Helicos BioSciences Corporation

2008 Annual Report

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2008

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

COMMISSION FILE NUMBER 001-33484

HELICOS BIOSCIENCES CORPORATION

(Exact name of registrant as specified in its charter)

DELAWARE (State or other jurisdiction of incorporation or organization)	**05-0587367** (I.R.S. Employer Identification No.)
One Kendall Square Building 700 Cambridge, Massachusetts (Address of principal executive offices)	**02139** (Zip Code)

Registrant's telephone number, including area code: **(617) 264-1800**

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.001 par value	The NASDAQ Global Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☐	Accelerated filer ☐	Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of the registrant's Common Stock held beneficially or of record by stockholders who are not affiliates of the registrant, based upon the closing price of the Common Stock on June 30, 2008, as reported by the NASDAQ Global Market, was approximately $41,061,033. For the purposes hereof, "affiliates" include all executive officers and directors of the registrant.

As of March 20, 2009, the Company had 64,553,002 shares of Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The Company intends to file a proxy statement pursuant to Regulation 14A within 120 days of the end of the fiscal year ended December 31, 2008. Portions of such proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated.

HELICOS BIOSCIENCES CORPORATION (a development stage company)
FORM 10-K
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2008
TABLE OF CONTENTS

PART I

ITEM 1. BUSINESS

OVERVIEW

Helicos BioSciences Corporation is a life sciences company focused on innovative genetic analysis technologies for the research, drug discovery and clinical diagnostics markets. Our products are based on our proprietary True Single Molecule Sequencing (tSMS)™ technology which enables rapid analysis of large quantities of genetic material by directly sequencing single molecules of DNA or single DNA copies of RNA. This approach differs from current methods of sequencing DNA because it analyzes individual molecules of DNA directly instead of analyzing a large number of copies of the molecule produced through complex sample preparation techniques. Our tSMS technology eliminates the need for costly, labor-intensive and time-consuming sample preparation techniques, such as amplification or cloning, which are required by other methods to produce a sufficient quantity of genetic material for analysis.

We believe that our tSMS technology represents the first comprehensive and universal solution for single molecule genetic analysis and that its adoption can expand the market for genetic analysis while substantially lowering the cost of individual analyses. Our goal is to enable production-level genetic analysis on an unprecedented scale by providing scientists and clinicians with the ability to compare genes and genomes from thousands of individuals. If our tSMS-based products are successful, the information generated from using these products may lead to improved drug therapies, personalized medical treatments and more accurate diagnostics for cancer and other diseases.

Our Helicos™ Genetic Analysis Platform is designed to obtain sequencing information by repetitively performing a cycle of biochemical reactions on individual DNA molecules and imaging the results after each cycle. The platform consists of an instrument called the HeliScope™ Single Molecule Sequencer, an image analysis computer tower called the HeliScope™ Analysis Engine, associated reagents, which are chemicals used in the sequencing process, and disposable supplies.

The imaging capability of the HeliScope Sequencer is designed to accommodate performance beyond what is needed to meet the platform's initial goals, providing the flexibility to introduce substantial throughput and cost improvements in the future without major changes to or replacement of the instrument. We believe that the Helicos Genetic Analysis Platform will ultimately enable the automated, parallel sequencing of billions of individual DNA molecules with greater speed and lower cost than other sequencing systems.

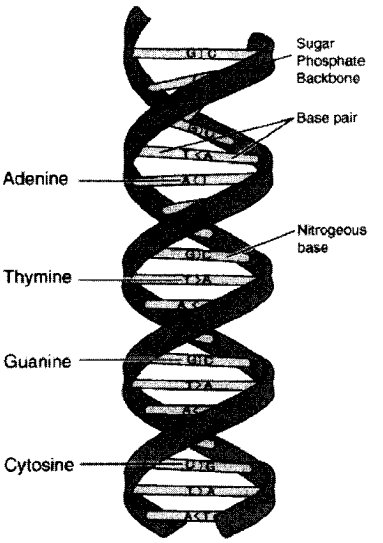
BACKGROUND ON DNA STRUCTURE AND FUNCTION

The genetic program that controls a living cell is encoded in its DNA. The diagram below shows the typical double-helix structure of DNA. The two strands are made 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 the polymer, and the bases face each other. The letters A, G, T and C represent the four types of nucleotide bases: adenine, guanine, thymine and cytosine.

The bases align with each other in a complementary structure held together by hydrogen bonds. A "T" on one strand always bonds with an "A" on the other strand, and a "G" on one strand always bonds with a "C" on the other strand. This bonding between DNA strands is called hybridization, and the resulting structure is called a base pair.

The genome of an organism is a complete DNA sequence of that organism. The human genome contains about three billion base pairs of DNA, which is represented twice in each cell. In a human, the individual acquires one version of the genome from the mother and one version from the father.



The human genome includes approximately 30,000 genes. Genes are segments of DNA that contain the information needed for a cell to make proteins. Each gene has one or more parts called coding regions that specify the sequence of amino acids for that protein. Genes also contain regulatory elements that determine when, where and how much protein is made. While it is currently understood that approximately 97% of the human genome does not code for proteins, recent research suggests that this non-coding DNA also contains important regulatory elements which plays an important role in controlling when and how much genes are expressed.

The process of making proteins using the information in DNA involves a process called gene expression. To express a gene, enzymes called RNA polymerases transcribe the coding region into molecules of messenger RNA, or mRNA. The mRNA moves from the nucleus into the cytoplasm, where the cell's protein synthesis machinery translates the genetic sequence information and assembles a chain of amino acids into a protein.

On June 26, 2000, scientists announced completion of the rough draft human genome sequence. This ten-year effort, known as the Human Genome Project, yielded many surprising discoveries. Among these was the realization that the human genome contains roughly the same number of genes, about 30,000, as other mammalian species. Moreover, the vast majority of genes and their sequences were found to be remarkably similar among different species. Much ongoing research involves understanding the subtle variations in genes and regulatory regions of the genome that make a human different from a mouse, and make individuals within a species different from each other.

Studying how genes and proteins differ between species and among individuals within a species helps scientists to determine their functions and their roles in health and disease. Inherited genetic variations among individuals contribute to differences in susceptibility to diseases and responses to drug treatments. Recent studies across the genomes of several individuals has begun to point to the fact that variation between any two individuals is significantly greater than anticipated, which opens the door for further understanding the spectrum of human diseases and differing responses to dietary, life style and environmental inputs in our daily lives.

Genetic mutations that arise in the body can lead to the development of cancer and other diseases. The current understanding of cancer suggests that relatively few changes to key elements in genes or regulatory regions can lead to the wildly differing phenotypes which are the characteristic of cancers. A research goal of cancer biology is to be able to understand how cancers differ at the genomic level and to use this information to match the correct therapy to a specific kind cancer therefore increasing probability of successful treatment.

In addition, cells of the immune system have the means to rearrange their genes to better fight infection, but faulty operation of this system can lead to inflammatory and autoimmune diseases. Increased understanding of genetic variation is expected to yield improvements in the diagnosis, treatment and even prevention of many diseases.

