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ILLUMINA, INC.,
UNIVERSITY OF WASHINGTON and
UAB RESEARCH FOUNDATION

UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF CALIFORNIA

ILLUMINA, INC., UNIVERSITY OF WASHINGTON AND UAB RESEARCH FOUNDATION, Plaintiffs, v. OXFORD NANOPORE TECHNOLOGIES LTD. AND OXFORD NANOPORE TECHNOLOGIES, INC., Defendants.	Case No. **'16CV0477 LAB MDD** **COMPLAINT FOR PATENT INFRINGEMENT** **DEMAND FOR JURY TRIAL**

Plaintiffs Illumina, Inc., University of Washington and UAB Research Foundation for their complaint allege as follows:

THE PARTIES

1. Plaintiff University of Washington is a public institution of higher education and an agency of the State of Washington having its principal place of business in the city of Seattle, Washington. UW CoMotion (formerly the UW Center

for Commercialization) is the department of University of Washington responsible for the licensing of university-owned intellectual properties, including patents.

2. Plaintiff UAB Research Foundation is a non-profit corporation organized under the laws of the State of Alabama and having its principal place of business in Birmingham, Alabama. Although the UAB Research Foundation retained its status as a separate corporate entity and still holds ownership rights in the patents-in-suit, it is now an affiliate of the University of Alabama at Birmingham's Institute for Innovation and Entrepreneurship.

3. Plaintiff Illumina, Inc. is a publicly traded corporation organized under the laws of the State of Delaware and having its principal place of business in the city of San Diego, California. Illumina, founded in 1998, is a leading developer, manufacturer, and marketer of life science tools and integrated systems for the analysis of genetic variation and function. Illumina is the market leader in genome sequencing, offering a broad range of genome sequencing instruments and components to meet the needs of scientists and researchers. Illumina's HiSeq X sequencing products recently achieved a milestone that researchers pursued for decades—scientists using Illumina's HiSeq X series can now sequence the entire human genome for under $1,000. Illumina continues to innovate and develop even better sequencing products. One of Illumina's approaches involves sequencing using nanopores, which, in this context, are small pores formed using various proteins. The patents-in-suit protect those nanopores and other important tools associated with this approach.

4. Defendant Oxford Nanopore Technologies Ltd. ("ONT") is a corporation organized under the laws of England and Wales, and, on information and belief, has its principal place of business located at Edmund Cartwright House, 4 Robert Robinson Avenue, Oxford Science Park, Oxford, OX4 4GA, UK and has an additional business location in Cambridge, UK. On information and belief, ONT designs, manufactures, has manufactured, uses, offers for sale, sells and/or imports into

the United States, Msp nanopores and sequencing products containing Msp nanopores, including but not limited to, MinION and PromethION, and/or components thereof.

5. Defendant Oxford Nanopore Technologies, Inc. is a corporation organized under the laws of Delaware, and, on information and belief, has its principal place of business located at 1 Kendall Square, Cambridge, MA 02139. On information and belief, Oxford Nanopore Technologies, Inc. is a wholly-owned subsidiary of ONT. On information and belief, Oxford Nanopore Technologies, Inc. designs, manufactures, has manufactured, uses, offers for sale, sells and/or imports into the United States, Msp nanopores and sequencing products containing Msp nanopores, including but not limited to MinION and PromethION, and/or components thereof.

JURISDICTION AND VENUE

6. This action arises under the patent laws of the United States, 35 U.S.C. § 1 *et seq.*, and thus this Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

7. This Court has personal jurisdiction over each of the Defendants consistent with the requirements of California Code of Civil Procedure § 410.10 and the Due Process Clause of the United States Constitution. Each Defendant has committed and continues to commit acts of patent infringement in California (and in this District) as alleged in this Complaint. For example, the Defendants have imported and used the accused MinION and PromethION devices in the United States, including at the American Society of Human Genetics annual meeting held from October 18 through October 22, 2014, in San Diego, California. *See* Exhibits 3, 4, and 5. As another example, ONT imported and used the MinION and PromethION devices in the United States, including at the Plant and Animal Genome XXIV conference in San Diego, California held from January 9-13, 2016. See Exhibits 6, 7, 8.

8. Venue is proper in this District under 28 U.S.C. §§ 1391 and 1400(b) because Defendants are subject to personal jurisdiction in this District, have committed

acts of patent infringement in this District in this District. Moreover, Illumina has its principal place of business in this District.

