

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

THE TRUSTEES OF COLUMBIA)
UNIVERSITY IN THE CITY OF NEW)
YORK and)
QIAGEN SCIENCES, LLC,)
Plaintiffs,)

Civil Action No. 19-1681-CFC

v.)

JURY TRIAL DEMANDED

ILLUMINA, INC.)

Defendant.)

AMENDED COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs The Trustees of Columbia University in the City of New York (“Columbia University”) and QIAGEN Sciences, LLC (“QIAGEN”) (collectively “Plaintiffs”), by and through their undersigned counsel, for their Amended Complaint against Defendant Illumina, Inc. (“Illumina”), allege as follows:

THE PARTIES

1. Plaintiff Columbia University is one of the world’s leading institutions of higher education, located at 535 West 116th Street, New York, New York 10027. It is a non-profit educational corporation formed by special act of the Legislature of the State of New York.

2. Plaintiff QIAGEN Sciences, LLC is a Delaware company having its principal place of business at 19300 Germantown Road, Germantown, MD 20874. QIAGEN Sciences, LLC is the successor-in-interest to QIAGEN Waltham, Inc. as a result of a merger effective December 31, 2017.

3. Upon information and belief, Defendant Illumina, Inc. is a Delaware corporation having its principal place of business at 5200 Illumina Way, San Diego, California 92122.

JURISDICTION AND VENUE

4. This action arises under the Patent Laws of the United States of America, 35 U.S.C. § 1 *et seq.*

5. This Court has subject matter jurisdiction over this action under 28 U.S.C. § 1331 and 28 U.S.C. § 1338(a) because this is a civil action arising under the Patent Act.

6. This Court has personal jurisdiction over Illumina because Illumina is incorporated in the State of Delaware.

7. Venue is proper in this District under 28 U.S.C. § 1400(b) because Illumina is incorporated in the State of Delaware and thus resides in this District.

BACKGROUND

The Patents-in-Suit

8. On September 10, 2019, the United States Patent and Trademark Office (“USPTO”) duly issued United States Patent No. 10,407,458 (“the ’458 Patent”), entitled “Massive Parallel Method for Decoding DNA and RNA,” in the names of inventors Jingyue Ju, Zengmin Li, John Robert Edwards, and Yasuhiro Itagaki. A true and correct copy of the ’458 Patent is attached hereto as Exhibit 1.

9. On September 10, 2019, the USPTO duly issued United States Patent No. 10,407,459 (“the ’459 Patent”), entitled “Massive Parallel Method for Decoding DNA and RNA,” in the names of inventors Jingyue Ju, Zengmin Li, John Robert Edwards, and Yasuhiro Itagaki. A true and correct copy of the ’459 Patent is attached hereto as Exhibit 2.

10. On October 1, 2019, the USPTO duly issued United States Patent No. 10,428,380 (“the ’380 Patent”), entitled “Massive Parallel Method for Decoding DNA and RNA,” in the

names of inventors Jingyue Ju, Zengmin Li, John Robert Edwards, and Yasuhiro Itagaki. A true and correct copy of the '380 Patent is attached hereto as Exhibit 3.

11. On October 8, 2019, the USPTO duly issued United States Patent No. 10,435,742 ("the '742 Patent"), entitled "Massive Parallel Method for Decoding DNA and RNA," in the names of inventors Jingyue Ju, Zengmin Li, John Robert Edwards, and Yasuhiro Itagaki. A true and correct copy of the '742 Patent is attached hereto as Exhibit 4.

12. On October 29, 2019, the USPTO duly issued United States Patent No. 10,457,984 ("the '984 Patent"), entitled "Massive Parallel Method for Decoding DNA and RNA," in the names of inventors Jingyue Ju, Zengmin Li, John Robert Edwards, and Yasuhiro Itagaki. A true and correct copy of the '984 Patent is attached hereto as Exhibit 5.

13. Columbia University owns by assignment all right, title, and interest in and to the '458 Patent, the '459 Patent, the '380 Patent, the '742 Patent, and the '984 Patent (collectively "the Patents-in-Suit").

14. QIAGEN is the exclusive licensee of the Patents-in-Suit.

15. On January 31, 2019, the applications that issued as the '458 Patent, the '380 Patent, and the '742 Patent published as US2019/0031704, US2019/0031706, and US2019/0031705, respectively.

16. On March 21, 2019, the applications that issued as the '459 Patent and the '984 Patent published as US2019/0085014 and US2019/0085015 (collectively with US2019/0031704, US2019/0031706, and US2019/0031705, "the Published Applications").

17. The inventions as claimed in the Patents-in-Suit are identical to the inventions as claimed in the Published Applications.

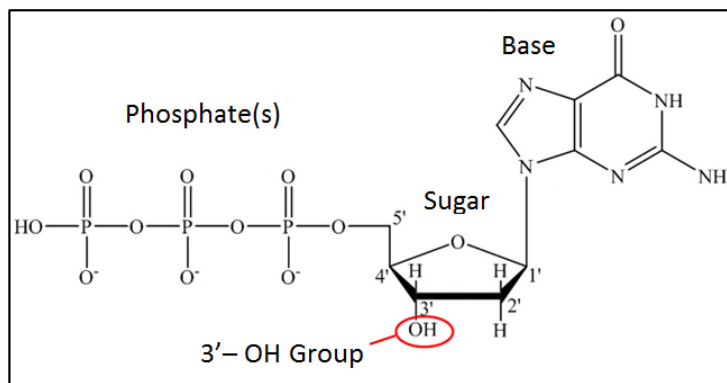
18. Illumina is a large and sophisticated company that has been a party to patent

litigation with Columbia University and QIAGEN, and thus, on information and belief, Illumina monitors patent applications involving DNA sequencing technology and was aware of the content of each of the claims of the '458 Patent, the '380 Patent, and the '742 Patent on or after they were published on January 31, 2019, and the content of each of the claims of the '459 Patent and the '984 Patent on or after they were published on March 21, 2019.

