suite 400, Wilmington, Delaware 19808. On information and belief, Defendant Orthofix Holdings, Inc. has carried out business in this District, has induced and/or contributed to infringement of the '239 Patent in this District, and will continue to engage in such acts of infringement in this District.

12. Defendants Orthofix Spinal Implants and Orthofix Biologics (collectively and formerly "Blackstone") are incorporated under the laws of the State of Massachusetts with each having a principal place of business at 1720 Bray Central Drive, McKinney, Texas 75069. On information and belief, Defendants Orthofix Spinal Implants and Orthofix Biologics have carried out business in this District, have induced and/or contributed to infringement of the '239 Patent in this District, and will continue to engage in such acts of infringement in this District.

13. Defendant the Musculoskeletal Transplant Foundation is incorporated under the laws of the State of New Jersey and is headquartered at 125 May Street, Edison, New

Jersey 08837, which is within this District. Upon information and belief, Defendant Musculoskeletal Transplant Foundation has induced and/or contributed to infringement of the '239 Patent in this District, and will continue to engage in such acts of infringement in this District.

JURISDICTION AND VENUE

14. This Court has subject matter jurisdiction over this action under 28 U.S.C. §§ 1331, 1338(a), 2201 and 2202.

15. This Court has personal jurisdiction over Defendants because: i) they each have established minimum contacts with the State of New Jersey by purposefully availing themselves of the laws and benefits of this forum, as evidenced by the acts of infringement they have induced and/or contributed to within this State; and ii) the exercise of jurisdiction over each Defendant would not offend traditional notions of fair play and substantial justice.

16. Venue is proper in this District under 28 U.S.C. §§ 1391 (b), (c) and 1400(b).

THE PATENT-IN-SUIT AND SUBJECT MATTER CLAIMED

17. The '239 Patent, entitled "Uses for Non-Autologous Mesenchymal Stem Cells," was duly and lawfully issued on March 12, 2002. By virtue of their respective interests in the '239 Patent, Plaintiffs have the right to sue and secure legal and equitable relief for infringement of the '239 Patent.

18. The '239 Patent claims, *inter alia*, methods for treating a human subject with allogeneic MSCs to promote connective tissue (*e.g.*, cartilage or bone) growth. The '239 Patent represents an important break-through in the use of stem cells to repair connective tissue defects, as discussed in greater detail below.

19. The phrase "stem cells" refers to those cells within the human body that have not yet "differentiated" (or transformed) into cells having specialized functions, such as those that make up tissues such as bone, cartilage or muscle. Hence, stem cells have the inherent capacity to differentiate into any (if they are "totipotent") or many closely related (if they are "multipotent") or not so closely related (if they are "pluripotent") types of specialized cells.

20. There are certain pluripotent stem cells known as MSCs that are useful transplants in surgical procedures, such as knee and spinal surgeries, because they can promote the formation of new connective tissue, such as bone.

21. There are two types of transplants that can be used in surgical procedures: (i) allogeneic; and (ii) autologous. Allogeneic transplants are derived from a donor (such as a cadaver) other than the patient. Autologous transplants are derived from the patient's own body.

22. A major advantage historically associated with using autologous transplants is that the transplant is derived from the patient. Hence, there is no risk that the patient's immune system will consider the transplant foreign and, in turn, reject it.

23. However, an autologous transplant, like MSCs, requires harvesting the transplant from one part of a patient's body for use in another part of the patient's body. Hence, in addition to the surgery necessary to graft a transplant to the patient (for example, to correct a bone defect), the harvesting of an autologous transplant, like MSCs, requires exposing the patient to another invasive and potentially painful procedure, which presents its own risks of potential complications. In many cases, the pain and discomfort associated with such harvesting is more severe than the restorative surgery.

24. In contrast, allogeneic transplants can be more readily and easily made available inasmuch as they can be collected from a donor other than the patient (including a cadaver) and subject to quality assurance testing and off-the-shelf use at any time.

25. Prior to the invention of the '239 Patent, allogeneic transplants were understood to pose a risk when used as transplants. Allogeneic materials were understood to display cell-surface proteins that were expected to be recognized as "foreign" by the recipient's immune system and, in turn, trigger an adverse immune response. Indeed, the response was expected to be so significant as to impede the success of the transplant therapy.

