UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

HELICOS BIOSCIENCES CORPORATION, Plaintiff, v. PACIFIC BIOSCIENCES OF CALIFORNIA, INC., LIFE TECHNOLOGIES CORPORATION, and ILLUMINA, INC., Defendants.	C.A. No. 10-735-SLR **DEMAND FOR JURY TRIAL**

AMENDED COMPLAINT

Plaintiff Helicos Biosciences Corporation ("Helicos") for its Amended Complaint against defendants Pacific Biosciences of California, Inc. ("PacBio"), Life Technologies Corporation ("Life") and Illumina, Inc. ("Illumina") (collectively "Defendants"), alleges as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement stemming from Defendants' unauthorized manufacture, use, sale, offer for sale and/or importation of Helicos's patented technology.

THE PARTIES

2. Plaintiff Helicos is a Delaware corporation with a principal place of business at One Kendall Square, Building 700, Cambridge, Massachusetts 02139.

3. Founded in 2004, Helicos is a life science company in the business of developing innovative genetic analysis technologies for the research, discovery, and clinical diagnostics markets.

4. PacBio is a Delaware corporation with a principal place of business at 1380

Willow Road, Menlo Park, California 94025.

5. Life is a Delaware corporation with a principal place of business at 5791 Van Allen Way, Carlsbad, California 92008.

6. Illumina is a Delaware corporation with a principal place of business at 9865 Towne Centre Drive, San Diego, California 92121.

7. Defendants are also a life sciences companies and are direct competitors of Helicos.

JURISDICTION AND VENUE

8. This action arises under the Patent Laws of the United States, 35 U.S.C. §§ 1 *et seq.*, and accordingly, this Court has jurisdiction over this case pursuant to 28 U.S.C. §§ 1331 and 1338.

9. Venue is proper in this district pursuant to 28 U.S.C. § 1391(b) and (c) and § 1400(a) and (b). Both plaintiff Helicos and Defendants are Delaware corporations.

DNA SEQUENCING

10. Genetic analysis and the study of genomic information has become a critical tool for understanding the mechanics of life, environmental effects on biological systems, and the diagnosis and treatment of disease. Studying how genes and proteins differ between species and among individuals within a species helps scientists to determine their functions and roles in health and disease. Genomic information enables the possibility of personalized medicine and the study of this information hopefully will provide individuals with access to their own genetic information to make informed decisions concerning the prevention and treatment of disease.

11. The genetic program that controls a living cell is incorporated in its DNA. DNA typically exists in a double-helix form. Each of the two strands of DNA that form the double-

helix are made up of subunits called nucleotides, each of which contains a phosphate, a sugar, and a side-chain called a base. The phosphates and sugars form the backbone of each strand of the helix, and the interactions between the bases of each strand hold the two strands together. The letters A, G, T and C are typically used to denote the four nucleotide bases: adenine, guanine, thymine and cytosine. The genome of an organism is the complete DNA sequence of that organism.

12. The analysis of genetic material has become a mainstay of biological research. In the past twenty years, scientists have developed a variety of genetic analysis methods, including DNA sequencing, gene expression analysis, and genotyping. DNA and RNA sequencing provide the most comprehensive information about the genome of an organism; however, traditional methods of genetic analysis suffer from significant drawbacks.

13. For example, traditional DNA sequencing methods lack the sensitivity to analyze single DNA molecules and therefore require the use of amplification or cloning to make thousands to millions of copies of DNA to obtain sufficient genetic material for sequencing. A preferred method of amplification involves a biochemical process known as polymerase chain reaction, or PCR. PCR, however, introduces errors in the analyzed genetic sequence in the copying process, which can result in incorrect and possibly misleading results.

14. Helicos has developed powerful sequencing technologies that directly analyze the sequences of single molecules of DNA, without the need for complex sample preparation techniques, amplification, or cloning required by traditional sequencing methods. Billions of these single molecules can be analyzed in parallel, permitting rapid and efficient analysis of many individual DNA sequences.

THE PATENTED TECHNOLOGY

15. Helicos owns and/or in-licenses various patents that cover methods for sequencing nucleic acids, including, among others: U.S. Patent Nos. 7,645,596; 7,037,687; 7,169,560; and 7,767,400.

16. These patents disclose methods for sequencing a single strand of DNA by synthesizing a complementary strand of DNA using labeled nucleotide bases that can be optically detected. The process is known as "sequencing-by-synthesis," as the sequencing of the nucleotides in one strand is accomplished through the synthesis of a complementary strand.

17. In sequencing-by-synthesis, a DNA strand to be sequenced, often referred to as a "template," is hybridized to a primer, which is a shorter nucleic acid strand complementary to a portion of the DNA strand to be sequenced. Where hybridized, the two strands together form a small duplex of double-stranded DNA. The bases of the two nucleic acid strands are complementary in that an A (adenine) in one strand pairs with T (thymine) in the other strand (the complementary strand), and G (guanine) on one strand pairs with C (cytosine) in the other strand. In this way, the sequence of bases in one strand dictates the sequence of bases in the complementary strand.

18. Sequencing-by-synthesis reactions employ an enzyme known as a DNA polymerase. Naturally occurring versions of DNA polymerase are responsible for replicating (i.e., copying) DNA. During sequencing-by-synthesis, the DNA polymerase adds additional nucleotides to the primer that are complementary to the nucleotides present in the template.