GENERAL ALLEGATIONS

9. Plaintiffs University of Washington and UAB Research Foundation co-own all rights, titles, and interests in and to U.S. Patent No. 8,673,550, entitled "Msp Nanopores and Related Methods," which was duly and legally issued on March 18, 2014. *See* Exhibit 1. Plaintiffs University of Washington and UAB Research Foundation also co-own all rights, titles, and interests in and to U.S. Patent No. 9,170,230, entitled "Msp nanopores and related methods," which was duly and legally issued on October 27, 2015. *See* Exhibit 2. The '550 and '230 patents are valid and enforceable. Illumina is the exclusive licensee of the '550 and '230 patents in the field of nucleic acid sequencing.

10. The patents-in-suit solve a difficult problem that had prevented nanopore sequencing from progressing—namely, scientists did not have a nanopore with the right characteristics to allow DNA to pass into the pore in a way that would generate current fluctuations that correlated with the identity of each individual base. At the time the inventors of the patents-in-suit began their project, almost everyone else was investigating protein nanopores made from α-hemolysin (α–HL), a protein derived from the *Staphylococcus aureus* bacteria. The conventional wisdom was that α–HL nanopores would be the key to sequencing was reflected in U.S. Patent No. 5,795,782, which was filed in 1995. For well over a decade after the '782 patent was filed, α–HL was considered the ideal protein nanopore to investigate.

11. Against this backdrop, the inventors of the patents-in-suit took an entirely different approach and began investigating nanopores made from a protein derived from *Mycobacterium smegmatis*. The inventors applied for a research grant in 2006 for projects where "the possible outcomes of the proposed feasibility study are unclear and it is not possible to propose sufficiently clear-cut and quantitative milestones for administrative evaluation." After many challenges, including skepticism from other

scientists that *Mycobacterium smegmatis* porin (Msp) would work, the inventors eventually showed that Msp is a far more promising type of nanopore than anyone expected. The inventors' work has shown that Msp is far better than even α–HL because, for example, it generates a signal that is 10-times stronger than that obtained with α–HL.

12. When the inventors published their remarkable results with Msp, others in the field immediately took notice and recognized the value of their work. For example, a 2010 article entitled "Proof-of-Principle Study Shows MspA is Superior to Alpha-Hemolysin for Protein Nanopore Sequencing," quoted several independent researchers who recognized that the inventors discovered a superior nanopore that finally enabled nanopore sequencing:

> Efforts to sequence DNA by threading it through protein-based nanopores have traditionally relied on one protein: alpha-hemolysin. But researchers from the University of Washington have diverged from that route, demonstrating in a recent proof-of-principle study that engineered Mycobacterium smegmatis porin A could yield a superior nanopore.
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> ***
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> "It's a proof of principle that nanopore sequencing is going to work. Now it's just a matter of fine-tuning the method," said David Deamer, a chemist at the University of California, Santa Cruz, who was not affiliated with the study but who also works with protein nanopores.
>
> "This is very impressive work that has, for the first time, generated real experimental data that mirrors the idealized cartoon where the nanopore current flips between four steady current levels, one corresponding to each base," said Ken Healy a physicist at the University College Cork in Ireland, and part of a University of Pennsylvania team that recently demonstrated DNA translocation through a graphene nanopore (IS 8/3/2010).

See Exhibit 9. Likewise, a scientist at Life Technologies, another company in the sequencing market, sent one of the inventors a glowing e-mail in 2012 about their results with Msp nanopores and expressed interest in licensing their technology:

> Lost in the frenzy around Oxford, seems no one noticed that you are the first person to ever show any actual sequencing AT ALL with a protein nanopore, and also the first to show directing reading of sequence BY ANY means of more than a few contiguous bases… which is an historic achievement. Congratulations!
>
> ***

> [I]s your technology still open for licensing and development? I do not know how you have proceeded with it, and whether you already have commitments to other parties. If there is still opportunity open, we should discuss.

See Exhibit 10 (capitalized words in original).

13. Illumina also recognized the commercial potential of the inventors' work. In May 2013, Illumina took an exclusive license to the patent applications covering their technology. The '550 patent was the first to issue from the inventors' work, and it did so in March 2014. The '230 patent subsequently issued on October 27, 2015.

14. Defendants learned of the inventors' work and recognized the value of using Msp porins for sequencing. ONT contacted the inventors in 2009-2011 about potentially commercializing the inventors' nanopore technology, as shown by the following exemplary statements:

- "Having read and discussed your recent publications, we would be most interested in exploring ways in which we could work with you and hopefully help commercialise your technology." Exhibit 11 (4/10/09 e-mail from Spike Willcocks, Business Development Director for ONT, to inventor Jens Gundlach).
- "Many thanks for your time today, Gordon and I thoroughly enjoyed the meeting. We are both very impressed with your work thus far, many congratulations! Please let us know if you have any further queries and I hope we can continue discussions towards a fruitful partnership." Exhibit 12 (7/1/09 e-mail from Willcocks to Gundlach).
- "I am really excited about MSPA and would like to discuss what we need to do to get you on board." Exhibit 13 (2/4/11 e-mail from Gordon Sanghera, CEO of ONT, to Jens Gundlach).