Nucleotides and DNA Sequencing

19. The Patents-in-Suit relate to modified versions of nucleotides (known as “nucleotide analogues”) and methods of using such nucleotide analogues for sequencing DNA (deoxyribonucleic acid). DNA encodes the genetic information of living organisms. DNA consists of smaller building blocks called nucleotides; the sequence of the nucleotides determines hereditary traits in living organisms. DNA sequencing—*i.e.*, determining the order of the nucleotides in a DNA strand—is of enormous importance for a wide variety of applications in medicine, biotechnology, and other fields. For example, by sequencing the DNA of individuals with a particular disease or the DNA in tumor cells, medical researchers and physicians may learn the genetic basis for the disease or tumor and may design or provide therapies specifically targeted to it.

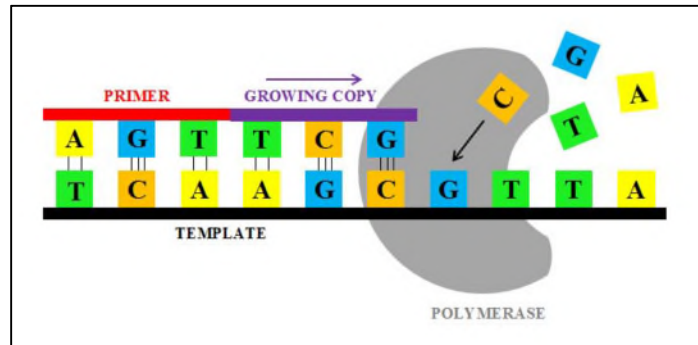
20. A nucleotide consists of a sugar, a base, and one or more phosphate groups, as shown below. Nucleotides are identified by their bases, which form the genetic code of DNA. There are four different nucleotide bases—an adenine (“A”), a guanine (“G”), a cytosine (“C”), and a thymine (“T”). A and G are known as “purine” bases, while C and T are “pyrimidine” bases. The sugar in the nucleotide contains five carbon atoms, conventionally numbered 1' through 5'. When the nucleotide is found in isolation, a hydroxyl group (OH) is attached at the 3' position and is referred to as the 3'-OH group (circled below). The nucleotide depicted below is called a deoxyribonucleotide triphosphate.



21. DNA consists of a chain of nucleotides, held together by bonds between a phosphate group of one nucleotide and a 3'-OH group of another nucleotide. In nature, two such chains of nucleotides form a double helix structure (forming a DNA double helix). Bonds between complementary base pairs hold the chains together, and base pairs always bond in the same way: A always pairs with T; C always pairs with G. These bonds between complementary base pairs form the “cross-bars” in the DNA double helix while the bonds between the phosphate group of one nucleotide and the 3'-OH group of the adjacent nucleotide form the “backbone” of the DNA double helix.

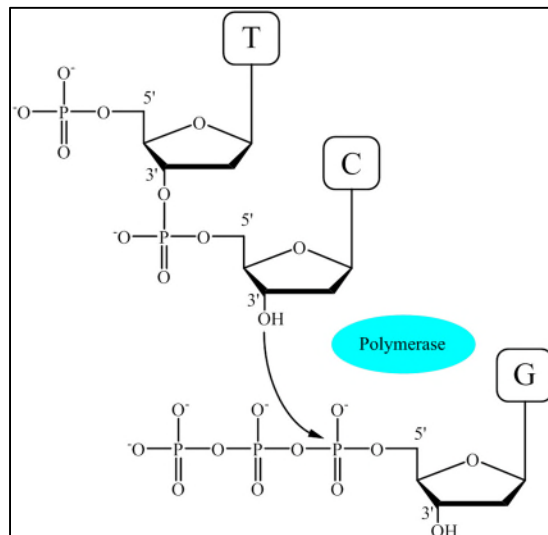
22. To duplicate, or “synthesize,” DNA, the two strands of the DNA double helix are first unwound and separated. Each strand of nucleotides can then serve as the *template* for the production (or *copying*) of a complementary strand. Synthesis of DNA typically begins with the use of a short strand of nucleotides, called a *primer*, which is designed to match, and therefore bind to, the corresponding nucleotides at the beginning of the *template* strand to be copied, as shown below. An enzyme called a *polymerase* extends the primer along the template by adding nucleotides with bases that are complementary to the nucleotides of the template being copied via the base-pairing rules: A-T and C-G. For example, if the next nucleotide in the template to be copied has a G base, the polymerase would incorporate into the growing primer chain a

nucleotide with a complementary C base.



23. As shown above, each letter in a square is a nucleotide. The polymerase also facilitates the formation of a bond between a phosphate group at the 5'-position of a free nucleotide and the 3'-OH group of the last nucleotide incorporated into the growing copy, thus adding the next nucleotide to the growing strand.

24. This reaction can only occur when the last nucleotide in the growing strand has a 3'-OH group available for linking to a phosphate group of an incoming nucleotide, as shown below.