26. The inventors of the '239 Patent put those fears to rest. They taught that allogeneic MSCs can be used in place of autologous MSCs without having to control for or prevent an adverse immunological response by the patient. In other words, the inventors of the '239 Patent surprisingly discovered that allogeneic MSCs do not provoke an adverse immunological response by the patient. The inventors' teaching that allogeneic MSCs can be used in this fashion marked a significant advancement in the art.

DEFENDANTS' WILLFUL INFRINGEMENT OF THE '239 PATENT

27. In the mid-1990s, Osiris was a small tissue regeneration company exploring whether MSC-based therapies could be developed for, among other things, treating bone defects.

28. Osiris conducted time-consuming and expensive research in developing MSC-based products and therapies in which they could be used. To protect the fruits of those efforts, Osiris, among other things, filed patent applications that matured into the '239 Patent, which issued in March 2002.

29. In mid-2005, Osiris launched Osteocel®, the first commercial product line in the United States that contained adult (allogeneic mesenchymal) stem cells for use as a transplant. In August 2006, the company went public with an initial public offering that resulted in a valuation of $300 million, making it the second-largest public stem cell company in the United States.

30. Blackstone, founded in 1996, was in the business of developing, marketing and selling medical products for use in spinal surgeries. In or about March 2006, Blackstone entered into an agreement with Osiris whereby Blackstone was authorized to distribute OsteoCel® for use in promoting bone growth. While Osiris sold the product line under the trade name "OsteoCel®," Blackstone sold it under the trade name "Trinity®."

31. In or about September 2006, Blackstone was acquired by Orthofix International N.V. Notwithstanding, the acquisition did not affect the ability of Blackstone/Orthofix to lawfully distribute Trinity®. Blackstone/Orthofix promoted the product line as unique in the field of biologics because, among other things, it was a safe alternative to autologous MSC preparations as evidenced by its failure to provoke a significant immunogenic response upon implantation.

32. In 2008, Osiris decided to divest itself of its OsteoCel® business. On information and belief, both Blackstone/Orthofix and NuVasive appreciated the business' commercial value and, in turn, made offers to acquire the same. In or about May 2008, Osiris accepted NuVasive's $85 million offer and entered into a definitive asset purchase and manufacturing agreement with NuVasive. The transferred product line is now currently being sold by NuVasive under the trade name "OsteoCel® Plus." By virtue of

the sale to NuVasive, Blackstone/Orthofix lost their distributorship rights to the Trinity® product line.

33. In September 2008, on the eve of the close of the asset purchase agreement between Osiris and NuVasive, Blackstone/Orthofix tried to block the sale by filing a lawsuit and seeking injunctive relief. *See Blackstone Med'l, Inc. v. Osiris Thers.*, 08-CV-30145 MAP (D. Mass. 2008). However, because, among other things, Blackstone/Osiris violated the provisions of their distributorship agreement with Osiris (which called for alternative dispute resolution procedures in lieu of court proceedings), Blackstone/Orthofix had no choice but to voluntarily dismiss the suit.

34. Undeterred, Blackstone/Orthofix thereafter partnered with MTF to produce a rival product line that is sold under the trade name "Trinity® Evolution™." This rival product line directly competes with OsteoCel® Plus, and Defendants' selling of the same for use in promoting bone growth squarely infringes upon Plaintiffs' rights in the '239 Patent.

COUNT I – PATENT INFRINGEMENT

35. Upon information and belief, Defendants, acting on their own, and/or in concert with and/or as alter egos or agents of one another, have manufactured, sold, and/or offered for sale in the United States, an allogeneic MSC-based bone growth product line, particularly Trinity® Evolution™.

36. Upon information and belief, Defendants have infringed one or more claims of the '239 Patent in violation of 35 U.S.C. § 271(b) by actively and knowingly inducing others to perform, and, hence, directly infringe, the method claimed in one or more claims of the '239 Patent in the United States, including in this District. Upon further information

and belief, the Defendants' sales and marketing of an allogeneic MSC-based bone growth product line, particularly Trinity® Evolution™, reflects a specific intent on their part to induce others to have performed, and, hence directly infringed, one or more claims of the '239 Patent.