19. The patents asserted here describe, for example, sequencing-by-synthesis methods that use labeled nucleotides. The nucleotides are labeled with detectable markers, such as fluorescent markers, that enable determination of each nucleotide incorporated into the DNA

strand being extended by the polymerase. The patents describe processes that involve, for example, identifying each new nucleotide by observing its detectable label and neutralizing or removing the label before addition of the next nucleotide.

20. Helicos also owns U.S. Patent No. 7,593,109, which covers an apparatus and method for analyzing biological samples, including DNA sequencing samples.

21. The '109 patent describes a system for analyzing biological samples, such as nucleic acids. The system includes a flow cell, a lighting system for illuminating the sample in the flow cell, and an optical instrument for viewing the sample in the flow cell.

PACBIO

22. PacBio's website contains a "Technology Backgrounder" describing its Single Molecule Real Time (SMRT™) DNA Sequencing technology. A copy of PacBio's Technology Backgrounder is attached hereto as Exhibit F. PacBio describes its technology as "based on eavesdropping on a single DNA polymerase molecule working in a continuous, processive manner." (Technology Backgrounder at 1.)

23. On October 20, 2010, PacBio filed its Fifth Amended Form S-1 Registration Statement ("PacBio Fifth Amended S-1") with the Securities and Exchange Commission also detailing its SMRT™ technology. Portions of PacBio's Firth Amended Form S-1 are attached hereto as Exhibit G. PacBio also published an article in *Science* ("*Science* Article") explaining its technology. A copy of that article is attached hereto as Exhibit H.

24. Like Helicos's patented technology, "the initial application for [PacBio's SMRT™ technology] is DNA sequencing." (PacBio Fifth Amended S-1 at 61; *see also* Technology Backgrounder at 1; PacBio Fifth Amended S-1 at 58-60; *Science* Article.)

25. PacBio reported in its S-1 Registration Statement that "[t]he DNA sequencing market is expected to grow from $1.2 billion in 2009 to more than $3.6 billion by 2014." (PacBio Fifth Amended S-1 at 2.)

26. Like Helicos's patented technology, PacBio's SMRT™ technology uses a single strand of DNA hybridized to a complementary nucleic acid sequence. (*See* Technology Backgrounder at Fig. 10, Step 1 and Fig. 17; PacBio Fifth Amended S-1 at 60; *Science* Article at Fig. 2A.)

27. Like Helicos's patented technology, PacBio's SMRT™ technology uses labeled nucleotides to synthesize a strand of DNA using DNA polymerase: "SMRT sequencing is a real-time approach that uses alternatively labeled phospholinked nucleotides." (Technology Backgrounder at 5; *see also* PacBio Fifth Amended S-1 at 59.) The synthesized strand is complementary to a template strand, and therefore reveals the sequence of the template.

28. Like Helicos's patented technology, the SMRT™ technology allows "the identity of the incorporated base [to be] determined" (Technology Backgrounder at Fig. 13) based on the label:

> When the DNA polymerase encounters the nucleotide complementary to the next base in the template, it is incorporated into the growing DNA chain. During incorporation, the DNA polymerase holds the nucleotide for tens of milliseconds…While held by the polymerase, the fluorescent label emits colored light. The PacBio *RS* detects this as a higher intensity flash of light whose color corresponds to the base identity, which is recorded.

(PacBio Fifth Amended S-1 at 59; Technology Backgrounder at 1, 6, 8 and Figure 10, Step 2; *Science* Article at 134 and Figs. 1A, 1B.)

29. Like Helicos's patented technology, in PacBio's SMRT™ technology the label is removed from the incorporated nucleotide. In the SMRT™ technology, "the DNA polymerase

naturally cleaves the dye molecule from the nucleotide when it cleaves the phosphate chain." (Technology Backgrounder, at 6; *see also* Technology Backgrounder at 1; PacBio Fifth Amended S-1 at 59; *Science* Article at Fig. 1B.)

30. And, like Helicos's patented technology, in PacBio's SMRT™ technology "the polymerase advances to the next base and the process continues to repeat." (Technology Backgrounder at 6; *see also* Technology Backgrounder at 1-2, 7 and Figs. 10 and 14; PacBio Fifth Amended S-1 at 60; *Science* Article at Fig. 1B.)

31. PacBio stated in its S-1 that it has received orders for machines incorporating its SMRT technology from the following customers: Baylor College of Medicine, the Broad Institute of MIT and Harvard, Cold Spring Harbor Laboratory, the U.S. Department of Energy Joint Genome Institute, The Genome Center at Washington University, Monsanto Company, the National Cancer Institute/SAIC-Frederick, the National Center for Genome Resources, the Ontario Institute for Cancer Research, Stanford University and Wellcome Trust Sanger Institute. PacBio also stated that, "[a]s of September 15, 2010, [PacBio has] shipped a total of seven PacBio *RS* limited production release instruments, and [PacBio] intend[s] to ship the remaining four later this year." (PacBio Fifth Amended S-1 at 68.)

LIFE

32. Life gave a presentation entitled "Single Molecule Real-Time DNA Sequencing of a Quantum-dot Nanocrystal" and dated February 27, 2010 at the AGBT (Advances in Genome Biology and Technology) Meeting in Marco Island, Florida ("Life Meeting Presentation"). The presentation states that it was given by Joseph M. Beecham, Chief Technology Officer, Head of Advanced Research, Single Molecule Sequencing for Life. The Life Meeting Presentation

describes its single molecule DNA sequencing system. A copy of the Life Meeting Presentation is attached hereto as Exhibit I.

