

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS**

MASSACHUSETTS INSTITUTE OF
TECHNOLOGY,

and

CHILDREN'S MEDICAL CENTER
CORPORATION,

Plaintiffs,

v.

SHIRE PHARMACEUTICALS, INC.,

and

SHIRE REGENERATIVE
MEDICINE, INC.,

Defendants

Civil Action No. 13-cv-10020

SECOND AMENDED COMPLAINT

Plaintiffs Massachusetts Institute of Technology ("MIT") and Children's Medical Center Corporation ("CMCC") (collectively, "Plaintiffs"), by and through their undersigned counsel, file this Amended Complaint for infringement of United States Patent Nos. 5,759,830, and 5,770,193 (collectively, the "patents-in-suit") against Defendants Shire Regenerative Medicine, Inc. ("SRM") and Shire Pharmaceuticals, Inc. ("Shire Pharmaceuticals") (collectively, "Defendants").

PARTIES

1. MIT is a nonprofit educational corporation organized under the laws of the Commonwealth of Massachusetts and is located at 77 Massachusetts Avenue, Cambridge, Massachusetts 02139.

2. CMCC is a nonprofit corporation organized under the laws of the Commonwealth of Massachusetts and is located at 55 Shattuck Street, Boston, MA 02115.

3. Upon information and belief, defendant SRM is a corporation organized under the laws of the state of Delaware, with a principal place of business at 11095 Torreyana Road, San Diego, CA 92121.

4. Upon information and belief, Shire Pharmaceuticals is a corporation organized under the laws of the state of Delaware, with a principal place of business at 725 Chesterbrook Boulevard, Wayne, PA 19007. Upon information and belief, Shire plc is a public limited company organized under the laws of the Bailiwick of Jersey, with a principal place of business at 5 Riverwalk, Citywest Business Campus, Dublin 24, Republic of Ireland. Upon information and belief, Shire plc is the indirect corporate parent of Shire Pharmaceuticals.

JURISDICTION AND VENUE

5. This action for patent infringement arises under the Patent Act, 35 U.S.C. § 1 *et seq.*

6. This Court has subject matter jurisdiction over these claims pursuant to 28 U.S.C. §§ 1331 and 1338(a).

7. This Court has personal jurisdiction over SRM. Upon information and belief, SRM has engaged and currently engages in continuous and systematic contacts with the Commonwealth of Massachusetts. Specifically, and upon information and belief, SRM has marketed and placed medical products, including the accused product in this case, into the stream of commerce via established distribution channels, with the knowledge, intent, and/or understanding that such products are marketed and/or sold within this District. SRM has purposefully directed sales and marketing of Dermagraft and other products to Massachusetts residents. Furthermore, upon information and belief, SRM has caused injury to Plaintiffs in

Massachusetts based on its infringement within and outside of Massachusetts while regularly doing business in Massachusetts and deriving substantial revenue from goods sold and used in Massachusetts.

8. This Court has personal jurisdiction over Shire Pharmaceuticals. Upon information and belief, Shire Pharmaceuticals engages in continuous and systematic contacts within the Commonwealth of Massachusetts. Upon information and belief, Shire Pharmaceuticals is the parent company of SRM and was, prior to the expiration of the patents-in-suit, directly involved in the manufacturing, marketing, and selling of the accused product in this case, including the offer for sale and sale of accused products in this District.

9. Upon information and belief, Shire Pharmaceuticals recruited, interviewed and hired the sales and sales support personnel for Dermagraft, including personnel who serviced customers in this District. Upon information and belief, upon appointment in April 2013 as Shire plc's Chief Executive Officer, Dr. Flemming Ornskov moved to Massachusetts and established his office in Lexington, Massachusetts. Upon information and belief, Dr. Ornskov reorganized Shire plc's businesses, including the business of SRM, into a simplified, flatter structure, which he called the "One Shire" strategy. Upon information and belief, Dr. Ornskov established an "In-Line" marketed products group consisting of five business units, one of which was the Regenerative Medicine business unit. Upon information and belief, Dr. Ornskov chaired the In-Line marketed products group, and executives of Shire Pharmaceuticals participated in the In-Line marketed products group. Upon information and belief, prior to the expiration of the patent, Dr. Ornskov relieved the then President of SRM of operational responsibilities for portions of the Dermagraft business, and the In-Line marketed products group, with the active participation of Shire Pharmaceuticals, made decisions for and about the Dermagraft business.