INDUSTRY OVERVIEW

Genomic information has become a critical tool to understanding the mechanics of life, the environmental effect on biological systems, diagnosis of disease and treatment of disease. Life science tools that analyze genomic material have provided tremendous insights into the complexity and variability of the genome and have changed the methods and strategies by which scientists conduct their research. Genomic information enables the possibility and promise of personalized medicine and should bring forth a new era in patient knowledge whereby individuals now can have access to their own genetic information to make informed decisions concerning the prevention and treatment of disease.

Genomic analysis market opportunity

Since the development of genetic engineering techniques in the 1970s, the analysis of genetic material has become a mainstay of biological research. The first automated DNA sequencer was invented in 1986, based on technology developed by Frederick Sanger and his colleagues in 1975, which is commonly referred to as Sanger sequencing. Subsequent versions of commercial DNA sequencers have increased the speed of DNA sequencing by 3,000 fold, making possible the Human Genome Project. In 1996 the first commercial microarray was introduced and enabled a new era of RNA analysis by measuring gene expression across many genes in a single experiment. Subsequent versions of the commercial microarrays including DNA and RNA have significantly increased the amount of information per run and provided selected single nucleotide polymorphisms, or SNPs of the whole human genome on a single chip, enabled large scale genome-wide SNP association studies and have been commercialized for several diagnostic applications. Today, manufacturers of systems, supplies and reagents for performing genetic analysis, which includes DNA sequencing, genotyping, and gene expression analysis, serve a worldwide market of approximately $5 billion, according to Strategic Directions International. Strategic Directions International estimates that DNA sequencing serves approximately 17% of this demand for genetic analysis. The remainder of this market is addressed by other genetic analysis methods, such as gene expression analysis and genotyping. Recent studies have demonstrated the complexity and variability of the human genome. This new information will necessitate larger scale studies, and require new methods and strategies that combine different application and data analysis techniques across these larger studies. Sanger methods of DNA and RNA sequencing and microarray based technologies will have limited utility in these new strategies based on their inherent technology limitations, throughput, cost and complexity of sample preparation. Therefore, high throughput technologies that provide complete sequence and quantitative information with simplified workflows and low cost per sample will be required.

The problem

To explore the next frontier of biomedical research, scientists must design comprehensive experiments on a larger scale than previously thought possible. Current methods of genetic analysis include DNA sequencing, gene expression analysis, genotyping and epigenetics. DNA and RNA

sequencing provide the most comprehensive genome-wide information without any prior knowledge of the sequence or sequence variation; however, the limitations of Sanger sequencing technologies restrict their use in large-scale studies and as a replacement for multiple technologies. In particular, limitations of Sanger sequencing include:

- *Low throughput.* Scientists measure the throughput of a DNA sequencing technology based on the number of bases analyzed per unit of time. We believe the highest-throughput automated Sanger sequencers can produce up to 2.9 million bases of genomic sequence data per day, or approximately 120,000 bases per hour, based on their performance specifications. Accordingly, we estimate it would take a single Sanger sequencer nearly 50 years to sequence an entire individual human genome at the 10x coverage required for accuracy. This timeframe is impractical for population disease studies as well as for individualized patient analysis and diagnostics.
- *Lack of sensitivity.* Sanger sequencing instruments inherently lack the sensitivity to analyze single 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 a polymerase chain reaction, or PCR. However, PCR introduces new errors in the analyzed genetic sequence in each round of the copying process, which may result in incorrect and possibly misleading results. In an important recent study of mutations in cancer cells published in the October 2006 edition of *Science*, PCR-related errors accounted for more than one-third of the putative candidate mutations. In addition, the use of amplification or cloning results in a population of molecules, the sequences of which are averaged together, thus making it difficult to detect low-prevalence sequence variations in the starting sample.
- *High cost.* The cost of sample preparation and sequence analysis for a complete individual human genome using current Sanger sequencing methods is approximately $15 million according to the National Institutes of Health. The high cost of sequencing has restricted scientific research. For example, for almost twenty years the scientific community has understood that cancer is a disease arising from mutations of the tumor genome yet not a single complete cancer genome has been sequenced to date.
- *Complex and hard-to-use.* Sanger sequencing technologies require extensive, labor-intensive and time-consuming sample preparation processes. These sample preparation processes often involve costly additional capital equipment, reagents, supplies and physical space as well as experimental redundancy to account for human error or limitations in accuracy. Thus, the complexity of sample preparation creates workflow bottlenecks in applying Sanger sequencing to large numbers of samples.

In response to these limitations, next generation sequencing technologies seek to improve the speed and reduce the per base cost of sequencing. However, these technologies continue to be limited by their sensitivity to the need for amplification or cloning to obtain enough DNA or RNA from a sample for their instruments to adequately read the sequence. As with Sanger-based sequencing technologies, this requirement for amplification or cloning adds to the cost and complexity of these sequencing methods, limits the scalability of sample preparation and may limit the accuracy of the data they produce. Moreover, these next generation sequencing technologies appear to possess biases and are hampered by their lack of quantitative accuracy which may limit their applicability to the broader genetic analysis space.

In the past, the prohibitive cost of high-volume sequencing at the genome scale has caused scientists to use other genetic analysis technologies to examine discrete aspects of gene structure or function. For example, researchers use gene expression analysis to compare amounts of mRNA made from different genes, and genotyping to examine specific gene segments known to contain sequence

variations, called single nucleotide polymorphisms, or SNPs. Technologies available for gene expression analysis and genotyping include:

- chip- or bead-based microarrays, in which collections of short DNA molecules are attached to the surface of a glass chip or to beads and used to determine the identity and abundance of particular DNA or RNA molecules in a sample; and
- real-time PCR, also called RT-PCR, which is the method of biochemically copying or amplifying the DNA in a sample through a process called PCR in which the identity and quantity of amplified DNA from the sample is measured as the analysis is performed.

While these other genetic analysis technologies address the cost limitations of DNA and RNA sequencing, they generally provide only limited information and suffer from a range of technical limitations, the most important of which is the high cost of replacement as new sequence information is added and products are updated. The following table summarizes the advantages and disadvantages of the genomic analysis technologies described above:

Comparison of established genomic analysis technologies

Analysis	Description	Technology	Advantages	Disadvantages
Sequencing	Determination of the complete sequences of DNA or RNA molecules	Automated Sanger-based instruments	• Comprehensive sequence information • Industry standard technology	• High cost • Low throughput • Complex sample preparation
Next Generation Sequencing	Determination of the complete sequences of DNA and RNA molecules	Ensemble-on-bead based technologies	• Comprehensive sequence information • High throughput/lower cost per sequence • Seen as "upgrade" to Sanger sequencers	• Complex sample preparation • Limited scalability • High cost of sample preparation • Limited quantitation
Gene Expression Analysis	Detection and quantitation of RNA to determine gene expression levels	DNA arrays on chips or beads	• Can perform genome-wide analysis of expressed genes • Widely available	• Low sensitivity • Relative quantitation • Limited sequence information • Limited to known genomic sequences • Biased based on templates
		RT-PCR	• Absolute quantitation • Highest sensitivity	• Higher cost per gene than arrays • Labor intensive • Not scalable
Genotyping	Analysis of short specific sequences within genomic DNA to look for known variants	DNA arrays on chips or beads	• High throughput/low cost per genotype • Can be applied to large numbers of samples	• Provides only limited genomic information • Only interrogates known sequence variants
		RT-PCR	• Higher sensitivity than arrays	• Provides very limited genomic information • Higher cost per genotype than arrays • Biased based on templates