33. On information and belief, Mr. Beecham gave similar presentations concerning Life's sequencing system since the February 2010 at the AGBT Meeting. A Life Inventor's Day presentation dated June 2, 2010 ("Life Inventor's Day Presentation") contains nearly identical information about Life's sequencing system as that presented at the AGBT meeting. Portions of the Life Inventor's Day Presentation are attached hereto as Exhibit J. In September 2010, Mr. Beecham gave a presentation also entitled "Single Molecule Real-Time DNA Sequencing of a Quantum-dot Nanocrystal" at a Cold Spring Harbor Laboratory Meeting in New York. Mr. Beecham is scheduled to give an identically titled presentation at the American Society of Human Genetics in Maryland on November 4, 2010.

34. Like Helicos's patented technology, Life's sequencing system uses "single DNA template molecules" and uses a "primed immobilized single DNA template molecule" for sequencing. (Life Meeting Presentation at 3, 20.)

35. Like Helicos's patented technology, Life's sequencing system uses labeled nucleotides equipped with "fluorescently tagged phosphate-dye" for incorporation into the DNA strand. (*Id.* at 3.)

36. Like Helicos's patented technology, in Life's sequencing system one nucleotide at a time is added to the DNA chain resulting in a measurable "specific base-call signal" that identifies the base-pair that is added. (*Id.* at 6, 15, 29-31.) The synthesized strand is complementary to the template strand, and therefore reveals the sequence of the template.

37. Like Helicos's patented technology, in Life's sequencing system the fluorescent label is removed from the incorporated nucleotide. As shown in one step of the Life sequencing system, "[f]luorescently-tagged phosphate-dye leaves complex." (*Id.* at 3.)

38. And, like Helicos's patented technology, Life's sequencing system then repeats the process of incorporating the labeled nucleotides into the complementary DNA strand continuing to reveal the sequence of the template: "polymerase translocates; prepares to incorporate next base." (*Id.* at 3.)

ILLUMINA

39. Illumina's website contains an "Illumina Sequencing Technology" presentation describing its single molecule DNA sequencing ("Illumina Presentation"). A copy of the Illumina Presentation is attached hereto as Exhibit K. Metzker, et al. also published an article in 2010 in the National Review of Genetics describing the Illumina Sequencing Technology ("Metzker"). A copy of Metzker is attached hereto as Exhibit L.

40. Like Helicos's patented technology, the Illumina sequencing technology uses a single strand of DNA hybridized to a complementary nucleic acid sequence. The Illumina sequencing technology "[b]ind[s] single-stranded fragments randomly to the inside surface of flow cell channels." (Illumina Presentation at 2.)

41. Like Helicos's patented technology, the Illumina sequencing technology uses DNA polymerase to create a complementary strand of DNA. (*Id.* at 3.) The synthesized strand is complementary to the template strand, and therefore reveals the sequence of the template.

42. Like Helicos's patented technology, the Illumina sequencing technology uses "fluorescently-labeled nucleotides," which are incorporated one at a time into the growing complementary DNA chain. (*Id.* at 1, 3; *see also Metzker* at Fig. 2(a)).

43. Like Helicos's patented technology, Illumina's sequencing technology uses the label to identify the incorporated base pair: "After laser excitation, the emitted fluorescence from each cluster is captured and the first base is identified." (Illumina Presentation at 3.)

44. Also like Helicos's patented technology, in Illumina's sequencing technology the label is removed from the incorporated nucleotide and "[t]he sequencing cycles are repeated to determine the sequence of bases in a fragment, one base at a time." (*Id.* at 3.)

45. Illumina's website also contains a information concerning its platforms for genetic analysis. Illumina's Genome Analyzer, HiSeq 2000 and its Sq Module in combination with its iScan and HiScan platforms (collectively, the "Illumina DNA Sequencing Platforms") are capable of performing the DNA sequencing described above. *See*, *e.g.,* Genome Analysis User Guide ("User Guide"), portions of which are attached hereto as Exhibit M. Bentley, et al. also published an article in Nature in 2008 ("Bentley") describing Illumina's sequencing technology and the operation of Illumina's Genome Analyzer. A copy of the Bentley article is attached hereto as Exhibit N.

46. Like Helicos's patented apparatus claimed in the '109 patent, the Illumina DNA Sequencing Platforms contain a flow cell. (User Guide at 4; Bentley, Supplementary Information at 15.)

47. Like Helicos's patented apparatus, the Illumina DNA Sequencing Platforms utilize a lighting system for illuminating the sample in the flow cell. Specifically, "high sensitivity fluorescence detection is achieved using laser excitation and total internal reflection optics." (User Guide at 36; Bentley, Supplementary Information at 15.)

48. Like Helicos's patented apparatus, the Illumina DNA Sequencing Platforms use an optical instrument for viewing the flow cell, namely "image capture us[ing] a CCD camera." (User Guide at 132.)

49. Like Helicos's patented apparatus, the Illumina DNA Sequencing Platforms use lasers to autofocus the image for image acquisition. (*Id.* at 132; Bentley, Supplementary Information at 15.)

50. It appears from Illumina's Annual Report on Form 10K for the fiscal year ending January 3, 2010 that Illumina's sales of its instruments and related products for its sequencing technology accrued approximately $300 million in sales in the last year.

COUNT I

INFRINGEMENT OF U.S. PATENT NO. 7,645,596 BY PACBIO

51. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-50.

52. On January 12, 2010, the U.S. Patent and Trademark Office duly and legally issued United States Patent No. 7,645,596, titled "Method of Determining the Nucleotide Sequence of Oligonucleotides and DNA Molecules," (the "'596 patent"), a copy of which is attached as Exhibit A.

