IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

SHIRE VIROPHARMA INCORPORATED,	)	
	)	
Plaintiff,	)	
	)	
v.	)	C.A. No. 17-_____
	)	
CSL BEHRING LLC,	)	
	)	
Defendant.	)	

COMPLAINT

Plaintiff Shire ViroPharma Incorporated ("Shire"), by its undersigned attorneys, brings this action against defendant CSL Behring LLC ("CSL") and hereby alleges as follows:

NATURE OF THE ACTION

1. This action for patent infringement and declaratory judgment is brought pursuant to the patent laws of the United States, 35 U.S.C. § 1 *et seq.*, and the Federal Declaratory Judgment Act, 28 U.S.C. § 2201 *et seq.* Shire seeks judgment that CSL has infringed, is infringing, and/or will infringe, and/or has induced, is inducing, and/or will induce others to infringe U.S. Patent No. 9,616,111 (the "'111 Patent"), attached hereto as Exhibit 1.

PARTIES

2. Plaintiff Shire ViroPharma Incorporated is a Delaware corporation, with a principal place of business located at 300 Shire Way, Lexington, MA 02421.

3. Shire is a global biotechnology company focused, *inter alia*, on serving people with rare diseases and other highly specialized conditions.

4. On information and belief, CSL is a Delaware limited liability company, with its principal place of business located at 1020 First Avenue, King of Prussia, PA 19406.

5. On information and belief, CSL is in the business of developing, manufacturing, and marketing pharmaceutical drug products and biologics and selling them throughout the United States and the world.

JURISDICTION AND VENUE

6. This Court has subject matter jurisdiction over this action, pursuant to 28 U.S.C. §§ 1331, 1338(a), 2201 and 2202, because the action arises under the patent laws of the United States and the Federal Declaratory Judgment Act.

7. This Court has general personal jurisdiction over CSL because CSL is incorporated in Delaware and because CSL knowingly transacts business in Delaware and, on information and belief, has engaged in, and made meaningful preparations to engage in, imminent infringing conduct in Delaware.

8. Venue is proper in this Court pursuant to 28 U.S.C. §§ 1391(b), and 1400(b), because the defendant resides in Delaware, is subject to personal jurisdiction in Delaware, transacts business in Delaware and, on information and belief, has committed, or made meaningful preparations to commit, acts of infringement in Delaware.

SHIRE'S '111 PATENT

9. Hereditary angioedema ("HAE") is a rare genetic disorder causing insufficient natural production of functional or adequate amounts of a protein called C1 esterase inhibitor. This protein is needed to help regulate several complex processes involved in immune system function (complement, contact system) and fibrinolytic system function (blood clotting, bleeding). The main function of C1 esterase inhibitor is to prevent the spontaneous activation of the complement system, which can cause local or systemic inflammation. Patients suffering

from HAE experience symptoms including unpredictable, recurrent attacks of swelling commonly affecting the hands, feet, arms, legs, face, abdomen, tongue, genitals, and larynx.

10. HAE can be treated by administering to patients with the disorder a drug product containing a C1 esterase inhibitor in order to restore the levels of C1 esterase inhibitor to levels sufficient to prevent or reduce the frequency or severity of HAE attacks.

11. Shire, including through corporate affiliates, makes and sells products for the treatment of HAE, including CINRYZE, FIRAZYR, and KALBITOR products, along with other products in development, namely, products currently known as SHP616 and SHP643.

12. CINRYZE contains a human plasma-derived C1 esterase inhibitor as its active ingredient. CINRYZE currently is the only C1 esterase inhibitor replacement therapy approved by the United States Food and Drug Administration (the "FDA") for routine prophylactic treatment of angioedema attacks in adolescent and adult patients with HAE. It is indicated for intravenous ("IV") administration at a concentration of 100 U/mL of human C1 esterase inhibitor. CINRYZE is sold by plaintiff Shire.

13. FIRAZYR is a peptide drug product approved for subcutaneous administration to treat acute attacks of HAE.

14. KALBITOR is a subcutaneously administered plasma kallikrein inhibitor indicated for treatment of acute attacks of HAE.