Even ONT's founder, Dr. Hagan Bayley, published a 2015 article that described the work of the inventors of the '550 patent as a "significant discovery" in the "steps towards nanopore sequencing." *See* Exhibit 14.

15. Defendants have had actual notice of the '550 Patent and their infringement of it since the day the patent issued (March 18, 2014). For example, ONT filed two petitions for *inter partes* review of the '550 Patent on March 18, 2014, so they must have known of it by at least then. Moreover, on information and belief, ONT knew upon learning of the '550 patent that it covered Msp porins, and methods and

systems for using Msp to sequence nucleic acids, and ONT knew that its sequencing products also use Msp. Defendants have had actual notice of the '230 patent at least as of the date the '230 patent issued (October 27, 2015).

16. On information and belief, Defendants' MinION product more likely than not includes Msp porins. As an example only, a member of ONT's technology advisory board, Dr. Mark Akeson, has publicly implied that ONT uses Msp nanopores through his comments on a paper published by one of the inventors of the patents-in-suit, Dr. Gundlach, about Msp nanopores. In particular, Dr. Akeson commented that Dr. Gundlach's paper is a "very nice set of experiments and important ***confirmation*** **of the work being done at Oxford Nanopore**." *See* Exhibit 15. Dr. Gundlach's paper describes "recent progress with respect to nanopore resolution and DNA control to interpret the procession of ion current levels observed during the translocation of DNA through the pore ***MspA***." *See* Exhibit 16 (abstract). Dr. Akeson's comments demonstrate that ONT is also using MspA nanopores—otherwise, Dr. Gundlach's paper could not provide "confirmation" of anything happening at ONT.

17. What is more, ONT's founder stated recently that ONT's process for getting data "could be deduced in outline, at least, from presentations and ***patent filings***," Exhibit 17, at p. 5 (emphasis added), and ONT's pending patent applications tout the advantages of Msp nanopores for sequencing, disclose and claim Msp nanopores covered by the patents-in-suit, and include working examples that use Msp nanopores covered by the patents-in-suit. *See, e.g.*, Exhibits 17-21. For example, one of ONT's patent applications, which was filed well after the priority date of the patents-in-suit, states that "the inventors have surprisingly demonstrated that novel mutants of Msp display improved properties for estimating the characteristics, such as the sequence of nucleic acids." *See* Exhibit 17 (U.S. Patent Appl. Publ. No. 2014/0186823) at ¶ 0007. All the Msp nanopores in that ONT patent application are derived from one of the mutant Msp nanopores disclosed in the patents-in-suit. *Compare* Exhibit 22 at 45:56-59 ('230 patent, disclosing MspA nanopore with mutations at positions 90, 91,

93, 118, 134, and 139), *and* Exhibit 1 at 45:55-58 ('550 patent, disclosing same), *with* Exhibit 17 at ¶ 120 (ONT patent application starting from the same MspA nanopore with mutations at positions 90, 91, 93, 118, 134, and 139). Many of ONT's other published applications include working examples that exclusively use MspA nanopores. *See, e.g.,* Exhibit 17 at 47, ¶ 0006, and ¶¶ 0111-0117; Exhibit 18 at ¶¶ 0193-94, and ¶ 217; Exhibit 19 at ¶¶ 197, 211, 216; Exhibit 20 at p. 78, lines 11-13 and p. 80, lines 19-20; Exhibit 21 at p. 69, lines 19-21, p. 72, lines 21-22, p. 74, lines 16-17; *see also* Exhibits 22-25 (claim charts). Based on this evidence, it is thus reasonable to infer that ONT's Accused Products more likely than not include the Msp nanopores described and claimed in its pending patent applications.

18. On information and belief, Defendants' MinION product includes MspA porins with mutations at amino acid positions 90, 91, and/or 93.

19. For example, one recent paper by a team of Harvard researchers in Boston, MA posted on June 30, 2015, entitled "Thermal motion of DNA in an MspA pore," states that "[t]he MspA protein nanopore was provided by Oxford Nanopore Technologies, Inc., and is the G75S/G77S/L88N/D90N/D91N/D93N/D118R/Q126R/D134R/E139K mutant of wild-type MspA." *See* Exhibit 26 at 5.