53. Helicos has the exclusive right and license to manufacture, use, sell, offer for sale, and import the technology covered by the '596 patent, as well as the sole and exclusive right to enforce the patent against infringers and to recover damages resulting therefrom.

54. On information and belief, PacBio has notice of the '596 patent.

55. PacBio has directly infringed, and is directly infringing, the '596 patent in the United States by at least making, using, offering to sell and selling its SMRT™ technology for

single molecule sequencing of DNA, which technology is within the scope of one or more claims of the '596 patent including, for example, its method of DNA sequencing using labeled nucleotides in the synthesis of a strand of DNA that is complementary to a template nucleic acid sequence, determining the identity of each nucleotide incorporated into the synthesized strand, and thereby determining the sequence of the complementary DNA template.

56. On information and belief, PacBio has actively induced, and is actively inducing, the infringement of the '596 patent by third parties, including genome centers, clinical, government and academic institutions, genomics service providers and agricultural companies. PacBio had actual or constructive knowledge of the '596 patent, encouraged and instructed such third parties to use its SMRT™ technology, and knew or should have known that such use would directly infringe the '596 patent. Upon information and belief, PacBio had and has a specific and actual intent to cause this direct infringement.

57. On information and belief, PacBio has contributed to and is contributing to the infringement of the '596 patent by third parties, including genome centers, clinical, government and academic institutions, genomics service providers and agricultural companies. PacBio offers to sell and sells its PacBio *RS* DNA sequencing platform that it knows is especially made or especially adapted for use in infringing the '596 patent. For example, PacBio has offered for sale and sold its PacBio *RS* DNA sequencing platform which is specifically designed to practice PacBio's infringing SMRT™ technology. PacBio has sold in the United States the PacBio *RS* DNA sequencing platform during the time the '596 patent has been in force. PacBio had actual or constructive knowledge of the '596 patent and knew or should have known that the PacBio *RS* DNA sequencing platform has no substantial non-infringing uses.

58. On information and belief, PacBio's infringement of the '596 patent has been, and continues to be, willful. For example, upon information and belief, PacBio knew that there was an objectively high likelihood that its actions would constitute infringement of the '596 patent, but it nevertheless proceeded with such actions and infringed the '596 patent.

59. PacBio manufactures, uses, sells, and/or offers for sale its SMRT™ technology throughout the United States.

60. Helicos is without an adequate remedy at law, because PacBio's continued infringement of the '596 patent will irreparably harm Helicos unless PacBio is enjoined by the Court from the actions complained of herein.

61. As a direct and proximate result of PacBio's infringement of the '596 patent, Helicos has suffered damages and continue to suffer damages in an amount to be determined at trial.

COUNT II

INFRINGEMENT OF U.S. PATENT NO. 7,037,687 BY PACBIO

62. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-61.

63. On May 2, 2006, the U.S. Patent and Trademark Office duly and legally issued United States Patent No. 7,037,687, titled "Method of Determining the Nucleotide Sequence of Oligonucleotides and DNA Molecules," (the "'687 patent"), a copy of which is attached as Exhibit B.

64. Helicos has the exclusive right and license to manufacture, use, sell, offer for sale, and import the technology covered by the '687 patent, as well as the sole and exclusive right to enforce the patent against infringers and to recover damages resulting therefrom.

65. On information and belief, PacBio has notice of the ’687 patent.

66. PacBio has directly infringed, and is directly infringing, the ’687 patent in the United States by at least making, using, offering to sell and selling its SMRT™ technology for single molecule sequencing of DNA, which technology is within the scope of one or more claims of the ’687 patent, for example its method of DNA sequencing using labeled nucleotides in the synthesis of a strand of DNA that is complementary to a template nucleic acid sequence, determining the identity of each nucleotide incorporated into the synthesized strand, and thereby determining the sequence of the complementary DNA template.

67. On information and belief, PacBio has actively induced, and is actively inducing, the infringement of the ’687 patent by third parties, including genome centers, clinical, government and academic institutions, genomics service providers and agricultural companies. PacBio had actual or constructive knowledge of the ’687 patent, encouraged and instructed such third parties to use its SMRT™ technology, and knew or should have known that such use would directly infringe the ’687 patent. Upon information and belief, PacBio had and has a specific and actual intent to cause this direct infringement.

68. On information and belief, PacBio has contributed to and is contributing to the infringement of the ‘687 patent by third parties, including genome centers, clinical, government and academic institutions, genomics service providers and agricultural companies. PacBio offers to sell and sells its PacBio *RS* DNA sequencing platform that it knows is especially made or especially adapted for use in infringing the ’687 patent. For example, PacBio has offered for sale and sold its PacBio *RS* DNA sequencing platform which is specifically designed to practice PacBio’s infringing SMRT™ technology. PacBio has sold in the United States the PacBio *RS* DNA sequencing platform during the time the ’687 patent has been in force. PacBio had actual

or constructive knowledge of the ’687 patent and knew or should have known that the PacBio *RS* DNA sequencing platform has no substantial non-infringing uses.

69. On information and belief, PacBio’s infringement of the ’687 patent has been, and continues to be, willful. For example, upon information and belief, PacBio knew that there was an objectively high likelihood that its actions would constitute infringement of the ’687 patent, but it nevertheless proceeded with such actions and infringed the ’687 patent.