The scope and pace of much important research, and the routine application of genomic information in clinical medicine, remain limited by the cost and throughput of the currently available genomic analysis systems. Many scientists believe that a further 10,000-fold decrease in the cost per

base of reagents and supplies for DNA sequencing using basic Sanger techniques would enable unprecedented research and large-scale clinical and other scientific studies. This goal is endorsed by the National Institutes of Health, whose National Human Genome Research Institute established the "Revolutionary Genome Sequencing Technologies—The $1,000 Genome," grant program to fund researchers' efforts to develop technology to enable the complete sequencing of an individual human genome at a cost of approximately $1,000. This goal is measured by the cost of the consumables used in the sequencing of the human genome and without regard to the cost of the sequencing instrument. In September 2006, we received a $2 million grant under this program to foster our technology development on the path to the $1,000 genome.

Scientists have long realized that many of the disadvantages of ensemble based sequencing could be addressed through the direct sequencing of single molecules. This ability to directly measure individual sequences would reduce the cost and complexity of large scale experiments while increasing sensitivity. The simplicity of the sample preparation and detection would also provide the capability to combine multiple application techniques in order to get the most comprehensive view of each sample. For nearly 20 years, researchers have attempted without success to develop such a single molecule sequencing technology. Past efforts fell short largely due to complexity or technological hurdles in signal detection, surface materials, biochemistry, enzymology, bioinformatics, automation or engineering. In 2003, one of our co-founders, Stephen R. Quake, DPhil, demonstrated, we believe for the first time, that sequence information could be obtained from single molecules of DNA. We have replicated and improved upon Professor Quake's approach to develop our True Single Molecule Sequencing (tSMS)™ technology. (Harris T et al. Single Molecule DNA Sequencing of a Viral Genome. *Science*. Vol. 320, no. 5872, pp. 106-109. 2008.)

THE HELICOS SOLUTION

Our True Single Molecule Sequencing (tSMS)™ technology is a powerful new approach that directly measures single molecules and will enable the large-scale analysis of DNA and RNA. We believe our Helicos™ Genetic Analysis System, based on this technology, has the potential to deliver unprecedented performance compared to the current market-leading sequencing and microarray methods. This novel approach allows our system to directly measure billions of individual sequences in parallel and avoids the need for complex sample preparation techniques, amplification or cloning required by existing methods. Our products utilizing our tSMS technology will benefit from simple, scalable sample preparation techniques and automated high-throughput sequencing processes that will enable sequencing at significantly greater speed and lower cost than other methods. This technology will provide scientists and clinicians with extensive capabilities for basic and translational research, for pharmaceutical research and development, and for the development and clinical application of genomic diagnostics. We believe that our products based on our technology will ultimately make it practical to compare genes, genomes, and transcriptomes from thousands of individuals, thereby enabling revolutionary biomedical research. In turn, subsequent discoveries may lead to more accurate molecular diagnostics for cancer and other diseases, improved drug therapies and personalized medical treatments.

Our Helicos Genetic Analysis System is designed to provide the following advantages over current Sanger sequencing technologies:

- *Enhanced throughput.* Scientists measure the throughput of a DNA sequencing technology based on the number of bases analyzed per unit of time. By the end of 2008, the HeliScope™ Single Molecule Sequencer had achieved throughput rates of approximately 100 million analyzable bases per hour, depending on the application. This compares to a throughput of approximately 120,000 bases per hour for Sanger sequencing technologies and approximately 50 million bases per hour for next-generation Sanger sequencers. In addition, we have designed the imaging capability of the HeliScope Sequencer to accommodate a maximum throughput approaching one

billion bases per hour, which would represent a more than 20-fold improvement over the published specifications of current market-leading sequencing technologies. To achieve this additional increase in throughput, we will need to improve the efficiency and accuracy of the system's sequencing chemistry, increase the density of strands of DNA that bind to the surface of the flow cell in which the sequencing reactions take place and make corresponding enhancements to the image processing software.

- *Increased sensitivity.* Our tSMS technology has the sensitivity to directly image and analyze single DNA and RNA molecules. Therefore, our HeliScope Sequencer will not require the sample preparation processes of existing sequencing technologies, which are costly, time-consuming and may introduce errors.
- *Simplicity.* Because the sample preparation process for genome sequencing using our HeliScope Sequencer involves only small quantities of reagents and a few simple steps, we believe that it will be less costly, less time-consuming, and less error prone than the sample preparation processes used in current technologies.
- *Lower cost.* According to published price quotes from research core laboratories and other sequencing providers, the price of sequencing using current Sanger sequencing methods is approximately $3 per thousand bases of sequencing data. We believe that the largest genome sequencing centers charge approximately $1 per thousand bases. The Helicos System generates sequencing information at a cost per thousand bases for reagents and supplies that is 1000 fold lower. We are planning improvements, some of which are under way, that are designed to achieve a further per base cost reduction of approximately 100-fold without requiring major modifications to the instrument. These improvements relate to enhancing the performance of the system's reagents and disposable supplies and enhancing the image processing subsystem, increasing the number of DNA molecules that the HeliScope Sequencer can analyze per run and improving fluid handling to decrease reagent consumption.
- *Scalability.* The sample preparation process is highly scalable because it does not require the need for complex sample preparation techniques, amplification or cloning required by existing methods.

We believe that our Helicos System can be used as a universal method of genetic analysis potentially replacing existing methods of gene expression analysis and genotyping. Based on its anticipated performance, we believe that the initial version of our Helicos System will be able to perform applications of gene expression analysis at a comparable cost per sample, and in the case of high volume analyses, a significantly lower cost, in comparison with current technologies.

Our True Single Molecule Sequencing (tSMS)™ Technology

Our True Single Molecule Sequencing (tSMS)™ technology enables the simultaneous sequencing of large numbers of strands of single DNA molecules. The first step of our single molecule sequencing approach is to cut, or shear, a sample of DNA into relatively small fragments. The double helix of each fragment is then separated into its two complementary strands. Each strand is used as a template for synthesis of a new complementary strand. This is accomplished through a series of biochemical reactions in which each of the four bases are successively introduced. If the introduced base is complementary to the next base in the template, it will be added to the new strand. Each of the added bases is tagged with a fluorescent dye, which is illuminated, imaged and then removed. The sequence of each new DNA strand is determined by collating the images of the illuminated bases from each cycle of highly specific incorporation and imaging. The raw sequencing data is then analyzed by computer algorithms.

The series of figures below outlines an example of how our tSMS technology operates to sequence single molecules from genomic DNA. The actual process our HeliScope™ Single Molecule Sequencer will utilize to sequence DNA molecules will depend on the application.