Columbia University's Patents-in-Suit

25. The Patents-in-Suit disclose and claim nucleotide analogues that are useful in a

type of “next generation sequencing” (or “NGS”) technology called “sequencing by synthesis” (“SBS”). NGS technologies are used in a variety of medical and research applications, including identifying genes and polymorphisms associated with disease and with individual variability in drug response, and are important to genomics research and discovery, particularly in the emerging field of personalized precision medicine, which seeks to use a patient’s own genomic DNA sequence information as the basis for individualized healthcare.

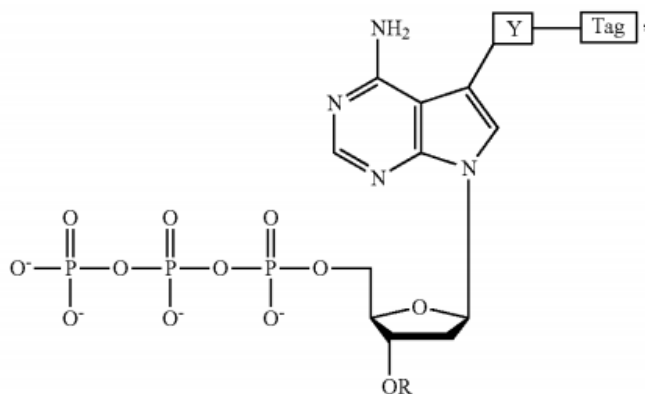
26. Generally speaking, SBS involves the use of modified nucleotides that take advantage of the foregoing reaction used to grow a DNA strand. The method uses modified nucleotides with removable “caps” (also called “protecting groups,” or “blocking groups”) attached to the 3’-OH group on the sugar portion of the nucleotide. The modified nucleotides also have detectable labels attached to them, to signal whether the nucleotides are an A, C, T, or G. When a polymerase incorporates such a nucleotide into a growing chain, the synthesis stops because the 3’-OH group—where the polymerase would otherwise be used to join with the phosphate group of the next nucleotide—is blocked by the cap. Once the process is stopped, the label on the nucleotide is detected to identify which base was incorporated. After the label is detected, the label and the cap are removed (or “cleaved”), allowing the polymerase to add another labeled nucleotide to the chain for continuous DNA sequencing.

27. The Patents-in-Suit teach nucleotide analogues that use a small cleavable chemical moiety with certain structural features to cap the 3’-OH group of the deoxyribose, along with cleavable labels attached to the base of each nucleotide. They further teach that the cleavable chemical cap “is stable during the polymerase reaction” and “does not interfere with the recognition of the nucleotide analogue by polymerase as a substrate,” and that “the growing strand of DNA should survive the . . . cleavage process[]”

28. In addition to teaching the use of small chemically cleavable capping groups, the Patents-in-Suit also *exclude* certain chemical groups for use as caps in this SBS method. For example, the Patents-in-Suit claim that the “OR” of the nucleotide is not a methoxy or an ester group, and the “R” of the nucleotide does not contain a ketone group. Similarly, certain claims of the Patents-in-Suit recite that the “R” group (*i.e.*, the cap) is not a $-\text{CH}_2\text{CH}=\text{CH}_2$ group, and certain claims of the Patents-in-Suit recite that the “OR” group is not an allyl ether group.

29. For example, claim 1 of the '459 Patent recites:

1. An adenine deoxyribonucleotide analogue having the structure:



wherein R (a) represents a small, chemically cleavable, chemical group capping the oxygen at the 3' position of the deoxyribose of the deoxyribonucleotide analogue, (b) does not interfere with recognition of the analogue as a substrate by a DNA polymerase, (c) is stable during a DNA polymerase reaction, (d) does not contain a ketone group, and (e) is not a $-\text{CH}_2\text{CH}=\text{CH}_2$ group;

wherein OR is not a methoxy group or an ester group;

wherein the covalent bond between the 3'-oxygen and R is stable during a DNA polymerase reaction;

wherein tag represents a detectable fluorescent moiety;

wherein Y represents a chemically cleavable, chemical linker which (a) does not interfere with recognition of the analogue as

a substrate by a DNA polymerase and (b) is stable during a DNA polymerase reaction; and

wherein the adenine deoxyribonucleotide analogue:

- i) is recognized as a substrate by a DNA polymerase,
- ii) is incorporated at the end of a growing strand of DNA during a DNA polymerase reaction,
- iii) produces a 3'-OH group on the deoxyribose upon cleavage of R,
- iv) no longer includes a tag on the base upon cleavage of Y, and
- v) is capable of forming hydrogen bonds with thymine or a thymine nucleotide analogue.

Illumina Makes, Uses, and Sells Nucleotide Analogues that Infringe the Patents-in-Suit

30. Illumina manufactures, uses, imports and/or sells DNA sequencing instruments that infringe the Patents-in-Suit (the “Accused Instruments”). These Accused Instruments include, but are not limited to, at least the following:

- a. HiSeq X Ten system, HiSeq X Five system, HiSeq 2500 system, HiSeq 3000 system, HiSeq 4000 system, MiSeq system, MiSeqDx system, and MiSeq FGx system (collectively “4-Channel Accused Instruments”),
- b. MiniSeq system, NextSeq 500 system, NextSeq 550 system, NextSeq 550Dx system, NovaSeq 5000 system, and NovaSeq 6000 system (collectively “2-Channel Accused Instruments”), and
- c. iSeq 100 (“1-Channel Accused Instrument”).