70. PacBio manufactures, uses, sells, and/or offers for sale its SMRT™ technology throughout the United States.

71. Helicos is without an adequate remedy at law, because PacBio’s continued infringement of the ’687 patent will irreparably harm Helicos unless PacBio is enjoined by the Court from the actions complained of herein.

72. As a direct and proximate result of PacBio’s infringement of the ’687 patent, Helicos has suffered damages and continue to suffer damages in an amount to be determined at trial.

COUNT III

INFRINGEMENT OF U.S. PATENT NO. 7,169,560 BY PACBIO

73. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-72.

74. On January 30, 2007, the U.S. Patent and Trademark Office duly and legally issued United States Patent No. 7,169,560, titled “Short Cycle Methods for Sequencing Polynucelotides,” (the “’560 patent”), a copy of which is attached as Exhibit C.

75. Helicos is the assignee of the ’560 patent.

76. On information and belief, PacBio has notice of the ’560 patent.

77. PacBio has directly infringed, and is directly infringing, the '560 patent in the United States by at least making, using, offering to sell and selling its SMRT™ technology for single molecule sequencing of DNA, which technology is within the scope of one or more claims of the '560 patent, for example, its method of DNA sequencing using labeled nucleotides in the synthesis of a strand of DNA that is complementary to a template nucleic acid sequence, determining the identity of each nucleotide incorporated into the synthesized strand, and thereby determining the sequence of the complementary DNA template.

78. On information and belief, PacBio has actively induced, and is actively inducing, the infringement of the '560 patent by third parties, including genome centers, clinical, government and academic institutions, genomics service providers and agricultural companies. PacBio had actual or constructive knowledge of the '560 patent, encouraged and instructed such third parties to use its SMRT™ technology, and knew or should have known that such use would directly infringe the '560 patent. Upon information and belief, PacBio had and has a specific and actual intent to cause this direct infringement.

79. On information and belief, PacBio has contributed to and is contributing to the infringement of the '560 patent by third parties, including genome centers, clinical, government and academic institutions, genomics service providers and agricultural companies. PacBio offers to sell and sells its PacBio *RS* DNA sequencing platform that it knows is especially made or especially adapted for use in infringing the '560 patent. For example, PacBio has offered for sale and sold its PacBio *RS* DNA sequencing platform which is specifically designed to practice PacBio's infringing SMRT™ technology. On information and belief, PacBio has sold in the United States the PacBio *RS* DNA sequencing platform during the time the '560 patent has been in force. PacBio had actual or constructive knowledge of the '560 patent and knew or should

have known that the PacBio *RS* DNA sequencing platform has no substantial non-infringing uses.

80. On information and belief, PacBio's infringement of the '560 patent has been, and continues to be, willful. For example, upon information and belief, PacBio knew that there was an objectively high likelihood that its actions would constitute infringement of the '560 patent, but it nevertheless proceeded with such actions and infringed the '560 patent.

81. PacBio manufactures, uses, sells, and/or offers for sale its SMRT™ technology throughout the United States.

82. Helicos is without an adequate remedy at law, because PacBio's continued infringement of the '560 patent will irreparably harm Helicos unless PacBio is enjoined by the Court from the actions complained of herein.

83. As a direct and proximate result of PacBio's infringement of the '560 patent, Helicos has suffered damages and continue to suffer damages in an amount to be determined at trial.

COUNT IV

INFRINGEMENT OF U.S. PATENT NO. 7,767,400 BY PACBIO

84. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-83.

85. On August 3, 2010, the U.S. Patent and Trademark Office duly and legally issued United States Patent No. 7,767,400, titled "Paired-end Reads in Sequencing by Synthesis," (the "'400 patent"), a copy of which is attached as Exhibit D.

86. Helicos is the assignee of the '400 patent.

87. On information and belief, PacBio has notice of the '400 patent.

88. PacBio has directly infringed, and is directly infringing, the ’400 patent in the United States by at least making, using, offering to sell and selling its SMRT™ technology for single molecule sequencing of DNA, which technology is within the scope of one or more claims of the ’400 patent including, for example, its method of Strobe Sequencing and its use of the SMRTbell™ Template technology.

89. On information and belief, PacBio has actively induced, and is actively inducing, the infringement of the ’400 patent by third parties, including genome centers, clinical, government and academic institutions, genomics service providers and agricultural companies. PacBio had actual or constructive knowledge of the ’400 patent, encouraged and instructed such third parties to use its SMRT™ technology, and knew or should have known that such use would directly infringe the ’400 patent. Upon information and belief, PacBio had and has a specific and actual intent to cause this direct infringement.

90. On information and belief, PacBio has contributed to and is contributing to the infringement of the ’400 patent by third parties, including genome centers, clinical, government and academic institutions, genomics service providers and agricultural companies. PacBio offers to sell and sells its PacBio *RS* DNA sequencing platform that it knows is especially made or especially adapted for use in infringing the ’400 patent. For example, PacBio has offered for sale and sold its PacBio *RS* DNA sequencing platform which is specifically designed to practice PacBio’s infringing SMRT™ technology. PacBio has sold in the United States the PacBio *RS* DNA sequencing platform during the time the ’400 patent has been in force. PacBio had actual or constructive knowledge of the ’400 patent and knew or should have known that the PacBio *RS* DNA sequencing platform has no substantial non-infringing uses.

91. On information and belief, PacBio's infringement of the '400 patent has been, and continues to be, willful. For example, upon information and belief, PacBio knew that there was an objectively high likelihood that its actions would constitute infringement of the '400 patent, but it nevertheless proceeded with such actions and infringed the '400 patent.