Figure 1

To prepare the sample for sequencing, the genomic DNA is first cut into small pieces of about 100 bases. The enzyme called terminal transferase is then used to add a string of "A" nucleotides to one end of each strand. Then, a nucleotide labeled with a single fluorescent dye molecule is added to the end of the strand.

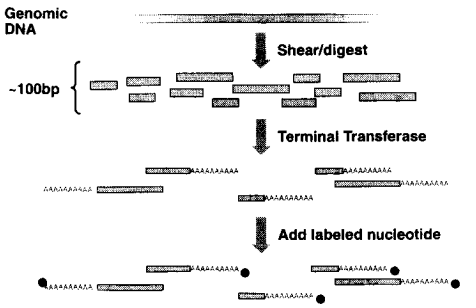


Figure 2

Inside the flow cell, short strands of "T" nucleotides, called primers, have already been attached to the surface.

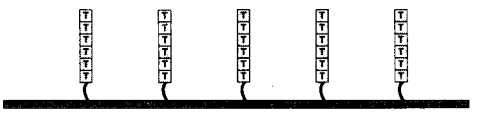


Figure 3

When the DNA sample is added, the strings of "As" on each DNA strand hybridize with the strands of "Ts" on the surface, anchoring the sample strands to be sequenced. The sample strands will act as a template and the strand of Ts as a "primer" for DNA synthesis. A laser subsystem illuminates the flow cell and the camera records the location of each captured sample strand. A mechanical stage moves the flow cell in sequential steps to allow the camera to image the entire active area of the flow cell. The dye molecules are then cleaved and washed away.

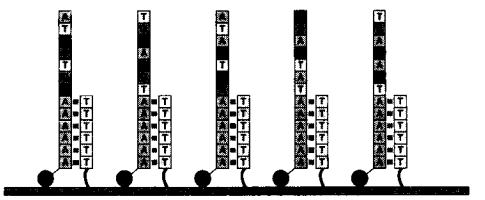


Figure 4

An enzyme called DNA polymerase and the first of the four types of our proprietary fluorescently labeled nucleotides are added. If the nucleotide is complementary to the next base in the template strand, the polymerase will add it to the primer strand. The nucleotides are designed to inhibit the polymerase from incorporating more than one base at a time on the same strand. Excess polymerase and unincorporated nucleotides are then washed away.

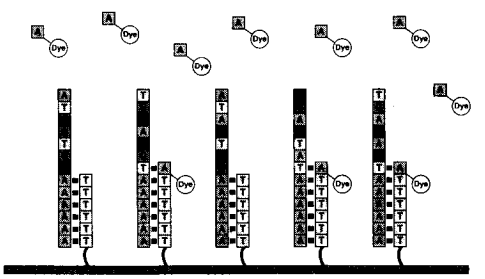


Figure 5

The laser subsystem illuminates the flow cell and the camera records the locations where fluorescently labeled nucleotides were added. The fluorescent dye molecules are then cleaved from the labeled nucleotides and washed away.

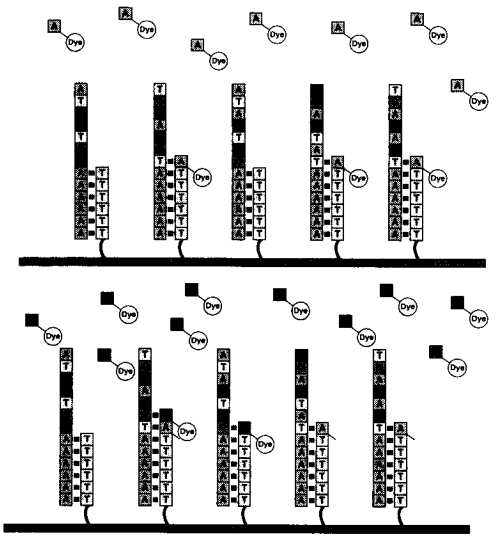
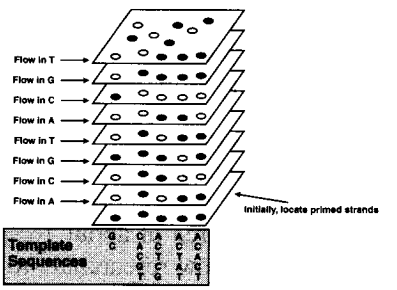


Figure 6

The process outlined in Figures 4 and 5 is repeated with each of the four types of labeled nucleotides. Repeating this cycle for a total of 120 times adds an average of more than 29 nucleotides to the primer strand. The number of bases added to a primer is the "read length."

Figure 7

The system's computer analyzes the series of images from each cycle and determines the sequence of bases in the template strand. The sequence is "read" by correlating the position of a fluorescent molecule in its vertical track with the knowledge of which base was added at that cycle. Finally, the sequence data is exported to another computer system for further analysis depending on the application.



The Helicos™ Genetic Analysis Platform

The Helicos™ Genetic Analysis Platform consists of the following components:

- **Helicos™ Genetic Analysis System**—The instrument component of the Helicos Genetic Analysis Platform which consists of three major components:
  - *The HeliScope™ Single Molecule Sequencer* which performs the True Single Molecule Sequencing (tSMS)™ chemistry and directly analyzes images of single molecules, producing accurate sequences of billions of templates at a time. The HeliScope system consists of a high-speed mechanical stage and a laser illumination subsystem, an image acquisition subsystem, a fluid handling subsystem and computer subsystems that control and analyze the sequencing reactions. To operate the instrument, a user loads a prepared sample of DNA or complementary DNA (cDNA) onto our flow cell using the HeliScope™ Sample Loader, places the flow cell on the mechanical stage and inserts our consumable reagent pack into the fluid handling system. From that point onward, all sequencing reactions are conducted automatically by the instrument. After each base is added, the mechanical stage moves the flow cells under a microscope lens. Four lasers illuminate the fluorescent tags of the bases, and a camera images the flow cells through the microscope lens.
  - *HeliScope™ Analysis Engine* provides computing power for near real-time image analysis and on-board data storage. The on-board data storage is appropriately sized to support two complete runs, enabling flexibility of operation and maximizing uptime. The Analysis Engine operates downstream from the HeliScope™ Sequencer in the data pipeline. It consists of the System Server, Object Finders, and an uninterruptible power supply (UPS). Components are mounted in a single enclosure for locating convenience and installation ease. Data

communication between the HeliScope Sequencer and Analysis Engine is accomplished across Gigabit Ethernet (GigE) lines, providing high reliability and allowing for considerable physical distance between components.

- *HeliScope™ Sample Loader* speeds the loading of samples into the Helicos™ flow cells. It provides 25 discreet loading ports to ensure proper separation of samples and ease of loading.

- **Helicos True Single Molecule Sequencing (tSMS)™ Kits.** Application specific reagent kits for sequencing which consists of proprietary formulations of a DNA polymerase enzyme, our proprietary fluorescently tagged bases, our proprietary imaging reagent, a proprietary formulation of a cleavage reagent and our proprietary application specific flow cells that have a proprietary surface coating with the chemical and optical properties needed for single molecule sequencing.