37. Upon information and belief, Defendants have infringed one or more claims of the '239 Patent in violation of 35 U.S.C. § 271(c) by contributing to others' performance and, hence, direct infringement, of the method claimed in one or more claims of the '239 Patent in the United States, including this District, through the sale of an allogeneic MSC-based bone growth product line, particularly Trinity® Evolution™.

38. Upon information and belief, the acts of infringement discussed in paragraphs 35-37 were engaged in with the Defendants' actual knowledge of the '239 Patent and the scope of protection it affords. Hence, the Defendants' infringing conduct has been willful, deliberate, and intentional.

39. Plaintiffs have been and will continue to be irreparably damaged by Defendants' infringement of the '239 Patent.

COUNT II – DECLARATORY JUDGMENT OF PATENT INFRINGEMENT

40. Upon information and belief, Defendants, acting on their own, and/or in concert with and/or as alter egos or agents of one another, will continue to manufacture, sell, or offer for sale in the United States an allogeneic MSC-based bone growth product line, particularly Trinity® Evolution™.

41. Upon information and belief, Defendants will continue to infringe one or more claims of the '239 Patent in violation of 35 U.S.C. § 271(b) by continuing to actively and knowingly inducing others to perform, and, hence, directly infringe, the method

claimed in one or more claims of the '239 Patent in the United States, including in this District. Upon further information and belief the Defendants' continued sales and marketing of an allogeneic MSC-based bone growth product line, particularly Trinity® Evolution™, reflects a specific intent on their part to induce others to perform, and, hence directly infringe, one or more claims of the '239 Patent.

42. Upon information and belief, Defendants will continue to infringe one or more claims of the '239 Patent in violation of 35 U.S.C. § 271(c) by continuing to contribute to others' performance, and, hence, direct infringement, of the method claimed in one or more claims of the '239 Patent in the United States, including this District, through the continued sale of an allogeneic MSC-based bone growth product line, particularly Trinity® Evolution™.

43. Upon information and belief, the acts of infringement discussed in paragraphs 40-42 will be engaged in with the Defendants' actual knowledge of the '239 Patent and the scope of protection it affords. Hence, the Defendants' infringing conduct will be willful, deliberate, and intentional.

44. Plaintiffs will be irreparably damaged by Defendants' continued infringement of the '239 Patent.

45. A judicial declaration that the Defendants' continued manufacture, use, sale, offer for sale, distribution, promotion and/or marketing of an allogeneic MSC-based bone growth product line such as Trinity® Evolution™ constitutes contributory and/or indirect infringement of the '239 Patent is necessary and appropriate so that Plaintiffs may protect their rights in the '239 Patent.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that the Court enter a Judgment against Defendants, including:

a. Adjudging the '239 Patent to be valid and enforceable;

b. Adjudging that Defendants have contributed to and induced infringement of one or more claims of the '239 Patent;

c. Adjudging that Defendants continued manufacture, use, sale, offer for sale, distribution, promotion and/or marketing of an MSC-based bone growth product in the United States, such as Trinity® Evolution™, will constitute contributory and/or induced infringement of the '239 Patent;

d. Permanently enjoining Defendants; their officers, agents, servants, employees, and attorneys; all parent and subsidiary corporations; all assigns and successors-in-interest to the foregoing; and those persons in active concert or participation with any of the foregoing who receive notice of the injunction from engaging in any act of infringement of one or more claims of the '239 Patent, pursuant to 35 U.S.C. § 283;

e. Adjudging that an accounting be had for damages caused by Defendants' infringement, together with pre- and post-judgment interest;

f. Adjudging that Defendants are willful infringers and augmenting the aforesaid damages pursuant to 35 U.S.C. § 284;

g. Adjudging that this case is exceptional and awarding Plaintiffs costs, expenses, and reasonable attorney's fees pursuant to 35 U.S.C. § 285; and

h. Such other and further relief as this Court may deem just and proper.

JURY DEMAND

Pursuant to Fed. R. Civ. P. 38(b), Plaintiffs hereby demand a trial by jury on all issues so triable.

Respectfully submitted,

RIKER, DANZIG, SCHERER, HYLAND & PERRETTI LLP

Dated: April 20, 2010.

By s/ Robert J. Schoenberg

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