92. PacBio manufactures, uses, sells, and/or offers for sale its SMRT™ technology throughout the United States.

93. Helicos is without an adequate remedy at law, because PacBio's continued infringement of the '400 patent will irreparably harm Helicos unless PacBio is enjoined by the Court from the actions complained of herein.

94. As a direct and proximate result of PacBio's infringement of the '400 patent, Helicos has suffered damages and continues to suffer damages in an amount to be determined at trial.

COUNT V

INFRINGEMENT OF U.S. PATENT NO. 7,645,596 BY LIFE

95. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-94.

96. On January 12, 2010, the U.S. Patent and Trademark Office duly and legally issued United States Patent No. 7,645,596, titled "Method of Determining the Nucleotide Sequence of Oligonucleotides and DNA Molecules," (the "'596 patent"), a copy of which is attached as Exhibit A.

97. Helicos has the exclusive right and license to manufacture, use, sell, offer for sale, and import the technology covered by the '596 patent, as well as the sole and exclusive right to enforce the patent against infringers and to recover damages resulting therefrom.

98. On information and belief, Life has notice of the ’596 patent.

99. Life has directly infringed, and is directly infringing, the ’596 patent in the United States by at least making, using and offering to sell its Single Molecule Real-Time DNA Sequencing of a Quantum-dot Nanocrystal technology for single molecule sequencing of DNA, which technology is within the scope of one or more claims of the ’596 patent including, for example, its method of DNA sequencing using labeled nucleotides in the synthesis of a strand of DNA that is complementary to a template nucleic acid sequence, determining the identity of each nucleotide incorporated into the synthesized strand, and thereby determining the sequence of the complementary DNA template.

100. On information and belief, Life’s infringement of the ’596 patent has been, and continues to be, willful. For example, upon information and belief, Life knew that there was an objectively high likelihood that its actions would constitute infringement of the ’596 patent, but it nevertheless proceeded with such actions and infringed the ’596 patent.

101. On information and belief, Life uses its Single Molecule Real-Time DNA Sequencing of a Quantum-dot Nanocrystal technology throughout the United States.

102. Helicos is without an adequate remedy at law, because Life’s continued infringement of the ’596 patent will irreparably harm Helicos unless Life is enjoined by the Court from the actions complained of herein.

103. As a direct and proximate result of Life’s infringement of the ’596 patent, Helicos has suffered damages and continues to suffer damages in an amount to be determined at trial.

COUNT VI

INFRINGEMENT OF U.S. PATENT NO. 7,037,687 BY LIFE

104. Helicos realleges and incorporates by reference as if set forth in full the

allegations of paragraphs 1-103.

105. On May 2, 2006, the U.S. Patent and Trademark Office duly and legally issued United States Patent No. 7,037,687, titled "Method of Determining the Nucleotide Sequence of Oligonucleotides and DNA Molecules," (the "'687 patent"), a copy of which is attached as Exhibit B.

106. Helicos has the exclusive right and license to manufacture, use, sell, offer for sale, and import the technology covered by the '687 patent, as well as the sole and exclusive right to enforce the patent against infringers and to recover damages resulting therefrom.

107. On information and belief, Life has notice of the '687 patent.

108. Life has directly infringed, and is directly infringing, the '687 patent in the United States by at least making, using and offering to sell its Single Molecule Real-Time DNA Sequencing of a Quantum-dot Nanocrystal technology for single molecule sequencing of DNA, which technology is within the scope of one or more claims of the '687 patent, for example its method of DNA sequencing using labeled nucleotides in the synthesis of a strand of DNA that is complementary to a template nucleic acid sequence, determining the identity of each nucleotide incorporated into the synthesized strand, and thereby determining the sequence of the complementary DNA template.

109. On information and belief, Life's infringement of the '687 patent has been, and continues to be, willful. For example, upon information and belief, Life knew that there was an objectively high likelihood that its actions would constitute infringement of the '687 patent, but it nevertheless proceeded with such actions and infringed the '687 patent.

110. On information and belief, Life uses its Single Molecule Real-Time DNA Sequencing of a Quantum-dot Nanocrystal technology throughout the United States.

111. Helicos is without an adequate remedy at law, because Life's continued infringement of the '687 patent will irreparably harm Helicos unless Life is enjoined by the Court from the actions complained of herein.

112. As a direct and proximate result of Life's infringement of the '687 patent, Helicos has suffered damages and continues to suffer damages in an amount to be determined at trial.

COUNT VII

INFRINGEMENT OF U.S. PATENT NO. 7,169,560 BY LIFE

113. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-112.

114. On January 30, 2007, the U.S. Patent and Trademark Office duly and legally issued United States Patent No. 7,169,560, titled "Short Cycle Methods for Sequencing Polynucelotides," (the "'560 patent"), a copy of which is attached as Exhibit C.

115. Helicos is the assignee of the '560 patent.

116. On information and belief, Life has notice of the '560 patent.

117. Life has directly infringed, and is directly infringing, the '560 patent in the United States by at least making, using and offering to sell its Single Molecule Real-Time DNA Sequencing of a Quantum-dot Nanocrystal technology for single molecule sequencing of DNA, which technology is within the scope of one or more claims of the '560 patent for example, its method of DNA sequencing using labeled nucleotides in the synthesis of a strand of DNA that is complementary to a template nucleic acid sequence, determining the identity of each nucleotide incorporated into the synthesized strand, and thereby determining the sequence of the complementary DNA template.

