UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

HELICOS BIOSCIENCES CORPORATION, Plaintiff, v. PACIFIC BIOSCIENCES OF CALIFORNIA, INC. Defendant.	C.A. No. _____ **DEMAND FOR JURY TRIAL**

COMPLAINT

Plaintiff Helicos Biosciences Corporation ("Helicos") for its Complaint against defendant Pacific Biosciences of California, Inc. ("PacBio"), alleges as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement stemming from defendant PacBio's unauthorized manufacture, use, sale, and offer for sale 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. PacBio is also a life sciences company and is a direct competitor of Helicos.

JURISDICTION AND VENUE

6. 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.

7. 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 defendant PacBio are Delaware corporations.

DNA SEQUENCING

8. 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.

9. 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.

10. 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.

11. 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.

12. 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

13. 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.

14. 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.

15. 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.

16. 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.

17. 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.

PACBIO

18. 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 E. PacBio describes its technology as "based on

eavesdropping on a single DNA polymerase molecule working in a continuous, processive manner." (Technology Backgrounder at 1.)

19. On August 16, 2010, PacBio filed a Form S-1 Registration Statement with the Securities and Exchange Commission also detailing its SMRT™ technology. Portions of PacBio's Form S-1 are attached hereto as Exhibit F. PacBio also published an article in *Science* explaining its technology. A copy of that article is attached hereto as Exhibit G.

20. Like Helicos's patented technology, "the initial application for [PacBio's SMRT™ technology] is DNA sequencing." (PacBio S-1 at 56; *see also* Technology Backgrounder at 1; PacBio S-1 at 54, 55; *Science* Article.)

21. PacBio reported in its S-1 Registration Statement that "the DNA sequencing market is expected to grow from $1.2 billion in 2009 to more than $3.6 billion by 2014." (PacBio S-1 at 2.)

22. 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 S-1 at 55; *Science* Article at Fig. 2A.)

23. 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 S-1 at 54.) The synthesized strand is complementary to a template strand, and therefore reveals the sequence of the template.

24. 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 flash whose color corresponds to the base identity, which is recorded.

(PacBio S-1 at 55; *see also* Pac-Bio S-1 at 54; Technology Backgrounder at 1, 6, 8 and Figure 10, Step 2; *Science* Article at 136 and Figs. 1A, 1B.)

25. 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 S-1 at 54; *Science* Article at Fig. 1B.)

26. 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; Pac-Bio S-1 at 55; *Science* Article at Fig. 1B.)

27. 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 August 15, 2010, [PacBio has] shipped a total of five PacBio *RS*

limited production release instruments, and [PacBio] intend[s] to ship the remaining six later this year." (PacBio S-1 at 61.)

COUNT I

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

28. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-27.

29. 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.

30. 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.

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

32. 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.

33. 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.

34. 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.

35. 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.

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

37. 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.

38. 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

39. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-38.

40. 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.

41. 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.

42. On information and belief, PacBio has notice of the '687 patent.

43. 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.

44. 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.

45. 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.

46. 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.

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

48. 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.

49. 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

50. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-49.

51. 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.

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

53. On information and belief, PacBio has notice of the '560 patent.

54. 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.

55. 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.

56. 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.

57. 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.

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

59. 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.

60. 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

61. Helicos realleges and incorporates by reference as if set forth in full the allegations of paragraphs 1-60.

62. 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.

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

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

65. 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.

66. 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.

67. 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.

68. 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.

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

70. 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.

71. 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.

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

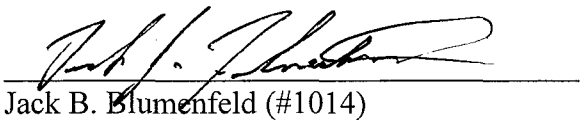
H. An award of pre-judgment and post-judgment interest; and

I. 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.

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