31. Illumina manufactures, uses, imports, and/or sells a number of reagent kits containing nucleotide analogues that are sold for use with the Accused Instruments and infringe the Patents-in-Suit (the “Accused Kits”). These Accused Kits include, but are not limited to, at

least the following:

- a. HiSeq 3000/4000 SBS Kit, HiSeq Rapid SBS Kit v2, HiSeq SBS Kit v4, HiSeq X Reagent Kits, MiSeq FGx Reagent Kit, MiSeq Reagent Kit v3, MiSeq Reagent Kits v2, MiSeq Cystic Fibrosis 139-Variant Assay, MiSeq Cystic Fibrosis Clinical Sequencing Assay, MiSeq Universal Kit, VeriSeq PGS Kit, TruSight Cardio Sequencing Kit, TruSight One Sequencing Panels, TruSight Inherited Disease Sequencing Panel, Extended RAS Panel, TruSeq Rapid SBS Kits (200 Cycle and 50 Cycle) – HS, TruSeq SBS Kit v3-HS, and TruSeq SBS Kit v5-GA (collectively “4-Channel Accused Kits”),
- b. MiniSeq Reagent Kit, NextSeq 500/550 v2 and v2.1 Kits, NextSeq 500/550 v2.5 Kits, NextSeq 550Dx Reagents, and NovaSeq Reagent Kits (collectively “2-Channel Accused Kits”), and
- c. iSeq 100 Reagents (“1-Channel Accused Kit”).

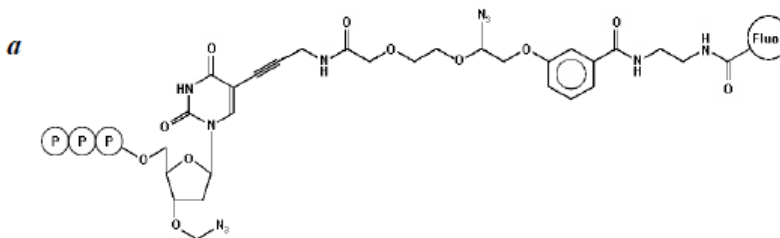
32. Illumina also offers DNA sequencing services, including Illumina FastTrack Sequencing Services, Illumina Clinical Sequencing Services, and Verifi Prenatal Test (collectively “Accused Services”), in which it tests samples for a fee, on information and belief using the Accused Kits and Accused Instruments to do so. For example, as Illumina states on its website, “Illumina offers a diverse portfolio of array and next-generation sequencing (NGS) services to support a broad range of genomic applications. . . . Armed with proven Illumina NGS and array technologies and a network of scientific experts, customers are increasingly empowered to accelerate opportunities for discovery.” *See* <https://www.illumina.com/services.html> (emphasis added) (attached as Exhibit 6).

33. On November 6, 2008, authors from Illumina and others published an article in *Nature* titled “Accurate Whole Human Genome Sequencing using Reversible Terminator

Chemistry” (“Bentley article”). A true and correct copy of the Bentley article is attached hereto as Exhibit 7. Along with the Bentley article, *Nature* also published “Supplementary Information” that provides more detail regarding Illumina’s sequencing methods that Illumina published in the Bentley article. A true and correct copy of the Supplementary Information is attached hereto as Exhibit 8.

34. Illumina states in the Bentley article that the sequencing methods shown in the article are “the basis for the standard protocols now available from Illumina, Inc.” Ex. 7 at 58. Accordingly, on information and belief, the nucleotide analogues described in the Bentley article and Supplementary Information are the same as (or substantially the same as) the nucleotide analogues contained in the Accused Kits.

35. Illumina’s disclosures in the Bentley article and its Supplementary Information confirm that Illumina uses the claimed deoxyribonucleotide analogues in Illumina’s sequencing technology. For example, the Bentley article provides that “[t]o ensure base-by-base nucleotide incorporation in a stepwise manner, [Illumina uses] a set of four reversible terminators, 3’-O-azidomethyl 2’-deoxynucleoside triphosphates (A, C, G and T), each labelled with a different removable fluorophore (Supplementary Fig. 1a).” Ex. 7 at 53. Fig. 1a from the Supplementary Information provides the “[s]tructure of the reversible terminator 3’-O-azidomethyl 2’-deoxythymine triphosphate (T) labelled with a removable fluorophore.” Ex. 8 at 14, Fig. S1.a.



Although only the structure for the thymine (T) nucleotide is provided, the Bentley article

indicates that the A, C, and G nucleotides each have the same protecting group. Ex. 7 at 53.

36. On information and belief, the adenine, cytosine, guanine, and thymine nucleotides contained in the 4-Channel Accused Kits, the adenine, cytosine, and thymine nucleotides contained in the 2-Channel Accused Kits, and the adenine and thymine nucleotides contained in the 1-Channel Accused Kit each have the same general structure as the nucleotide shown in paragraph 35 (*i.e.*, an azidomethyl capping group attached to the 3' oxygen and a fluorophore attached to the base via a cleavable linker). *See* Illumina CMOS Chip and One-Channel SBS Chemistry at p. 2 (attached as Exhibit 9).

37. On information and belief, during the use of the 1-Channel Accused Kit in the 1-Channel Accused Instrument, the cytosine nucleotide has the same general structure as the nucleotide shown in paragraph 35 (*i.e.*, an azidomethyl capping group attached to the 3' oxygen and a fluorophore attached to the base via a cleavable linker). Ex. 9 at 2.

38. To demonstrate how Illumina's nucleotide analogues and/or their use in sequencing methods infringe the Patents-in-Suit, attached as Exhibits 10-14 are preliminary and exemplary claim charts. These charts are illustrative only and not intended to limit Plaintiffs' right to modify these charts or provide any other claim charts or allege that other Illumina nucleotide analogues infringe each of the Patents-in-Suit. Exhibits 10-14 are hereby incorporated by reference in their entirety.