118. On information and belief, Life's infringement of the '560 patent has been, and continues to be, willful. For example, upon information and belief, Life knew that there was an objectively high likelihood that its actions would constitute infringement of the '560 patent, but it nevertheless proceeded with such actions and infringed the '560 patent.

119. Life uses its Single Molecule Real-Time DNA Sequencing of a Quantum-dot Nanocrystal technology throughout the United States.

120. Helicos is without an adequate remedy at law, because Life's continued infringement of the '560 patent will irreparably harm Helicos unless Life is enjoined by the Court from the actions complained of herein.

121. As a direct and proximate result of Life's infringement of the '560 patent, Helicos has suffered damages and continues to suffer damages in an amount to be determined at trial.

COUNT VII

INFRINGEMENT OF U.S. PATENT NO. 7,037,687 BY ILLUMINA

122. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-121.

123. On May 2, 2006, the U.S. Patent and Trademark Office duly and legally issued United States Patent No. 7,037,687, titled "Method of Determining the Nucleotide Sequence of Oligonucleotides and DNA Molecules," (the "'687 patent"), a copy of which is attached as Exhibit B.

124. Helicos has the exclusive right and license to manufacture, use, sell, offer for sale, and import the technology covered by the '687 patent, as well as the sole and exclusive right to enforce the patent against infringers and to recover damages resulting therefrom.

125. On information and belief, Illumina has notice of the '687 patent.

126. Illumina has directly infringed, and is directly infringing, the ’687 patent in the United States by at least making, using, offering to sell, selling and importing its sequencing technology for single molecule sequencing of DNA, which technology is within the scope of one or more claims of the ’687 patent, for example its method of DNA sequencing using labeled nucleotides in the synthesis of a strand of DNA that is complementary to a template nucleic acid sequence, determining the identity of each nucleotide incorporated into the synthesized strand, and thereby determining the sequence of the complementary DNA template.

127. On information and belief, Illumina has actively induced, and is actively inducing, the infringement of the ’687 patent by third parties, including genome centers, clinical, government and academic institutions, genomics service providers, molecular diagnostic companies and agricultural companies, among others. Illumina had actual or constructive knowledge of the ’687 patent, encouraged and instructed such third parties to use its sequencing technology, and knew or should have known that such use would directly infringe the ’687 patent. Upon information and belief, Illumina had and has a specific and actual intent to cause this direct infringement.

128. On information and belief, Illumina has contributed to and is contributing to the infringement of the ‘687 patent by third parties, including genome centers, clinical, government and academic institutions, genomics service providers, molecular diagnostic companies and agricultural companies, among others. Illumina offers to sell and sells the Illumina DNA Sequencing Platforms, that it knows are especially made or especially adapted for use in infringing the ’687 patent. For example, Illumina has offered for sale and sold the Illumina DNA Sequencing Platforms, which are specifically designed to practice Illumina’s infringing sequencing technology. Illumina has sold in the United States the Illumina DNA Sequencing

Platforms during the time the ’687 patent has been in force. Illumina had actual or constructive knowledge of the ’687 patent and knew or should have known that the Illumina DNA Sequencing Platforms have no substantial non-infringing uses.

129. On information and belief, Illumina’s infringement of the ’687 patent has been, and continues to be, willful. For example, upon information and belief, Illumina knew that there was an objectively high likelihood that its actions would constitute infringement of the ’687 patent, but it nevertheless proceeded with such actions and infringed the ’687 patent.

130. Illumina manufactures, uses, sells, offers for sale and/or imports its sequencing technology throughout the United States.

131. Helicos is without an adequate remedy at law, because Illumina’s continued infringement of the ’687 patent will irreparably harm Helicos unless Illumina is enjoined by the Court from the actions complained of herein.

132. As a direct and proximate result of Illumina’s infringement of the ’687 patent, Helicos has suffered damages and continue to suffer damages in an amount to be determined at trial.

COUNT IX

INFRINGEMENT OF U.S. PATENT NO. 7,169,560 BY ILLUMINA

133. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-132.

134. On January 30, 2007, the U.S. Patent and Trademark Office duly and legally issued United States Patent No. 7,169,560, titled “Short Cycle Methods for Sequencing Polynucelotides,” (the “’560 patent”), a copy of which is attached as Exhibit C.

135. Helicos is the assignee of the ’560 patent.

136. On information and belief, Illumina has notice of the ’560 patent.

137. Illumina has directly infringed, and is directly infringing, the ’560 patent in the United States by at least making, using, offering to sell, selling and importing its sequencing technology for single molecule sequencing of DNA, which technology is within the scope of one or more claims of the ’560 patent, for example its method of DNA sequencing using labeled nucleotides in the synthesis of a strand of DNA that is complementary to a template nucleic acid sequence, determining the identity of each nucleotide incorporated into the synthesized strand, and thereby determining the sequence of the complementary DNA template.

138. On information and belief, Illumina has actively induced, and is actively inducing, the infringement of the ’560 patent by third parties, including genome centers, clinical, government and academic institutions, genomics service providers, molecular diagnostic companies and agricultural companies, among others. Illumina had actual or constructive knowledge of the ’560 patent, encouraged and instructed such third parties to use its sequencing technology, and knew or should have known that such use would directly infringe the ’560 patent. Upon information and belief, Illumina had and has a specific and actual intent to cause this direct infringement.