15. Shire and its affiliates are in the process of developing certain other products for the treatment of HAE, including a prophylactic C1 esterase inhibitor treatment to be administered subcutaneously rather than intravenously (known as SHP616), as well as lanadelumab, a human monoclonal anti-kallikrein antibody for subcutaneous self-administration for routine prophylaxis of angioedema attacks in patients with HAE (known as SHP643).

16. On April 11, 2017, the United States Patent and Trademark Office lawfully issued the '111 patent, entitled "C1-INH Compositions and Methods for the Prevention and Treatment of Disorders Associated with C1 Esterase Inhibitor Deficiency."

17. The claims of the '111 patent are directed generally to methods "for treating hereditary angioedema (HAE) . . . comprising subcutaneously administering . . . a composition comprising a C1 esterase inhibitor, a buffer selected from citrate or phosphate, and having a pH ranging from 6.5-8.0, wherein the C1 esterase inhibitor is administered at a concentration of at least about 400 U/mL and a dose of at least about 1000 U. . . " The administration of the composition "increases the level of C1 esterase inhibitor in the blood of the subject to at least about 0.4 U/mL," and "the C1 esterase inhibitor comprises an amino acid sequence at least 95% identical to residues 23 to 500 of SEQ ID NO:1," which amino acid sequence is identified in the '111 patent.

18. Shire is the assignee and owner of all rights, title, and interest in the '111 patent, and has the right to sue for past and present infringement.

CSL'S PLANS TO MARKET AND SELL HAEGARDA

19. On information and belief, in the next few months, CSL intends to begin selling in the United States a prophylactic C1 esterase inhibitor treatment for subcutaneous administration. CSL will market its new C1 esterase inhibitor product as "HAEGARDA."

20. CSL's HAEGARDA product has infringed, is infringing, and/or will infringe and/or has induced, is inducing, and/or will induce others to infringe the '111 patent, and CSL has taken and is taking meaningful steps to infringe or to induce others to infringe the '111 patent.

21. On August 30, 2016, CSL announced that it had filed the HAEGARDA Biologics License Application ("BLA") with the FDA, seeking regulatory approval to sell HAEGARDA. The FDA accepted the HAEGARDA BLA on August 30, 2016. A true copy of CSL's press release, dated August 30, 2016, is attached hereto as Exhibit 2.

22. In order to file the BLA, CSL had to complete phase III clinical trials for HAEGARDA. 21 CFR 601.

23. In the United States, FDA regulatory approval typically takes no longer than one year from the date of BLA filing. 21 U.S.C. § 379(g). Accordingly, Shire is informed and believes that CSL will obtain regulatory approval for HAEGARDA no later than August 2017.

24. CSL has publicly stated that it anticipates HAEGARDA will receive FDA approval and launch in the second half of 2017. On February 15, 2017, CSL's CEO, Paul Perreault, stated: "[T]he U.S. FDA accepted for review the Biologics License Application for CSL 830, also known as Haegarda. . . . [It] is also expected to be approved and launched in the US in the second half of this calendar year." A true copy of CSL's interim earnings presentation is attached hereto as Exhibit 3.

25. Numerous analysts and thought leaders in the pharmaceutical industry have also publicized their understanding regarding the timing of HAEGARDA's approval and launch, confirming that the product will launch in or around the summer of 2017. *See* Exhibit 4, January 27, 2017 Leerink Analysis ("CSL's Haegarda – will likely have an FDA action date in the 2H'17. . . . According to CSL, the Haegarda NDA has been accepted and we would expect the FDA to approve the drug in 2H'2017"); Exhibit 5, January 19, 2017 Credit Suisse Analysis ("A near-term catalyst is the outcome of the FDA review for CSL's Haegarda (subcutaneous C1 esterase product), anticipated mid-CY17"); Exhibit 6, January 19, 2017 UBS Analysis ("Into the

medium term, CSL remains very optimistic on SubQ Berinert (Haegarda) for hereditary angioedema to triple sales off US$250m base over next 5 yrs"); Exhibit 7, January 18, 2017 Morningstar Analysis ("CSL recently announced that the U.S. Food and Drug Administration, or FDA, had accepted its Biologics License Application for review of CSL830. This is typically the final step before marketing and product launch subject to approval. . . . Given median FDA review times, we expect potential approval by mid-calendar 2017 with launch shortly after in the United States").