20. On information and belief, Defendants' MinION product includes MspA porins with mutations at amino acid positions 118, 134, and/or 139. *See* ¶ 18, *supra.*

21. On information and belief, Defendants' MinION product includes MspA porins with one or more of the following mutations: D118R, D134R, and/or E139K. *See* ¶ 18, *supra.*

22. On information and belief, Defendants' PromethION product includes Msp porins. *See* ¶ 16, *supra.*

23. On information and belief, Defendants' PromethION product includes Msp porins with mutations at amino acid positions 90, 91, and/or 93. *See* ¶ 18, *supra.*

24. On information and belief, Defendants' PromethION product includes Msp porins with mutations at amino acid positions 118, 134, and/or 139. *See* ¶ 18, *supra*.

25. On information and belief, Defendants' PromethION product includes Msp porins with one or more of the following mutations: D118R, D134R, and/or E139K. *See* ¶ 18, *supra*.

26. Each Defendant has directly infringed, and continues to infringe, literally or under the doctrine of equivalents, one or more claims of each of the patents-in-suit by acting without authority to make, have made, use, offer to sell, sell within the United States, or import into the United States, Msp nanopores and sequencing products containing Msp nanopores, including but not limited to MinION and PromethION, and/or components thereof. By way of example, Defendants import and distribute the MinION to scientists and researchers in the United States through MinION Access Programme ("MAP").[1] As another example, Defendants have imported the PromethION into the United States. As another example, Defendants have offered to sell the PromethION to scientists and researchers in the United States through PromethION Early Access Programme ("PEAP"), which is a similar program to the MAP and allows participants to purchase the PromethION.[2] As a further example, Defendants have provided Msp nanopores to third-parties in the United States, as evidenced by a recent scientific article in which a member of ONT's technical advisory board indicated that he received Msp nanopores from Defendants.[3]

27. In addition, Defendants actively induce others to infringe one or more claims of each of the patents-in-suit through the importation, sale, and offer to sell

[1] *See, e.g.*, Ex. 27 (https://nanoporetech.com/technology-users) ("MinION and consumables are now available to purchase by joining the MinION Access Programme.").
[2] *See, e.g.*, Ex. 28 (https://nanoporetech.com/community/peap-promethion-early-access-programme).
[3] *See, e.g.,* B. Lu, et al., *Thermal motion of DNA in an MspA pore*, at p. 5 ("The MspA protein nanopore was provided by Oxford Nanopore Technologies, Inc., and is the G75S/G77S/L88N/D90N/D91N/D93N/D118R/Q126R/D134R/E139K mutant of wild-type MspA.").

their nanopore sequencing devices and/or components thereof to customers in the United States along with directions, demonstrations, guides, manuals, training for use, and other materials that encourage the infringing use of Defendants' nanopore sequencing devices and/or components thereof. By way of example, to join the MAP, each participant must agree to certain "Terms and Conditions," which require, among others, each participant to conduct certain "burn-in experiments" that use the MinION or PromethION in a manner covered by the '550 and '230 patents.. *See* Exhibit 30; Exhibit 31 at 3-4; Exhibit 32 at 22. Based on its knowledge of the '550 and '230 patents, ONT knows that these mandatory "burn-in experiments" infringe one or more of the claims of each of the patents-in-suit. Moreover, on information and belief, Defendants' actions have actually encouraged MAP participants in the United States to use Defendants' products in an infringing manner. *See* Exhibits 33-40.

28. Furthermore, Defendants contributorily infringe one or more claims of each of the patents-in-suit through their sale and offer to sell within the United States and/or import into the United States of components of their nanopore sequencing devices and/or their nanopore sequencing devices for use in practicing a process, constituting a material part of one or more claims of each of the patents-in-suit, knowing the same to be especially made or especially adapted for use in an infringement of each of the patents-in-suit, and not a staple article or commodity of commerce suitable for substantial noninfringing use. By way of example, Defendants' nanopore sequencing devices are specifically designed for purposes of scientific use or research to identify analytes such as DNA, RNA and proteins. On information and belief, due to their specific design, Defendants' nanopore sequencing devices do not have any substantial non-infringing uses. Moreover, on information and belief, Defendants have actually provided their sequencing systems to third-parties who have used it to infringe the each of the patents-in-suit, as evidenced by the examples given in the previous paragraph of MAP program participants that have published articles describing or mentioning their experience using the MinION device.

29. Defendants' infringement of the patents-in-suit has caused injury and damage to Plaintiffs, and it will cause additional severe and irreparable injury and damages in the future.