139. On information and belief, Illumina has contributed to and is contributing to the infringement of the ‘560 patent by third parties, including genome centers, clinical, government and academic institutions, genomics service providers, molecular diagnostic companies and agricultural companies, among others. Illumina offers to sell and sells the Illumina DNA Sequencing Platforms that it knows is especially made or especially adapted for use in infringing the ’560 patent. For example, Illumina has offered for sale and sold the Illumina DNA Sequencing Platforms, which are specifically designed to practice Illumina’s infringing

sequencing technology. Illumina has sold in the United States the Illumina DNA Sequencing Platforms during the time the '560 patent has been in force. Illumina had actual or constructive knowledge of the '560 patent and knew or should have known that the Illumina DNA Sequencing Platforms have no substantial non-infringing uses.

140. On information and belief, Illumina's infringement of the '560 patent has been, and continues to be, willful. For example, upon information and belief, Illumina knew that there was an objectively high likelihood that its actions would constitute infringement of the '560 patent, but it nevertheless proceeded with such actions and infringed the '560 patent.

141. Illumina manufactures, uses, sells, offers for sale and/or importing its sequencing technology throughout the United States.

142. Helicos is without an adequate remedy at law, because Illumina's continued infringement of the '560 patent will irreparably harm Helicos unless Illumina is enjoined by the Court from the actions complained of herein.

143. As a direct and proximate result of Illumina's infringement of the '560 patent, Helicos has suffered damages and continue to suffer damages in an amount to be determined at trial.

COUNT X

INFRINGEMENT OF U.S. PATENT NO. 7,593,109 BY ILLUMINA

144. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-143.

145. On September 22, 2009, the U.S. Patent and Trademark Office duly and legally issued United States Patent No. 7,539,109, titled "Apparatus and Methods for Analyzing Samples," (the "'593 patent"), a copy of which is attached as Exhibit E.

146. Helicos is the assignee of the ’109 patent.

147. Helicos has the exclusive right and license to manufacture, use, sell, offer for sale, and import the technology covered by the ’109 patent, as well as the sole and exclusive right to enforce the patent against infringers and to recover damages resulting therefrom.

148. On information and belief, Illumina has notice of the ’109 patent.

149. Illumina has directly infringed, and is directly infringing, the ’109 patent in the United States by at least making, using, offering to sell, selling and importing the Illumina DNA Sequencing Platforms.

150. On information and belief, Illumina’s infringement of the ’109 patent has been, and continues to be, willful. For example, upon information and belief, Illumina knew that there was an objectively high likelihood that its actions would constitute infringement of the ’109 patent, but it nevertheless proceeded with such actions and infringed the ’109 patent.

151. Illumina manufactures, uses, sells, offers and/or imports for sale the Illumina DNA Sequencing Platforms throughout the United States.

152. Helicos is without an adequate remedy at law, because Illumina’s continued infringement of the ’109 patent will irreparably harm Helicos unless Illumina is enjoined by the Court from the actions complained of herein.

153. As a direct and proximate result of Illumina’s infringement of the ’109 patent, Helicos has suffered damages and continue to suffer damages in an amount to be determined at trial.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff prays for the following relief:

A. A finding that PacBio has infringed the ’596, ’687, ’560 and ’400 patents;

B. A finding that PacBio's infringement of the '596, '687, '560 and '400 patents has been willful;

C. A permanent injunction prohibiting PacBio, its officers, agents, servants, employees, attorneys, and all other persons in active concert or participation with PacBio who have notice of the injunction, from further infringing the '596, '687, '560 and '400 patents throughout their respective enforceable terms;

D. An accounting for damages arising from the infringement of the '596, '687, '560 and '400 patents by PacBio and those in privity with PacBio, including loss of market share;

E. An award of damages proximately caused by PacBio's unlawful acts, at least under 35 U.S.C. § 284;

F. An award of increased damages and punitive damages for the willful nature of PacBio's unlawful acts, said award to equal treble the amount of actual damages;

G. A finding that Life has infringed the '596, '687, and '560 patents;

H. A finding that Life's infringement of the '596, '687, and '560 patents has been willful;

I. A permanent injunction prohibiting Life, its officers, agents, servants, employees, attorneys, and all other persons in active concert or participation with Life who have notice of the injunction, from further infringing the '596, '687, and '560 patents throughout their respective enforceable terms;

J. An accounting for damages arising from the infringement of the '596, '687, and '560 patents by Life and those in privity with Life, including loss of market share;

K. An award of damages proximately caused by Life's unlawful acts, at least under 35 U.S.C. § 284;

L. An award of increased damages and punitive damages for the willful nature of Life's unlawful acts, said award to equal treble the amount of actual damages;

M. A finding that Illumina has infringed the '687, '560, and '109 patents;

N. A finding that Illumina's infringement of the '687, '560, and '109 patents has been willful;

O. A permanent injunction prohibiting Illumina, its officers, agents, servants, employees, attorneys, and all other persons in active concert or participation with Illumina who have notice of the injunction, from further infringing the '687, '560, and '109 patents throughout their respective enforceable terms;

P. An accounting for damages arising from the infringement of the '687, '560, and '109 patents by Illumina and those in privity with Illumina, including loss of market share;

Q. An award of damages proximately caused by Illumina's unlawful acts, at least under 35 U.S.C. § 284;

R. An award of increased damages and punitive damages for the willful nature of Illumina's unlawful acts, said award to equal treble the amount of actual damages;

S. An award of the costs and attorneys' fees Helicos has incurred in bringing and maintaining this action;

T. An award of pre-judgment and post-judgment interest; and

U. Such further and other relief as the Court deems just and proper.

JURY DEMAND

Helicos demands a trial by jury on all issues so triable.

BAYARD, P.A.

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October 22, 2010