26. On information and belief, CSL representatives at the November 10-14, 2016 Conference for the American College of Allergy, Asthma & Immunology publicly indicated that approval and launch are likely to occur as soon as June 2017. A CSL Sales Manager and a CSL Field Medical Team Director each stated that CSL was aiming to launch HAEGARDA in June 2017. A CSL Senior Global Clinical Program Director confirmed that launch was planned for "mid-2017," while a CSL Manager of Regulatory added that launch would be in the "second half of the year, probably earlier on."

27. CSL's public statements confirm its intention to market and sell HAEGARDA in the United States upon FDA approval. On February 15, 2017, Perreault stated: "A really exciting development for CSL is that it will be the first subcutaneous prophylactic therapy available on the market to prevent hereditary angioedema attacks. And given its safety profile, we believe Haegarda will become the standard of care for hereditary angioedema patients. . . . This is, in my view, a game changer for the treatment of HAE and for the lives of patients living with the disease. I'm sure most of you are familiar with the data, it's truly outstanding. We have high expectations for this product and we expect it will be a significant driver for us in the near to medium term." Exhibit 3.

28. On November 30, 2016, CSL's Executive Vice President of Global Commercial Operations, Robert Repella, stated: "Haegarda, I think it's pretty clear that this product changes the game in HAE. It clearly will be positioned in the marketplace as the product that's most effective in preventing attacks . . . when you add on top of it, the convenience of subcutaneous, we have high expectations for what this product can do for both patients and our business in the specialty segment. . . . [W]hen you look at our combined portfolio of Berinert for acute treatment and of course, Haegarda for prophylaxis and preventing attacks, we're looking at a revenue potential of somewhere in the range of $750 million to $1 billion . . . . So we do expect this to be a significant growth driver for us going forward." A true copy of the S&P Capital IQ Call, dated November 30, 2016, is attached hereto as Exhibit 8.

29. In anticipation of FDA approval to market and sell HAEGARDA in the United States, Shire is informed and believes that CSL has been and is making meaningful preparations to market and sell HAEGARDA in the United States.

30. CSL filed a United States trademark application for "HAEGARDA" on January 6, 2016, seeking to protect the mark for "pharmaceutical preparations, namely, C1 inactivator for the treatment of hereditary angioedema." Exhibit 9.

31. CSL has also announced an expansion of its production capability with respect to its existing IV treatment for HAE (Berinert) and the new subcutaneous treatment for HAE (HAEGARDA). Both drugs are derived from human plasma. In August 2015, Perreault stated: "We started our project to expand the Berinert production capacity, anticipating the R&D coming through on our Berinert subcutaneous high volume product – high concentration product." A true copy of CSL's Q4 Earnings Call Transcript, dated August 11, 2015, is attached hereto as Exhibit 10. More recently, on February 15, 2017, Perreault added: "We're currently

opening [plasma centers] at a run rate of two to three centers per month, not an easy exercise." Exhibit 3.

32. On information and belief, CSL plans to manufacture and package its HAEGARDA product in the same facilities it already has set up and fully operational for the manufacture and packaging of Berinert.

33. On information and belief, CSL plans to boost its staff in the first half of 2017 to support HAEGARDA. According to a CSL Senior Director of Global Commercial Development, "[CSL] plans to modestly boost [its] Medical Field staffing numbers, and should begin that process around Spring 2017" in preparation for the launch of HAEGARDA.

34. On information and belief, in connection with the launch of HAEGARDA, CSL intends to expand its "Berinert Expert Network" ("B.E.N."), which is an existing resource for HAE patients using Berinert, CSL's IV product. According to one CSL Senior Product Manager, "The plan, for now at least, is to expand out our B.E.N. resource program for patients so that it'll highlight the [HAEGARDA] formulation. What's so great about B.E.N. is that we have online marketing geared for HAE patients that's in the words and video of actual HAE patients who are on Berinert, which we'll re-fresh for [HAEGARDA] once it's launched. The other cool thing about it is that the focus is on stealthily influencing patients to do their own homework, get educated about other treatment options, even network with the other HAE patients that we've connected them to in order to get smart before they go into see their doctor. This way they'll be empowered about their treatment and be able to ask for [HAEGARDA] even if their doctor doesn't bring it up."