Upon information and belief, Shire plc and Shire Pharmaceuticals operated SRM as a division or business unit, and did not treat SRM as a separate corporate entity with independent decision-making authority. Accordingly, upon information and belief, Shire Pharmaceuticals, through the In-Line marketed products group, meeting in Massachusetts, directed infringing activities in Massachusetts and throughout the United States.

10. Upon information and belief, Shire Pharmaceuticals places products into the stream of commerce through distribution channels that it established, with the knowledge, intent, and/or understanding that such products are marketed and/or sold within this District. Shire Pharmaceuticals has purposefully directed sales and marketing of Dermagraft to Massachusetts residents. Furthermore, upon information and belief, Shire Pharmaceuticals has caused injury to Plaintiffs in Massachusetts based on its infringement within and outside of Massachusetts while regularly doing business in Massachusetts and deriving substantial revenue from goods sold and used in Massachusetts.

11. Upon information and belief, venue is proper in this Court pursuant to 28 U.S.C. §§ 1391(b) and (c) because this is the judicial District where (i) a substantial part of the events or omissions giving rise to the claims has occurred and is currently occurring; and (ii) where Defendants are subject to personal jurisdiction.

FACTUAL BACKGROUND

Plaintiffs

12. Plaintiff MIT is a world-renowned education and research institution. The mission of MIT is to advance knowledge and educate students in science, technology, and other areas of scholarship that will best serve the nation and the world. For more than 150 years, MIT

has produced an unending stream of engineering and scientific advancements, many of them world changing.

13. Plaintiff CMCC is the parent organization for The Children's Hospital Corporation which operates Boston Children's Hospital, a comprehensive center for pediatric health care and one of the largest pediatric medical centers in the United States. Boston Children's Hospital is home to the world's largest research enterprise based at a pediatric hospital, with more than 1,000 scientists working at or affiliated with the institution.

The Patents-in-Suit

14. United States Patent No. 5,759,830 (the "'830 patent") entitled "Three-dimensional fibrous scaffold containing attached cells for producing vascularized tissue in vivo" was duly and legally issued to Plaintiffs as assignees by the United States Patent and Trademark Office on June 2, 1998. A true and correct copy of the '830 patent is attached as Exhibit A. Since its date of issue, Plaintiffs have been and still are the owners of the '830 patent.

15. United States Patent No. 5,770,193 (the "'193 patent" and, collectively with the '830 patent, "the patents-in-suit") entitled "Preparation of three-dimensional fibrous scaffold for attaching cells to produce vascularized tissue in vivo" was duly and legally issued to Plaintiffs as assignees by the United States Patent and Trademark Office on June 23, 1998. A true and correct copy of the '193 patent is attached as Exhibit B. Since its date of issue, Plaintiffs have been and still are the owners of the '193 patent.

16. The patents-in-suit both name Dr. Robert Langer and Dr. Joseph Vacanti as inventors. Dr. Langer is an Institute Professor at MIT, and runs one of the world's leading research laboratories studying tissue regeneration. Dr. Vacanti is currently the John Homans Professor of Surgery at Harvard Medical School and a Director of the Laboratory for Tissue

Engineering and Organ Fabrication at Massachusetts General Hospital. Previously Dr. Vacanti served on the surgery staff at Boston Children's Hospital.

The Accused Product

17. Upon information and belief, Defendant SRM manufactured, marketed, and sold Dermagraft, a human fibroblast-derived dermal substitute indicated for use in treatment of full-thickness diabetic foot ulcers. Upon information and belief, Dermagraft is manufactured from human fibroblast cells derived from newborn foreskin tissue. Upon information and belief, during the manufacturing process, the human fibroblasts are seeded onto a bioabsorbable polyglactin three-dimensional mesh scaffold. Upon information and belief, the fibroblasts proliferate to fill the interstices of this scaffold and secrete human dermal collagen, matrix proteins, growth factors, and cytokines to create a three-dimensional human dermal substitute containing metabolically active, living cells.