39. Each claim element in Exhibits 10-14 that is mapped to Illumina's nucleotide analogues and/or Illumina's sequencing methods shall be considered an allegation within the meaning of the Federal Rules of Civil Procedure and therefore a response to each allegation is required.

40. On information and belief, Illumina directly and willfully infringes the claims of

each of the Patents-in-Suit pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making, using, offering for sale, selling, and/or importing into the United States the Accused Kits or by performing the Accused Services. Illumina also actively induces infringement of the Patents-in-Suit pursuant to 35 U.S.C. § 271(b).

COUNT I

Infringement of U.S. Patent No. 10,407,458

41. Plaintiffs re-allege and incorporate by reference the allegations contained in paragraphs 1-40 above.

42. Illumina directly infringes claims 1-2 of the '458 Patent, literally or under the doctrine of equivalents, by making, using, offering for sale, selling, and/or importing into the United States the 4-Channel Accused Kits, and/or by using the 4-Channel Accused Kits to perform the Accused Services in the United States. Attached as Exhibit 10 is a claim chart showing specifically element-by-element how Illumina's 4-Channel Accused Kits infringe claims 1-2 of the '458 Patent.

43. Illumina's sale of 4-Channel Accused Instruments also actively induces, and continues to actively induce, infringement of claims 1-2 of the '458 Patent in violation of 35 U.S.C. § 271(b). Users of the 4-Channel Accused Kits, including Illumina's customers, directly infringe claims 1-2 of the '458 Patent when they use the 4-Channel Accused Kits with the 4-Channel Accused Instruments. Illumina knowingly induces the users of the 4-Channel Accused Kits to infringe by selling to such users the 4-Channel Accused Instruments with instructions (attached hereto as Exhibit 15) that the 4-Channel Accused Instruments can only be used with the 4-Channel Accused Kits. *See, e.g.*, Ex. 15 at 9 ("The MiSeq Reagent Kit is a single-use reagent kit required to perform a sequencing run. It is available in different types and sizes. Each

type of MiSeq Reagent Kit includes a kit-specific flow cell type and all reagents required for performing a run.”). Based on the allegations in the Complaint (19-cv-1681, D.I. 1), this Amended Complaint, and the attached claim chart, Illumina has knowledge that use of the 4-Channel Accused Kits by its customers infringes claims 1-2 of the ’458 Patent.

44. Illumina’s infringement of the ’458 Patent is damaging and will continue to damage Plaintiffs.

45. Illumina’s continuing infringement of the ’458 Patent will irreparably harm Plaintiffs, and Illumina’s infringement will continue unless enjoined by this Court pursuant to 35 U.S.C. § 283.

46. Illumina is a large and sophisticated company that is highly experienced with patent litigation generally, and litigation involving Columbia University’s patents specifically. In July 2017, Plaintiffs sued Illumina on a patent from the same family as the Patents-in-Suit. *See The Trustees of Columbia University in the City of New York and QIAGEN Sciences, LLC v. Illumina Inc.*, C.A. No. 17-973 (CFC) (D. Del.). In that action, Plaintiffs thereafter amended the complaint three times to assert additional issued patents from the same patent family as the current Patents-in-Suit. In addition, Columbia University and Illumina are parties to IPR2018-00291, wherein on March 15, 2019, Columbia University filed Supplemental Mandatory Notices informing Illumina that Columbia University was prosecuting ten patent applications, including U.S. Application No. 16/149,098, which published as US2019/0031704 and issued as the ’458 Patent. *The Trustees of Columbia University in the City of New York v. Illumina, Inc.*, IPR2018-00291, Paper No. 60 (March 15, 2019). The ’458 Patent claims are identical to those published in US2019/0031704. On March 26, 2019, Illumina acknowledged in a Paper filed in IPR2018-00291 that it had actual knowledge of the pending patent applications, which were published.

The Trustees of Columbia University in the City of New York v. Illumina, Inc., IPR2018-00291, Paper No. 63 at 3 (March 26, 2019) (“Columbia is prosecuting an additional 10 pending applications . . . [s]hould any of those issue, it is likely that the Parties will be back before the Board yet again[.]”). Thus, on information and belief, Illumina was monitoring the patent applications in the family of the Patents-in-Suit and, thus, aware of the content of claims 1-2 of the ’458 Patent on or soon after they were published on January 31, 2019.

47. On information and belief, Illumina’s infringement of the ’458 Patent will be willful, justifying an award of increased damages and making this an exceptional case entitling Plaintiffs to reasonable attorneys’ fees pursuant to 35 U.S.C. § 285.

COUNT II

Infringement of U.S. Patent No. 10,407,459

48. Plaintiffs re-allege and incorporate by reference the allegations contained in paragraphs 1-47 above.

49. Illumina directly infringes claims 1-2 of the ’459 Patent, literally or under the doctrine of equivalents, by making, using, offering for sale, selling, and/or importing into the United States the Accused Kits, and/or by using the Accused Kits to perform the Accused Services in the United States. Attached as Exhibit 11 is a claim chart showing specifically element-by-element how Illumina’s Accused Kits infringe claims 1-2 of the ’459 Patent.