35. On information and belief, as evidenced by the various public statements by CSL and/or CSL representatives described herein, CSL has made and continues to make meaningful

preparation to sell its infringing HAEGARDA product on the date when or shortly after it receives FDA approval later this year.

CSL'S INFRINGING CONDUCT

36. CSL's imminent manufacture, importation, use, sale, and/or offer to sell HAEGARDA in the United States has infringed, and/or will infringe, and/or will induce others to infringe, either directly or under the doctrine of equivalents, one or more claims, including at least claims 1, 2, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, 15, 16, and 17 of Shire's '111 patent.

37. Shire's '111 patent claims a method for treating HAE by subcutaneously administering a composition comprising a C1 esterase inhibitor, a buffer selected from citrate or phosphate and having a pH ranging from 6.5-8, wherein the C1 esterase inhibitor is administered at a concentration of at least about 400 U/mL and a dose of at least about 1000 U, and wherein the administration of the composition comprising the C1 esterase inhibitor increases the level of C1 esterase inhibitor in the blood to at least about 0.4 U/mL, and wherein the C1 esterase inhibitor comprises an amino acid sequence at least 95% identical to residues 23 to 500 of SEQ ID NO:1, as disclosed in the patent.

38. As described above, CSL has stated that CSL830 is another name for HAEGARDA. CSL830 was the subject of a recent published study. Zuraw, B.L., et al., "Phase II study results of a replacement therapy for hereditary angioedema with subcutaneous C1-inhibitor concentrate," Allergy 70: 1319–1328 (2015) (hereinafter, "Zuraw Study," attached hereto as Exhibit 11).

39. The Zuraw Study confirmed that CSL830 (HAEGARDA) will be used as a "replacement therapy for hereditary angioedema with subcutaneous C1 inhibitor concentrate." The "final concentration of CSL830 is 500 IU/ml." Exhibit 11 at p. 1320. The Zuraw Study

found that subcutaneous administration of "CSL830 administered twice-weekly for 4 weeks leads to a dose-dependent increase in functional C1-INH activity and C4 levels, with the 3000 and 6000 IU doses achieving constant C1-INH activity levels above 40%. C1-INH functional levels approached the range of normal C1-INH values of healthy subjects with the 6000 IU dose." Zuraw at p. 1326. The Zuraw Study concluded that "C1-INH replacement through repeated SC dosing of a volume-reduced C1-INH concentrate (CSL830) led to a predictable dose-dependent increase in functional C1-INH levels in patients with mild-to-moderate HAE. Furthermore, consistent and sustained steady-state C1-INH levels reached values that are predicted to be efficacious in preventing angioedema attacks." Exhibit 11 at p. 1326.

40. The Medical Director of CSL Behring's Canadian arm also confirmed that the HAEGARDA formulation is "already available" in Canada, having been marketed as "Berinert 1500" for IV use in treating acute HAE attack.

41. Berinert 1500 contains 1500 IU of lyophilized C1 esterase inhibitor at a concentration of 500 IU/ml and contains sodium citrate (a citrate buffer). The C1 esterase inhibitor in Berinert 1500 inhibitor is derived from human plasma. Moreover, Berinert 1500 is lyophilized powder to be reconstituted in liquid form for injection.

42. The publicly available information regarding CSL830 and Berinert 1500 demonstrate that CSL's planned marketing and sales of HAEGARDA in the United States infringes, will imminently infringe, and/or actively induce others to infringe the '111 patent.

43. On information and belief, the HAEGARDA product label will direct that the product be administered in a way that necessarily infringes and/or will infringe the '111 patent.

44. On information and belief, CSL (a) has knowledge of the '111 patent and had knowledge of the application prior to issuance of the patent; (b) has knowledge of the acts of

infringement that will occur and/or are occurring when the HAEGARDA product is administered; and (c) has the specific intent to cause direct infringement when the HAEGARDA product is administered.

COUNT I
(Declaratory Judgment of Infringement of U.S. Patent No. 9,616,111)

45. Shire re-alleges, and incorporates herein by reference, the allegations of the preceding paragraphs of this Complaint as if fully set forth herein.