18. In 2001 the FDA approved Dermagraft for use in connection with treatment of full-thickness diabetic foot ulcers of greater than six weeks duration that extend through the dermis, but without tendon, muscle, joint capsule, or bone exposure.

19. In 2006, upon information and belief, SRM (then known as Advanced BioHealing, Inc.) acquired rights to Dermagraft. Upon information and belief, SRM began manufacturing and selling Dermagraft in the United States in 2007.

20. Upon information and belief, in 2011 Shire Pharmaceuticals acquired Advanced BioHealing, Inc., and in 2012 renamed the company Shire Regenerative Medicine.

21. On June 22, 2011 and July 27, 2011, MIT sent correspondence to both SRM and Shire Pharmaceuticals respectively, informing them of the patents-in-suit and inviting them to engage in discussions with MIT regarding the patents-in-suit. MIT received no response to its

letters. Copies of the 2011 correspondence to SRM and Shire Pharmaceuticals (collectively, the “2011 Letters”) are attached as Exhibit C and Exhibit D, respectively.

22. SRM and Shire Pharmaceuticals had actual knowledge of the existence of the patents-in-suit at least as early as June and July 2011, respectively, when they received the 2011 Letters. The 2011 Letters informed Defendants that the patents-in-suit were examples of patents owned by MIT that covered tissue engineering and regenerative medicine. The 2011 Letters also invited Defendants to engage in licensing discussions concerning Dermagraft, which was SRM’s only engineered tissue, regenerative medicine commercial product. Although the 2011 Letters did not allege infringement, in view of the 2011 Letters’ invitation to “licens[e] relevant MIT technology,” it would have been prudent for Defendants to perform an analysis of the patents-in-suit to determine whether Dermagraft infringed them, and whether they were relevant MIT technology.

23. Furthermore, had Defendants performed an analysis of the patents-in-suit, they would have discovered that the claims require a “fibrous, three-dimensional scaffold composed of fibers of a biocompatible, biodegradable, synthetic polymer.” According to Dermagraft product literature, “Dermagraft® is grown on a bioabsorbable mesh. The mesh provides a three-dimensional scaffolding to facilitate cell growth and tissue formation during the manufacturing process,” exactly as required by the claims. Defendants would have discovered that the claims require “cells derived from a vascularized tissue attached in vitro to the surface of the fibers of the scaffold.” According to Dermagraft product literature, “Dermagraft is manufactured from human fibroblast cells derived from newborn foreskin tissue,” which is a vascularized tissue. Likewise, Defendants would have discovered that the other limitations of the claims, requiring

sufficient attachment area, maximum diffusion distance and diffusion sufficient to maintain cell viability, are also present.

24. On November 7, 2012, MIT and CMCC sent correspondence to SRM, a copy of which is attached (without its original attachments) as Exhibit E (the “2012 Letter”), notifying SRM of MIT and CMCC’s belief that Dermagraft infringes the patents-in-suit. The 2012 Letter expressly referred to and attached the 2011 Letter to Shire Pharmaceuticals.

25. Both SRM and Shire Pharmaceuticals also had actual notice of MIT’s assertion that Dermagraft infringed the patents-in-suit upon filing of the original Complaint in this action.

COUNT I
(Infringement of United States Patent No. 5,759,830)

26. Plaintiffs repeat and reallege the allegations contained in paragraphs 1 through 25 above as if fully set forth herein.

27. SRM has infringed, either literally or under the doctrine of equivalents, one or more claims of the ‘830 patent under 35 U.S.C. § 271(a), by the manufacture, use, offer to sell, sale, or importation of Dermagraft, including the sale of Dermagraft in this District.

28. Upon information and belief, prior to the expiration of the patents-in-suit, Shire Pharmaceuticals recruited, interviewed and hired sales and sale support personnel to sell and support Dermagraft, and thereby directed activities that infringed the ‘830 patent. Upon information and belief, prior to the expiration of the patents-in-suit, Shire Pharmaceuticals directed SRM’s infringement of the ‘830 patent through the In-line marketed products group. Shire Pharmaceuticals knew, or should have known, that SRM’s manufacturing and sale of Dermagraft infringed the ‘830 patent.

29. Upon information and belief, Shire Pharmaceuticals actively induced, with the specific intent to induce, under 35 U.S.C. § 271(b), SRM’s infringement of one or more claims

of the '830 patent and knew or should have known that their actions would induce SRM to infringe.