50. Illumina’s sale of the Accused Instruments also actively induces, and continues to actively induce, infringement of claims 1-2 of the ’459 Patent in violation of 35 U.S.C. § 271(b). Users of the Accused Kits, including Illumina’s customers, directly infringe claims 1-2 of the ’459 Patent when they use the Accused Kits with the Accused Instruments. Illumina knowingly induces the users of the Accused Kits to infringe by selling to such users the Accused

Instruments with instructions (attached hereto as Exhibits 15-17) that the Accused Instruments can only be used with the Accused Kits. *See, e.g.*, Ex. 15 at 9 (“The MiSeq Reagent Kit is a single-use reagent kit required to perform a sequencing run. It is available in different types and sizes. Each type of MiSeq Reagent Kit includes a kit-specific flow cell type and all reagents required for performing a run.”); Ex. 16 at 5 (“Performing a sequencing run on the MiniSeq System requires a single-use MiniSeq Kit. Each kit includes a flow cell and the reagents required for a sequencing run.”); Ex. 17 at 7 (“Performing a run on the iSeq 100 System requires one single-use iSeq 100 i1 Reagents kit.”) Based on the allegations in the Complaint (19-cv-1681, D.I. 1), this Amended Complaint, and the attached claim chart, Illumina has knowledge that use of the Accused Kits by its customers infringes claims 1-2 of the ’459 Patent.

51. Illumina’s infringement of the ’459 Patent is damaging and will continue to damage Plaintiffs.

52. Illumina’s continuing infringement of the ’459 Patent will irreparably harm Plaintiffs, and Illumina’s infringement will continue unless enjoined by this Court pursuant to 35 U.S.C. § 283.

53. Illumina is a large and sophisticated company that is highly experienced with patent litigation generally, and litigation involving Columbia University’s patents specifically. In July 2017, Plaintiffs sued Illumina on a patent from the same family as the Patents-in-Suit. *See The Trustees of Columbia University in the City of New York and QIAGEN Sciences, LLC v. Illumina Inc.*, C.A. No. 17-973 (CFC) (D. Del.). In that action, Plaintiffs thereafter amended the complaint three times to assert additional issued patents from the same patent family as the current Patents-in-Suit. In addition, Columbia University and Illumina are parties to IPR2018-00291, wherein on March 15, 2019, Columbia University filed Supplemental Mandatory Notices

informing Illumina that Columbia University was prosecuting ten patent applications, including U.S. Application No. 16/149,114, which published as US2019/0085014 and issued as the '459 Patent. *The Trustees of Columbia University in the City of New York v. Illumina, Inc.*, IPR2018-00291, Paper No. 60 (March 15, 2019). The '459 Patent claims are identical to those published in US2019/0085014. On March 26, 2019, Illumina acknowledged in a Paper filed in IPR2018-00291 that it had actual knowledge of the pending patent applications, which were published. *The Trustees of Columbia University in the City of New York v. Illumina, Inc.*, IPR2018-00291, Paper No. 63 at 3 (March 26, 2019) ("Columbia is prosecuting an additional 10 pending applications . . . [s]hould any of those issue, it is likely that the Parties will be back before the Board yet again[.]"). Thus, on information and belief, Illumina was monitoring the patent applications in the family of the Patents-in-Suit and, thus, aware of the content of claims 1-2 of the '459 Patent on or soon after they were published on March 21, 2019.

54. On information and belief, Illumina's infringement of the '459 Patent will be willful, justifying an award of increased damages and making this an exceptional case entitling Plaintiffs to reasonable attorneys' fees pursuant to 35 U.S.C. § 285.

COUNT III

Infringement of U.S. Patent No. 10,428,380

55. Plaintiffs re-allege and incorporate by reference the allegations contained in paragraphs 1-54 above.

56. Illumina directly infringes claims 1-4 of the '380 Patent, literally or under the doctrine of equivalents, by using the Accused Instruments and Accused Kits, and by performing the Accused Services in the United States. Attached as Exhibit 12 is a claim chart showing specifically element-by-element how the use of Illumina's Accused Kits with the Accused

Instruments infringes claims 1-4 of the '380 Patent.

57. Illumina's sale of the Accused Instruments also actively induces, and continues to actively induce, infringement of claims 1-4 of the '380 Patent in violation of 35 U.S.C. § 271(b). Users of the Accused Kits and Accused Instruments, including Illumina's customers, directly infringe claims 1-4 of the '380 Patent when they use the Accused Kits with the Accused Instruments. Illumina knowingly induces the users of the Accused Kits to infringe by selling to such users the Accused Instruments with instructions (attached hereto as Exhibits 15-17) that the Accused Instruments can only be used with the Accused Kits. *See, e.g.*, Ex. 15 at 9 ("The MiSeq Reagent Kit is a single-use reagent kit required to perform a sequencing run. It is available in different types and sizes. Each type of MiSeq Reagent Kit includes a kit-specific flow cell type and all reagents required for performing a run."); Ex. 16 at 5 ("Performing a sequencing run on the MiniSeq System requires a single-use MiniSeq Kit. Each kit includes a flow cell and the reagents required for a sequencing run."); Ex. 17 at 7 ("Performing a run on the iSeq 100 System requires one single-use iSeq 100 i1 Reagents kit.") Based on the allegations in this Amended Complaint and the attached claim chart, Illumina has knowledge that use of the Accused Kits with the Accused Instruments by its customers infringes claims 1-4 of the '380 Patent.

58. Illumina's infringement of the '380 Patent is damaging and will continue to damage Plaintiffs.

59. Illumina's continuing infringement of the '380 Patent will irreparably harm Plaintiffs, and Illumina's infringement will continue unless enjoined by this Court pursuant to 35 U.S.C. § 283.

60. Illumina is a large and sophisticated company that is highly experienced with patent litigation generally, and litigation involving Columbia University's patents specifically.