Consumable reagents. The biochemical sequencing reactions that occur in the HeliScope Sequencer involve the use of a proprietary formulation of a DNA polymerase enzyme, proprietary fluorescently tagged bases and proprietary imaging reagents. We have developed proprietary nucleotide triphosphates, called Virtual Terminator™ Nucleotides, that allow us to add only one base at a time to each DNA strand. Our proprietary imaging reagents improve the stability of our fluorescent tags and increase their brightness. Our cleavage reagents are used to remove the fluorescent tags from the Virtual Terminators.

Disposable supplies. The HeliScope™ Single Molecule Sequencer is designed to perform sequencing reactions inside two glass flow cells. The system alternates between the flow cells, performing sequencing reactions in one flow cell while recording images from the other. Each flow cell has an active area of about 16 square centimeters and contains 25 separate channels. Our flow cells are designed to allow researchers to sequence separate samples in each channel, which will enable the simultaneous sequencing of at least 50 different DNA samples. The initial version of our flow cell is designed to permit binding of DNA strands at an average density of approximately 100 million strands of DNA per square centimeter, equaling an average of approximately 2.8 billion strands of DNA for both flow cells.

APPLICATIONS

The Helicos™ Genetic Analysis System provides new opportunities for large scale genomic studies which encompass many areas of research, development and diagnostic use. The areas where we believe Helicos offers significant opportunity include:

- *Studying the Human Genome.* The ENCODE studies published in 2007 and 2008 provided new insights into the complexity of the human genome. These initial studies published in 2007, which examined only 1% of the genome architecture revealed a much more dynamic and complex genome state at every level including organization, sequence, expression and regulation. New approaches which allow a window into the genome allowing unbiased interrogation are clearly required to fully understand the genome. During 2008, we have seen the emergence of next generation sequencing technology applied to a fuller understanding of the genome with particular emphasis focused on the transcriptome. Through deep resequencing of the transcriptome, we are gaining new insights in the truly remarkable resilience of the genome and the variety of coding and non-coding RNAs playing intimate roles in gene regulation. The need for new approaches was further validated in 2007 with the publication of two complete human genome sequences which demonstrated levels of human genome variation far exceeding initial expectations. During 2008, the continuing focus on full genome sequencing and the pace of technology advancements to drive costs of sequencing down, continued in earnest. The Helicos System provides the platform which is now well positioned for the depth and breadth of genomic studies required to fully unlock the secrets of the genome and the role of genome variation in health and disease.

- *Disease association studies.* 2007 and 2008 represented landmark years in the search for genes involved in common disease. As we have known common diseases and conditions involve complex genetic factors and environmental interactions to produce the visible measurements or features of disease. In 2007, large scale genetic association studies including the Wellcome Trust Case Control Consortium and the Genetic Association Information Network (GAIN) identified multiple genes and gene regions associated with diseases such as coronary artery disease, Type I and Type II diabetes, obesity, Crohn's Disease, rheumatoid arthritis, and bipolar disorder. In 2008, additional publications on a broad survey of diseases continued in earnest. Yet what we now have learned is that common variants associated with these diseases only begin to scratch the surface of the underlying individual variation contributing to these associations. By sequencing the genomes or selected genes from many individuals with a given condition, it may be possible to identify the causative mutations underlying the disease. Ongoing efforts are focused on the subsequent sequencing of the genomic regions associated with these common diseases to attempt the search for further genomic factors accounting for disease contributions. This research may lead to breakthroughs in disease diagnosis, prevention and treatment.
- *Cancer research.* Cancer genetics involves understanding the effects of the inherited genome as well as the tumor genome including acquired mutations and other genetic alterations. Diagnosing and treating cancer therefore requires a more comprehensive understanding of the individual patient tumor genome to better-predict responses to drug therapy. We believe the availability of low-cost genome sequencing on small samples or tumor cell biopsies to characterize acquired changes of the genome that contribute to cancer would enable improved diagnosis and treatment of cancer.
- *Pharmaceutical research and development.* Genomics touches every phase of the drug discovery and development process to varying degrees. This includes early target discovery, through candidate selection, clinical trial design and interpretation and ultimately into the marketplace with diagnostics linking genomic information with therapeutic intervention. In early discovery, single molecule sequencing could enable high-throughput screening in a cost-effective manner using large scale gene expression analysis, allowing the study of disease and target pathways to better identify promising drug leads. As lead matter is refined into preclinical candidates, expression profiling may allow a better understanding of compound toxicity and allow those candidates with minimal toxicity profiles to proceed to the clinic. The broad application of genomics in the later phase of drug development has been hampered by the lack of high throughput, cost effective methods to link patient variation with genomic information. In clinical development, our technology could potentially be used to generate individual gene profiles that can provide valuable information on likely response to therapy, both efficacy and adverse events, and provide insight into genomic biomarkers that may provide signatures for patient screening and individualization of therapy.
- *Infectious disease.* All viruses, bacteria and fungi contain DNA or RNA. The detection and sequencing of DNA or RNA from pathogens at the single molecule level would provide medically and environmentally useful information for the diagnosis, treatment and monitoring of infections and to predict potential drug resistance. Such sequencing would not require the growth or purification of organisms that can be difficult to culture or work with.
- *Autoimmune conditions.* Autoimmune conditions, such as multiple sclerosis, Type I diabetes and lupus, have important genetic components which can be reflected at both the DNA and RNA level. Monitoring the underlying genetic background of patients as well as monitoring RNA expression changes associated with these diseases and corresponding treatment may enable better patient management.

- *Clinical diagnostics.* Patients who present with the same disease symptoms often have different prognoses and responses to drugs based on their underlying genetic differences. We believe that delivering patient-specific genetic and genomic information at a reasonable cost represents a multi-billion dollar potential market waiting to be fully realized. Commercial markets for molecular diagnostics include gene- or expression-based diagnostic kits and services, companion diagnostic products for selecting and monitoring particular therapies, as well as patient screening for early disease detection and disease monitoring. Creating more effective and targeted molecular diagnostics and screening tests requires a better understanding of genes, regulatory factors and other disease- or drug-related factors, which we believe our single molecule sequencing technology has the potential to enable.
- *Agriculture.* Agricultural research has increasingly turned to genomics for the discovery, development and design of genetically superior animals and crops. The agribusiness industry has been a large consumer of genetic technologies—particularly microarrays—to identify relevant genetic variations across varieties or populations which will be especially useful in species not well studied in the past. Our sequencing technology may provide a more powerful, direct and cost-effective approach to gene expression analysis and population studies for this industry.

RESEARCH AND DEVELOPMENT

The wide variety of technical disciplines required for the development of a commercial single molecule sequencing system is represented within our research and development organization, which includes the following functional groups: methods development, organic synthesis, engineering, sequencing development and scientific informatics. Our research and development staff includes PhD scientists and PhD engineers.