FIRST CLAIM FOR RELIEF
Infringement of U.S. Patent No. 8,673,550

30. Plaintiffs incorporate by reference the allegations set forth in paragraphs 1 through 28 above as if specifically set forth herein.

31. Each Defendant has directly infringed at least claims 2-4, 7-10, 13-15, 17-18, 20-22, 24, 26-28, 31-33, 35-36, and 38-40 of the '550 Patent, literally and/or under the doctrine of equivalents, in violation of 35 U.S.C. §271. The infringing products include Defendants' nanopore sequencing devices such as MinION and PromethION and components thereof. Exemplary claim charts demonstrating how these representative accused products infringe claims 1, 17, 23, 32 and 33 of the '550 Patent are attached as Exhibits 22 and 23. The infringement remains ongoing.

32. In addition to its direct infringement, each Defendant has been and is now indirectly infringing by way of inducing infringement and/or contributing to the infringement of one or more claims of the '550 Patent.

33. As a consequence of Defendants' infringement, Plaintiffs are entitled to recover damages adequate to compensate it for the injuries complained of therein, but in no event less than a reasonable loyalty.

34. Defendants' infringement is willful because they have had knowledge of the '550 patent since its issuance on March 18, 2014, the Patent Office has denied multiple requests in which they have asked the U.S. Patent and Trademark Office to reevaluate the validity of claims of the '550 patent in *inter partes* review, and, on information and belief, Defendants have no good faith belief in non-infringement.

SECOND CLAIM FOR RELIEF
Infringement of U.S. Patent No. 9,170,230

35. Plaintiffs incorporate by reference the allegations set forth in paragraphs 1 through 27 above as if specifically set forth herein.

36. Each Defendant has directly infringed claims 1-31 of the '230 Patent, literally and/or under the doctrine of equivalents, in violation of 35 U.S.C. §271. The infringing products include Defendants' nanopore sequencing devices such as MinION and PromethION and components thereof. Exemplary claim charts demonstrating how these representative accused products infringe claims 1, 10, 15, 18, and 31 of the '230 Patent are attached as Exhibits 24 and 25. The infringement remains ongoing.

37. In addition to its direct infringement, each Defendant has been and is now indirectly infringing by way of inducing infringement and/or contributing to the infringement of one or more claims of the '230 Patent.

38. As a consequence of Defendants' infringement, Plaintiffs are entitled to recover damages adequate to compensate it for the injuries complained of therein, but in no event less than a reasonable loyalty.

39. Defendants' infringement is willful because they have had knowledge of the '230 patent since its issuance on October 27, 2015, and, on information and belief, Defendants have no good faith belief in non-infringement or invalidity, particularly given that the Patent Office has rejected their attempts to invalidate claims of the related '550 patent.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully requests that this Court enter judgment in Plaintiffs' favor against Defendants and issue an order that includes:

A. Enter judgment that Defendants' have infringed one or more claims of the '550 and '230 patents;

B. Enter judgment that Defendants' infringement of the patents-in-suit has been willful, deliberate, and intentional;

C. Enter an order, pursuant to 35 U.S.C. § 284, awarding to Plaintiffs damages adequate to compensate for Defendants' infringement of the patents-in-suit in an amount to be determined at trial, but not less than a reasonable royalty;

D. Enter an order, pursuant to 35 U.S.C. § 284, trebling damages awarded to Plaintiffs to the extent Defendants' infringement of the patents-in-suit is determined to have been willful;

E. Enter an order, pursuant to 35 U.S.C. § 285, deeming this to be an "exceptional case" and thereby awarding to Plaintiffs its reasonable attorneys' fees, costs, and expenses;

F. Enter an order that Defendants account for and pay to Plaintiffs the damages to which Plaintiffs are entitled as a consequence of the infringement, including any damages not covered by the jury verdict;

G. Enter an order awarding to Plaintiffs pre- and post-judgment interest at the maximum allowable rates allowable under the law; and

H. A permanent injunction enjoining Defendants, their officers agents, servants, employees, attorneys, and those persons in active concert or participation with any of them, from infringing in any manner the patents-in-suit;

I. Enter an order awarding to Plaintiffs such other and further relief, whether at law or in equity, that this Court deems just and proper.

JURY DEMAND

Plaintiffs hereby demand a trial by jury for all issues so triable.

Dated: February 23, 2016

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General Information

Court	United States District Court for the Southern District of California; United States District Court for the Southern District of California
Federal Nature of Suit	Property Rights - Patent[830]
Docket Number	3:16-cv-00477