46. On information and belief, CSL has made meaningful preparations to market and sell its HAEGARDA product, which will imminently infringe and/or actively induce others to infringe the '111 patent, including:

(a) completing its collection of data from phase III clinical trials for HAEGARDA;

(b) filing its BLA with the FDA for regulatory approval to sell HAEGARDA;

(c) announcing the impending launch of the product;

(d) obtaining trademark registration for HAEGARDA;

(e) hiring personnel to facilitate the production and sale of HAEGARDA;

(f) opening new plasma-collection centers to facilitate the production of HAEGARDA;

(g) expanding the patient resource network in anticipation of launch of the product, in order to elicit interest in HAEGARDA; and

(h) manufacturing commercial quantities of HAEGARDA in preparation for launch in the United States.

47. Upon receipt of regulatory approval to sell HAEGARDA in the United States, CSL's manufacture, importation, use, sale, and/or offer to sell HAEGARDA in the United States will infringe and/or induce others to infringe, either literally or under the doctrine of equivalents, one or more claims of the '111 patent.

48. Although, upon information and belief, CSL is aware of the '111 patent, CSL refuses to desist from continued and impending infringement of the '111 patent, such that a concrete controversy now exists between Shire and CSL.

49. CSL's actions have created a reasonable apprehension of Shire's imminent harm and loss resulting from CSL's threatened (and actual) actions. CSL's violation of Shire's exclusive rights under the '111 patent will cause Shire significant and irreparable injury.

50. Unless CSL is permanently enjoined by this Court from making, using, selling, and/or offering to sell, its HAEGARDA product, the administration of which infringes or imminently will infringe the '111 patent, Shire will be substantially and irreparably harmed by CSL's infringing conduct.

51. Shire seeks a judicial determination that CSL is infringing, and/or will infringe, and/or is currently inducing infringement, and/or upon FDA approval will infringe and/or induce infringement, of one or more claims of the '111 patent by making, importing, using, selling, and/or offering for sale HAEGARDA. Such a determination and declaration is necessary and appropriate in order that the parties may ascertain their rights and duties.

COUNT II
(Infringement of U.S. Patent No. 9,616,111)

52. Shire re-alleges, and incorporates herein by reference, the allegations of the preceding paragraphs of this Complaint as if fully set forth herein.

53. CSL has infringed, is infringing, will infringe, and/or has induced, is inducing, and/or will induce others to infringe, the '111 patent, either literally or under the doctrine of equivalents, by making, importing, using, selling, and/or offering for sale HAEGARDA for use in the methods claimed in the '111 patent.

54. CSL has not obtained a license to the '111 patent.

55. Unless CSL is permanently enjoined by this Court from making, importing, using, selling, and/or offering for sale its HAEGARDA product for use in the methods claimed in the '111 patent, Shire will be substantially and irreparably harmed by CSL's infringing conduct.

56. Shire seeks damages in an amount adequate to compensate Shire for CSL's infringement and a permanent injunction barring CSL from infringing and/or inducing others to infringe Shire's '111 patent.

PRAYER FOR RELIEF

WHEREFORE, the plaintiffs respectfully request:

(a) That the Court determine that CSL will imminently infringe, and/or will induce others to infringe, one or more claims of United States Patent No. 9,616,111;

(b) That the Court determine that CSL has infringed and/or is inducing others to infringe, one or more claims of United States Patent No. 9,616,111;

(c) That the Court enter a permanent injunction precluding CSL, and all persons in active concert or participation with them, from making, importing, using, selling, or offering to sell in the United States a product that necessarily will be administered to patients in a way that infringes one or more claims of United States Patent No. 9,616,111;

(d) That the Court determine the amount of damage caused to Shire by CSL's unlawful conduct and enter judgment for Shire in the amount of its damages, plus interest and the costs of this action;

(e) That the Court determine that this case is exceptional, within the meaning of 35 U.S.C. § 285, and order CSL to pay Shire's reasonable attorneys' fees pursuant to 35 U.S.C. § 285; and

(f) That the Court grant such other and further relief as it deems appropriate.

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