We have rapidly advanced the development of our True Single Molecule Sequencing (tSMS)™ technology since we began operations in 2003. In 2004, we began to produce sequence data from single molecules of DNA and in 2005, we sequenced genomic DNA from a small virus called M13 using our tSMS technology. Also in 2005, we began to design the Helicos™ Genetic Analysis System. In 2006, we received a $2 million grant from the National Human Genome Research Institute. Also in 2006, we completed the design of the critical components of the Helicos System. During 2007, we assembled two additional pre-production prototypes which are used for a variety of sub-system testing. In 2007, we substantially finished the assembly of five commercial grade Helicos Systems in advance of our first shipment of the Helicos System to our initial customer on March 5, 2008, which was later returned. During the fourth quarter of 2008, we shipped and installed a second Helicos System. Prior to shipment, our commercial grade systems are subject to extensive verification and validation testing with reagents and flow cells produced by our operations group in order to validate the performance that will be achieved by the customer. A part of our engineering effort has gone into assisting our operations group in establishing the documentation, test plans, and infrastructure required for scale-up of the manufacturing of additional Helicos Systems. During 2008, we introduced a second generation Virtual Terminator™ with improved performance and shelf-life stability. We also introduced a second generation image analysis software with improved performance.

We will continue to invest in research and development to further improve the performance of our Helicos System beyond its performance characteristics at commercial launch. Our goal is to achieve a further reduction of DNA sequencing cost per base of approximately 100 fold without requiring major modifications to the HeliScope™ Single Molecule Sequencer. We describe below some of the ways in which we have improved the performance of the tSMS technology for use in the HeliScope Sequencer and ways in which we believe we can further improve performance on an ongoing basis.

- *Improved flow cell surface stability.* By optimizing the surface coating of the flow cell and the reagents used in the HeliScope Sequencer, we have increased the stability of DNA attachment

to the flow cell surface. We are working on further increases in stability in order to increase the number of strands that remain present at the end of a run and thus the amount of sequence data produced.

- *Increased sequencing reaction efficiency and accuracy.* In the course of developing our proprietary sequencing process and reagents, we have significantly increased the efficiency with which new bases are added to a growing DNA strand and the accuracy with which they are detected. We are working to further increase efficiency and accuracy at each step of the sequencing process to continue to increase the number of DNA strands that are useful for genetic analysis.
- *Increased density of DNA strands.* We have successfully developed the flow cells in our HeliScope Sequencer to permit binding of DNA strands at an average density of approximately 100 million strands per square centimeter. We are performing additional development work in the area of surface chemistry in an effort to increase the number of DNA strands that can be anchored to the surface of the flow cells up to 400 million per square centimeter.
- *Enhanced speed of image processing subsystem.* We have developed high speed image processing that enables analysis of the images produced by the HeliScope Sequencer. We continue to enhance the speed of the image processing subsystem in order to enable reduction in the server hardware included as a part of the cost of a Helicos System.

We believe that each of the above improvements, if successful, would increase the throughput of the HeliScope Sequencer and reduce the cost per base of sequencing. We are also planning other improvements, such as reducing reagent consumption, reducing image acquisition time, and enhancing the performance of the system's mechanical components, with the goal of further increasing throughput and reducing cost.

In 2008 we continued our forward thinking research activities in genomic and measurement sciences. The Applications, Methods and Collaborations group emerged as a result of the intimate relationship between genomic sciences, applications and methods. The group has moved to supporting customers, prospective customers and collaborators who now can benefit from our expertise in sample preparation and novel methods for the application of single molecule sequencing to address important questions in biology. We have continued our collaborations with world class leaders in the field of genomics including members of the ENCODE consortium, genome sequencing centers and academic research institutions.

Our early research areas include:

- *Transcriptome analyses:* Digital gene expression provides a hypothesis free, global, and quantitative analysis of the entire transcriptome. Our research focuses on developing the single molecule sequencing method to allow the quantitative measurement of virtually all genes in a sample by counting the number of individual mRNA molecules produced from each gene. This allows one to examine all the genes present in a cell or tissue in a hypothesis independent manner with no bias as to those genes believed to be expressed. We believe the end result will be a highly sensitive and quantitative measurement which will allow not only for the detection of highly expressed transcripts but also for the detection of very rare transcripts represented by only a few molecules of RNA per cell. During 2008, we demonstrated a proof of principle for direct sequencing of RNA without an intermediate cDNA.
- *miRNA measurements:* microRNA (miRNA) represent important regulators of gene expression and are becoming increasingly important in disease studies, especially cancer. Helicos is using single molecule sequencing to investigate the ability to quantitatively measure miRNAs from human samples as well as identify novel miRNAs which have been limited by previous requirements for amplification of miRNAs and limited depth of coverage.

- *Candidate region sequencing:* Currently the cost of sequencing an entire human genome remains too high to enable routine whole genome sequencing. New methods are currently under development to allow a simplified, highly multiplexed candidate region capture method to facilitate large-scale studies of genomic regions of interest. We are almost ready to launch barcoding of samples which allows multiplexed sequencing of more than one sample per channel.
- *Paired end reads:* A paired end read strategy is critical for single molecule sequencing to enable whole genome sequencing. Our research focuses on reading both ends of a DNA molecule of selected sizes to accurate recapitulate the structural context of the genome to be sequenced. Optimizing the size of inserts for our paired end strategy to allow both short fragments (250-500 base pairs) and longer fragments (1 to 10 kb) remains our focus. Proof of principle was demonstrated on the HeliScope™ Single Molecule Sequencer which we expect will lead to commercialization in 2009.

In the years ended December 31, 2006, 2007, and 2008 we incurred $14.4 million, $24.8 million and $24.6 million respectively, of research and development expenses.

COLLABORATION

Our strategy is to establish the Helicos™ Genetic Analysis Platform as the platform of choice for analyzing large quantities of genetic information and to expand the applications of our technology. Accordingly, we have entered into and intend to enter into additional collaborative agreements to further this strategy. For example, in January 2008, Helicos announced a collaboration with Dr. Ambros at the University of Massachusetts Medical School (UMMS) to apply the quantitative power of True Single Molecule Sequencing (tSMS)™ to develop a single assay to characterize known species of miRNA as well as discover new non-coding RNAs. Dr. Victor Ambros, an elected member of the National Academy of Sciences and a recent addition to the UMMS Program of Molecular Medicine, discovered the existence of miRNAs by finding the Lin-4, a miRNA found during a study of developmental timing in ringworms. Dr. Ambros continues his research on microRNA function and gene regulation during development, focusing on understanding the genetic and molecular mechanisms that control cell division, differentiation and morphogenesis in animals. Results from the collaboration were presented at the Advances in Genome Biology and Technology meeting, held in Marco Island in February 2008.

MANUFACTURING AND RAW MATERIALS

We manufacture our products using a combination of outsourced components and subassemblies. In addition to in-house production capability we utilize subcontractors for parts of the manufacturing process where we have determined it is in our best interest to do so. We have purchased and are in the process of qualifying and installing production tooling, scale-up equipment and automation equipment for the production of our products. We are focused on increasing our manufacturing process capability and capacity as needed to produce products in sufficient quantity to meet all of our business plan objectives.

Our manufacturing operations require a wide variety of raw materials, electronic and mechanical components, chemicals and biochemicals, and other supplies. Certain of these raw materials are currently available only from a single source or limited sources. Where this is the case, we take such steps as we deem appropriate to ensure that materials and components from these suppliers are not materially delayed or interrupted. We have deployed a fully integrated Enterprise Planning Requirements, or ERP, System to assist in the planning, procurement, and control of our manufacturing operations and those of our subcontractors.