In July 2017, Plaintiffs sued Illumina on a patent from the same family as the Patents-in-Suit. *See The Trustees of Columbia University in the City of New York and QIAGEN Sciences, LLC v. Illumina Inc.*, C.A. No. 17-973 (CFC) (D. Del.). In that action, Plaintiffs thereafter amended the complaint three times to assert additional issued patents from the same patent family as the current Patents-in-Suit. In addition, Columbia University and Illumina are parties to IPR2018-00291, wherein on March 15, 2019, Columbia University filed Supplemental Mandatory Notices informing Illumina that Columbia University was prosecuting ten patent applications, including U.S. Application No. 16/150,191, which published as US2019/0031706 and issued as the '380 Patent. *The Trustees of Columbia University in the City of New York v. Illumina, Inc.*, IPR2018-00291, Paper No. 60 (March 15, 2019). The '380 Patent claims are identical to those published in US2019/0031706. On March 26, 2019, Illumina acknowledged in a Paper filed in IPR2018-00291 that it had actual knowledge of the pending patent applications, which were published. *The Trustees of Columbia University in the City of New York v. Illumina, Inc.*, IPR2018-00291, Paper No. 63 at 3 (March 26, 2019) ("Columbia is prosecuting an additional 10 pending applications . . . [s]hould any of those issue, it is likely that the Parties will be back before the Board yet again[.]"). Thus, on information and belief, Illumina was monitoring the patent applications in the family of the Patents-in-Suit and, thus, aware of the content of claims 1-4 of the '380 Patent on or soon after they were published on January 31, 2019.

61. On information and belief, Illumina's infringement of the '380 Patent will be willful, justifying an award of increased damages and making this an exceptional case entitling Plaintiffs to reasonable attorneys' fees pursuant to 35 U.S.C. § 285.

COUNT IV

Infringement of U.S. Patent No. 10,435,742

62. Plaintiffs re-allege and incorporate by reference the allegations contained in paragraphs 1-61 above.

63. Illumina directly infringes claims 1-2 of the '742 Patent, literally or under the doctrine of equivalents, by making, using, offering for sale, selling, and/or importing into the United States the Accused Kits, and/or by using the Accused Kits to perform the Accused Services in the United States. Attached as Exhibit 13 is a claim chart showing specifically element-by-element how Illumina's Accused Kits infringe claims 1-2 of the '742 Patent.

64. Illumina's sale of the Accused Instruments also actively induces, and continues to actively induce, infringement of claims 1-2 of the '742 Patent in violation of 35 U.S.C. § 271(b). Users of the Accused Kits, including Illumina's customers, directly infringe claims 1-2 of the '742 Patent when they use the Accused Kits with the Accused Instruments. Illumina knowingly induces the users of the Accused Kits to infringe by selling to such users the Accused Instruments with instructions (attached hereto as Exhibits 15-17) that the Accused Instruments can only be used with the Accused Kits. *See, e.g.*, Ex. 15 at 9 ("The MiSeq Reagent Kit is a single-use reagent kit required to perform a sequencing run. It is available in different types and sizes. Each type of MiSeq Reagent Kit includes a kit-specific flow cell type and all reagents required for performing a run."); Ex. 16 at 5 ("Performing a sequencing run on the MiniSeq System requires a single-use MiniSeq Kit. Each kit includes a flow cell and the reagents required for a sequencing run."); Ex. 17 at 7 ("Performing a run on the iSeq 100 System requires one single-use iSeq 100 i1 Reagents kit.") Based on the allegations in this Amended Complaint and the attached claim chart, Illumina has knowledge that use of the Accused Kits by its customers

infringes claims 1-2 of the '742 Patent.

65. Illumina's infringement of the '742 Patent is damaging and will continue to damage Plaintiffs.

66. Illumina's continuing infringement of the '742 Patent will irreparably harm Plaintiffs, and Illumina's infringement will continue unless enjoined by this Court pursuant to 35 U.S.C. § 283.

67. Illumina is a large and sophisticated company that is highly experienced with patent litigation generally, and litigation involving Columbia University's patents specifically. In July 2017, Plaintiffs sued Illumina on a patent from the same family as the Patents-in-Suit. *See The Trustees of Columbia University in the City of New York and QIAGEN Sciences, LLC v. Illumina Inc.*, C.A. No. 17-973 (CFC) (D. Del.). In that action, Plaintiffs thereafter amended the complaint three times to assert additional issued patents from the same patent family as the current Patents-in-Suit. In addition, Columbia University and Illumina are parties to IPR2018-00291, wherein on March 15, 2019, Columbia University filed Supplemental Mandatory Notices informing Illumina that Columbia University was prosecuting ten patent applications, including U.S. Application No. 16/150,185, which published as US2019/0031705 and issued as the '742 Patent. *The Trustees of Columbia University in the City of New York v. Illumina, Inc.*, IPR2018-00291, Paper No. 60 (March 15, 2019). The '742 Patent claims are identical to those published in US2019/0031705. On March 26, 2019, Illumina acknowledged in a Paper filed in IPR2018-00291 that it had knowledge of the pending patent applications. *The Trustees of Columbia University in the City of New York v. Illumina, Inc.*, IPR2018-00291, Paper No. 63 at 3 (March 26, 2019) ("Columbia is prosecuting an additional 10 pending applications . . . [s]hould any of those issue, it is likely that the Parties will be back before the Board yet again[.]"). Thus, on

information and belief, Illumina was monitoring the patent applications in the family of the Patents-in-Suit and, thus, aware of the content of claims 1-2 of the '742 Patent on or soon after they were published on March 21, 2019.