30. Upon information and belief, Defendants' infringement was willful despite knowledge of the '830 patent. Upon information and belief, Defendants acted despite an objectively high likelihood that their actions constituted infringement of a valid patent, and that objectively-defined risk was either known or so obvious that it should have been known to Defendants.

31. Plaintiffs have been damaged by Defendants' infringement and/or inducement of infringement of the '830 patent.

COUNT II
(Infringement of United States Patent No. 5,770,193)

32. Plaintiffs repeat and reallege the allegations contained in paragraphs 1 through 31 above as if fully set forth herein.

33. SRM has infringed, either literally or under the doctrine of equivalents, one or more claims of the '193 patent under 35 U.S.C. § 271(a), by the manufacture of Dermagraft.

34. SRM has actively induced infringement under 35 U.S.C. § 271(b) and contributed to the infringement, under 35 U.S.C. § 271(c), of one or more claims of the '193 patent, either literally or under the doctrine of equivalents.

35. SRM sold and offered to sell Dermagraft in the United States for treatment of diabetic foot ulcers, together with instructing, directing, and/or advising others how to carry out methods of treatment that infringe one or more claims of the '193 patent.

36. SRM sold Dermagraft with a package insert that includes instructions for treating diabetic foot ulcers in a manner that infringes one or more claims of the '193 patent. When physicians or others use Dermagraft according to the instructions set forth in the package insert

provided by SRM, such acts constitute direct infringement of one or more claims of the '193 patent, either literally or under the doctrine of equivalents.

37. SRM knew or should have known that its actions would induce others to infringe the '193 patent, had a specific intent to induce infringement, and knew that Dermagraft was especially made or adapted for use in an infringing manner. Dermagraft is a material component of the inventions claimed in the '193 patent and is not a staple article of commerce capable of substantial noninfringing use.

38. Upon information and belief, prior to the expiration of the patents-in-suit, Shire Pharmaceuticals recruited, interviewed and hired sales and sale support personnel to sell and support Dermagraft, and thereby directed activities that infringed the '193 patent. Upon information and belief, prior to the expiration of the patents-in-suit, Shire Pharmaceuticals directed SRM's infringement of the '193 patent through the In-line marketed products group. Shire Pharmaceuticals knew, or should have known, that SRM's manufacturing and sale of Dermagraft infringed the '193 patent.

39. Upon information and belief, Shire Pharmaceuticals has induced, with the specific intent to induce, under 35 U.S.C. § 271(b), SRM's infringement of one or more claims of the '193 patent and knew or should have known that their actions would induce SRM to infringe.

40. Upon information and belief, Defendants' infringement was willful despite knowledge of the '193 patent. Upon information and belief, Defendants acted despite an objectively high likelihood that their actions constituted infringement of a valid patent, and that objectively-defined risk was either known or so obvious that it should have been known to Defendants.

41. Plaintiffs have been damaged by Defendants' infringement or inducement of and/or contributory infringement of the '193 patent.

PRAYERS FOR RELIEF

WHEREFORE, Plaintiffs respectfully request the following relief:

- a. That the Court award damages arising out of Defendants' direct and indirect infringement of the '830 patent, including enhanced damages, together with prejudgment and post-judgment interest;
- b. That the Court award damages arising out of Defendants' direct and indirect infringement of the '193 patent, including enhanced damages, together with prejudgment and post-judgment interest;
- c. That this Court declare that this is an exceptional case and Plaintiffs be awarded their costs and reasonable attorneys' fees in this action as provided by 35 U.S.C. § 285 or as otherwise permitted by law; and
- d. That this Court award Plaintiffs such other and further relief that this Court deems just and proper.

JURY DEMAND

Plaintiffs demand a trial by jury of all claims so triable.

Dated: February 21, 2014

Respectfully submitted,

MASSACHUSETTS INSTITUTE OF
TECHNOLOGY and CHILDREN'S
MEDICAL CENTER CORPORATION

By their attorneys,

/s/ Daryl L. Wiesen

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CERTIFICATE OF SERVICE

I, Daryl L. Wiesen, hereby certify that this document filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies will be sent to those indicated as non-registered participants on February 21, 2014.

/s/ Daryl L. Wiesen