MARKETING, SALES, SERVICE AND SUPPORT

The market for high-performance genetic analysis tools is relatively concentrated among large genome sequencing centers, major biotechnology and pharmaceutical companies and major academic medical centers and research institutions. To address this market, we have a specialized sales, marketing and service force in the United States and Canada. We believe that we will be able to better access the market for genetic analysis instruments and support our customers through well-trained and experienced personnel under our direct control.

OUR SCIENTIFIC ADVISORY BOARD

We have established a scientific advisory board consisting of individuals whom we have selected for their particular expertise in the fields of genomics, physics, molecular biology, chemistry and engineering. We anticipate that our scientific advisory board members will consult with us on matters relating to:

- our research and development efforts;
- opportunities for strategic collaborations;
- new technologies relevant to our research and development efforts;
- scientific and technical issues relevant to our business; and
- our sales and marketing strategy.

All of our advisors are employed by organizations other than us and may have commitments to or consulting or advisory agreements with other entities that may limit their availability to us. Our scientific advisory board currently consists of the following members:

SAB Member	Current Affiliations
Stephen R. Quake, DPhil ..... *Chairman of the Scientific Advisory Board*	Professor of Bioengineering at Stanford University and Investigator of the Howard Hughes Medical Institute
George Church, PhD	Professor of Genetics at Harvard Medical School
Leroy Hood, PhD	President and co-founder of the Institute for Systems Biology in Seattle, Washington
David R. Liu, PhD	Professor of Chemistry and Chemical Biology at Harvard University; Investigator of the Howard Hughes Medical Institute and Associate Member of the Broad Institute of MIT and Harvard
Eugene W. Myers, PhD	Group Leader at the Janelia Farm Research Campus of the Howard Hughes Medical Institute
John Quackenbush, PhD	Faculty Member at the Dana-Farber Cancer Institute and Professor of Biostatistics and Computational Biology and Professor of Computational Biology and Bioinformatics at the Harvard School of Public Health
Floyd Romesberg. PhD	Associate Professor of Chemistry at The Scripps Research Institute in La Jolla, California
Victor E. Velculescu, MD, PhD	Assistant Professor of Oncology at The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

COMPETITION

Competition among entities developing or commercializing instruments, research tools or services for Genomic analysis is intense. A number of companies offer DNA sequencing equipment or consumables, including Applied Biosystems, who recently merged with Invitrogen to form a new entity called Life Technologies, Inc., Beckman Coulter, Inc., the Life Sciences Division of GE Healthcare, Illumina, Inc., Complete Genomics, Inc. and Roche Applied Science. Furthermore, a number of other companies and academic groups are in the process of developing novel techniques for DNA sequencing. These companies include, among others, Genizon BioSciences, Genovoxx, Intelligent Bio-Systems, Lucigen, Microchip Biotechnologies, Pacific Biosciences, Shimadzu Biotech, and ZS Genetics. For RNA analysis and/or genotyping there are a number of companies that offer equipment and supplies including Affymetrix, Inc., Agilent Technologies, Applera Corporation, and Bio-Rad Laboratories. Three companies provide a wide range of products that span both DNA and RNA analysis—Life Technologies, Inc., Affymetrix, Inc. and Illumina, Inc. However, the solutions that are provided are separate applications that require different sample preparation techniques, consumables, analysis software and instrumentation with limited correlation between platforms. In order to successfully compete against existing and future technologies, we will need to demonstrate to potential customers that the price and performance of our technologies and products and our customer support capabilities are superior to those of our competitors. In addition, we will have to demonstrate the scalability of the platform both through its application versatility and simplicity of sample preparation.

Many of our competitors have substantially greater capital resources, research and product development capabilities and greater financial, scientific, manufacturing, marketing, and distribution experience and resources, including human resources, than we do. These competitors may develop or commercialize genetic analysis technologies before us or that are more effective than those we are developing. Moreover, our competitors may obtain patent protection or other intellectual property rights that could limit our rights to offer genetic analysis products or services.

INTELLECTUAL PROPERTY

Developing and maintaining a strong intellectual property position is an important element of our business strategy. We have developed an extensive patent strategy. Our patent portfolio relating to our proprietary technology is comprised, on a worldwide basis, of various patents and pending patent applications, which, in either case, we own directly or for which we are the exclusive or semi-exclusive licensee. A number of these patents and patent applications are foreign counterparts of U.S. patents or patent applications. Among other things, our patent estate includes patents and/or patent applications having claims directed to:

- the overall True Single Molecule Sequencing (tSMS)™ method;
- certain components of the Helicos™ Genetic Analysis Platform, including our laser illumination subassembly, our flow cells and various methods for using our HeliScope Sequencer;
- methods for focusing our lasers and imaging our flow cell surfaces, and our use of combinations of laser optical paths;
- our Virtual Terminator™ Nucleotides and other nucleotides;
- various aspects of our sample preparation processes;
- algorithms for analysis of our data; and
- reagent formulations for imaging and for sequencing.

Patent law relating to the scope of claims in the technology field in which we operate is still evolving. The degree to which we will be able to protect our technology with patents, therefore, is

uncertain. Others may independently develop similar or alternative technologies, duplicate any of our technologies and, if patents are licensed or issued to us, design around the patented technologies licensed to or developed by us. In addition, we could incur substantial costs in litigation if we are required to defend ourselves in patent suits brought by third parties or if we initiate such suits.

We regard as proprietary any technology that we or our exclusive licensors have developed or discovered, including technologies disclosed in our patent estate, and that was not previously in the public domain. Aspects of our technology that we consider proprietary may be placed into the public domain by us or by our licensors, either through publication or as a result of the patent process. We may choose for strategic business reasons to make some of our proprietary technology publicly available whether or not it is protected by any patent or patent application.

With respect to proprietary know-how that is not patentable and for processes for which patents are difficult to obtain or enforce, we may rely on trade secret protection and/or confidentiality agreements to protect our interests. While we require all employees, consultants, collaborators, customers and licensees to enter into confidentiality agreements, we cannot be certain that proprietary information will not be disclosed or that others will not independently develop substantially equivalent proprietary information.

In addition to our patents, patent applications, confidential know-how, and potential trade secrets, we license technology that we consider to be material to our business.

Roche License Agreement. In June 2004, we entered into an agreement with Roche Diagnostics GmbH, or Roche, in which Roche granted us a worldwide, semi-exclusive royalty-bearing license, with the right to grant sublicenses under a patent relating to sequencing methods. In exchange for the rights licensed from Roche, we initially paid Roche an upfront license fee and are obligated to pay Roche certain additional annual minimum license fees. We have an option to convert our license to non-exclusive beginning in 2008, in which case our annual minimum license fees would be reduced. We are also required to pay royalties to Roche based on net product sales by us and our affiliates, against which we are entitled to credit our annual minimum license fee payments for the same year. We are also obligated to pay Roche a portion of specified sublicense income amounts that we receive based on sublicenses that we grant to third parties. Our royalty obligation, if any, under this agreement extends until the expiration of the last-to-expire of the licensed patents.