68. On information and belief, Illumina's infringement of the '742 Patent will be willful, justifying an award of increased damages and making this an exceptional case entitling Plaintiffs to reasonable attorneys' fees pursuant to 35 U.S.C. § 285.

COUNT V

Infringement of U.S. Patent No. 10,457,984

69. Plaintiffs re-allege and incorporate by reference the allegations contained in paragraphs 1-68 above.

70. Illumina directly infringes claims 1-2 of the '984 Patent, literally or under the doctrine of equivalents, by making, using, offering for sale, selling, and/or importing into the United States the Accused Kits, and/or by using the Accused Kits to perform the Accused Services in the United States. Attached as Exhibit 14 is a claim chart showing specifically element-by-element how Illumina's Accused Kits infringe claims 1-2 of the '984 Patent.

71. Illumina's sale of the Accused Instruments also actively induces, and continues to actively induce, infringement of claims 1-2 of the '984 Patent in violation of 35 U.S.C. § 271(b). Users of the Accused Kits, including Illumina's customers, directly infringe claims 1-2 of the '984 Patent when they use the Accused Kits with the Accused Instruments. Illumina knowingly induces the users of the Accused Kits to infringe by selling to such users the Accused Instruments with instructions (attached hereto as Exhibits 15-17) that the Accused Instruments can only be used with the Accused Kits. *See, e.g.*, Ex. 15 at 9 ("The MiSeq Reagent Kit is a single-use reagent kit required to perform a sequencing run. It is available in different types and

sizes. Each type of MiSeq Reagent Kit includes a kit-specific flow cell type and all reagents required for performing a run.”); Ex. 16 at 5 (“Performing a sequencing run on the MiniSeq System requires a single-use MiniSeq Kit. Each kit includes a flow cell and the reagents required for a sequencing run.”); Ex. 17 at 7 (“Performing a run on the iSeq 100 System requires one single-use iSeq 100 i1 Reagents kit.”) Based on the allegations in this Amended Complaint and the attached claim chart, Illumina has knowledge that use of the Accused Kits by its customers infringes claims 1-2 of the ’984 Patent.

72. Illumina’s infringement of the ’984 Patent is damaging and will continue to damage Plaintiffs.

73. Illumina’s continuing infringement of the ’984 Patent will irreparably harm Plaintiffs, and Illumina’s infringement will continue unless enjoined by this Court pursuant to 35 U.S.C. § 283.

74. Illumina is a large and sophisticated company that is highly experienced with patent litigation generally, and litigation involving Columbia University’s patents specifically. In July 2017, Plaintiffs sued Illumina on a patent from the same family as the Patents-in-Suit. *See The Trustees of Columbia University in the City of New York and QIAGEN Sciences, LLC v. Illumina Inc.*, C.A. No. 17-973 (CFC) (D. Del.). In that action, Plaintiffs thereafter amended the complaint three times to assert additional issued patents from the same patent family as the current Patents-in-Suit. In addition, Columbia University and Illumina are parties to IPR2018-00291, wherein on March 15, 2019, Columbia University filed Supplemental Mandatory Notices informing Illumina that Columbia University was prosecuting ten patent applications, including U.S. Application No. 16/150,180, which published as US2019/0085015 and issued as the ’984 Patent. *The Trustees of Columbia University in the City of New York v. Illumina, Inc.*, IPR2018-

00291, Paper No. 60 (March 15, 2019). The '984 Patent claims are identical to those published in US2019/0085015. On March 26, 2019, Illumina acknowledged in a Paper filed in IPR2018-00291 that it had actual knowledge of the pending patent applications, which were published. *The Trustees of Columbia University in the City of New York v. Illumina, Inc.*, IPR2018-00291, Paper No. 63 at 3 (March 26, 2019) (“Columbia is prosecuting an additional 10 pending applications . . . [s]hould any of those issue, it is likely that the Parties will be back before the Board yet again[.]”). Thus, on information and belief, Illumina was monitoring the patent applications in the family of the Patents-in-Suit and, thus, aware of the content of claims 1-2 of the '984 Patent on or soon after they were published on March 21, 2019.

75. On information and belief, Illumina's infringement of the '984 Patent will be willful, justifying an award of increased damages and making this an exceptional case entitling Plaintiffs to reasonable attorneys' fees pursuant to 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that this Court enter judgment against Illumina, granting Plaintiffs the following relief:

A. A judgment holding Illumina liable for direct and indirect infringement of the Patents-in-Suit and for violating Plaintiffs' provisional rights in the Patents-in-Suit;

B. Damages resulting from Illumina's infringement of the Patents-in-Suit in an amount to be proven at trial, but no less than a reasonable royalty, such damages to be increased up to three times as a result of Illumina's willful infringement, together with pre-judgment and post-judgment interest;

C. A reasonable royalty resulting from Illumina's violation of Plaintiffs' provisional rights under 35 U.S.C. § 154(d), together with pre-judgment and post-judgment interest;

D. An injunction permanently enjoining Illumina under 35 U.S.C. § 283 from infringing the Patents-in-Suit, including by specifically prohibiting Illumina from making, using, offering for sale, selling, and/or importing into the United States any product which falls within the scope of the Patents-in-Suit;

E. A judgment holding this to be an exceptional case, and an award to Plaintiffs of their attorneys' fees and costs pursuant to 35 U.S.C. § 285; and

F. Such other and further relief as the Court deems just and equitable.

DEMAND FOR JURY TRIAL

Pursuant to Federal Rule of Civil Procedure 38(b) and D. Del. LR 38.1, Plaintiffs hereby demand a trial by jury on all issues so triable.

MORRIS, NICHOLS, ARSHT & TUNNELL
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