AZTE License Agreement. In March 2005, we entered into an agreement with Arizona Technology Enterprises, or AZTE, in which AZTE granted us a worldwide, exclusive, irrevocable, royalty-bearing license, with the right to grant sublicenses, under specified patents and patent applications exclusively licensed by AZTE from Arizona State University and the University of Alberta. Our license from AZTE grants us rights to patents and patent applications claiming technology for determining DNA or RNA nucleotide sequences. In exchange for the rights licensed from AZTE, we initially paid AZTE an upfront license fee, committed to an annual license fee, committed to pay a three-year maintenance fee, and issued 88,888 shares of restricted common stock, which vest in two equal installments upon the achievement of separate milestones relating to the successful issuance of patents. We are also required to pay royalties to AZTE based on net product sales by us and our affiliates, against which we are entitled to credit the annual license payments described above. We are obligated to pay AZTE a portion of specified sublicense income amounts that we receive based on sublicenses that we grant to third parties. Our royalty obligation, if any, under this agreement extends until the expiration of the last-to-expire of the licensed patents. We are obligated to use our reasonable commercial efforts to develop, manufacture and commercialize licensed products. In addition, if we fail to meet specified development and commercialization deadlines, our license converts from exclusive to non-exclusive.

Caltech License Agreement. In November 2003, we entered into an agreement with California Institute of Technology, or Caltech, in which Caltech granted us a worldwide, exclusive, royalty-bearing

license, with the right to grant sublicenses, under specified patents and patent applications, and a worldwide, non-exclusive, royalty bearing license, with the right to grant sublicenses, under specified technology outside the scope of the licensed patents. Our license from Caltech grants us rights to patents, patent applications, and technology relating to sequencing methods. In March 2007, we amended the Caltech License Agreement to provide rights under an additional patent application under the terms of the existing license, but with an additional one-time payment. In exchange for the rights licensed from Caltech, we issued Caltech 46,514 shares of our common stock. We are also obligated to pay Caltech annual minimum royalty payments. We are also required to pay royalties to Caltech based on net product sales by us and our affiliates, which we are entitled to credit against our annual minimum royalty payments for such year. We are also obligated to pay Caltech a portion of specified license and sublicense income, proceeds from sales of specified intellectual property and specified service revenue amounts that we receive based on licenses and sublicenses that we grant, sales of intellectual property and services that we provide to third parties. Our royalty obligation with respect to any licensed product extends until the later of the expiration of the last-to-expire of the licensed patents covering the licensed product and three years after the first commercial sale of the licensed product in any country for non-patented technology covered under the agreement. We are obligated to use commercially reasonable efforts to commercialize licensed products.

PerkinElmer License Agreement. In April 2007, we entered into an agreement with PerkinElmer LAS, Inc., or PerkinElmer, in which PerkinElmer granted us a worldwide, non-exclusive, non-transferable, non-sublicensable, royalty bearing license under specified patents. Our license from PerkinElmer grants us rights under certain patents to produce and commercialize certain of the reagents used in some applications on the HeliScope system, which contain chemicals purchased by PerkinElmer, and further provides our customers with an implied license to use such reagents. In exchange for the rights licensed from PerkinElmer, we are obligated to pay PerkinElmer a portion of our net revenue from the sale of our reagents that contain chemicals covered by the patents licensed under the PerkinElmer agreement.

See Note 7 to the Consolidated Financial Statements contained in this Form 10-K for additional information on license agreements.

CORPORATE INFORMATION

We were incorporated in Delaware in May 2003. In 2003, one of our co-founders, Professor Stephen R. Quake, who was then at the California Institute of Technology, demonstrated, we believe for the first time, that sequence information could be obtained from a single strand of DNA. Shortly thereafter, Noubar Afeyan, Chief Executive Officer of Flagship Ventures, and Stanley Lapidus, then a Venture Partner at Flagship Ventures, met with Professor Quake and agreed to found a company to develop and commercialize technology based on Professor Quake's single molecule approach. Combining the experience of Professor Quake in single molecule methods, Dr. Afeyan in the sequencing technology and life sciences businesses, and Mr. Lapidus in diagnostics and entrepreneurship, we focused exclusively on the technical and commercial development of technology based on Professor Quake's approach. Professor Eric Lander, Director of the Broad Institute of MIT and Harvard, and a leader in the DNA sequencing field, provided helpful guidance and advice during our founding stages.

EMPLOYEES

We had 71 full time employees at December 31, 2008. We have never had a work stoppage and none of our employees are covered by collective bargaining agreements. We believe our employee relations are good. Our success depends in large part on our ability to attract and retain skilled and experienced employees.

AVAILABLE INFORMATION

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, definitive proxy statements on Form 14A, current reports on Form 8-K, and any amendments to those reports are made available free of charge on our website, www.helicosbio.com, as soon as reasonably practicable after such reports are electronically filed with or furnished to the Securities and Exchange Commission (SEC). Statements of changes in beneficial ownership of our securities on Form 4 by our executive officers and directors are made available on our website by the end of the business day following the submission to the SEC of such filings. In addition, the SEC's website, www.sec.gov, contains reports, proxy statements, and other information regarding reports that we file electronically with the SEC.

Item 1A. RISK FACTORS

The following important factors could cause our actual business, prospects, financial results or financial condition to differ materially from those contained in forward-looking statements made in this Annual Report on Form 10-K or elsewhere by management from time to time.

In or before the first quarter of 2010, we expect we will need to raise additional funding, which may not be available on favorable terms, if at all, or without dilution to our stockholders. If we do not raise the necessary funds, we may need to cut back or terminate some or all aspects of our operations, which would materially adversely affect our business prospects.

Because our Helicos™ Genetic Analysis System is complex and will be new to the market and involve significant capital expenditures by customers and a long sales cycle, it is very difficult to predict the actual rate of product sales. We will need additional financing to execute on our current and future business strategies. We expect capital outlays and operating expenditures to increase over the next several years as we expand our infrastructure, commercialization, manufacturing and research and development activities. The amount of additional capital we may need to raise depends on many factors, including:

- the level of research and development investment required to maintain and improve our technology position;
- the amount and growth rate of our revenues;
- changes in product development plans needed to address any difficulties in manufacturing or commercializing our Helicos System and enhancements to our system;
- the costs of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;
- competing technological and market developments;
- our need or decision to acquire or license complementary technologies or acquire complementary businesses; and
- changes in regulatory policies or laws that affect our operations.

The worldwide financial markets are currently experiencing turmoil. These events have materially and adversely impacted the availability of financing to a wide variety of companies, particularly early-stage companies such as Helicos. We do not know whether the additional capital which we will require will be available when and as needed, on favorable terms if at all, or that our actual cash requirements will not be greater than anticipated. In addition, if we raise additional funds through the issuance of equity or convertible debt securities, the percentage ownership of our stockholders could be significantly diluted, and these newly-issued securities may have rights, preferences or privileges senior to those of existing stockholders. If we obtain additional debt financing, a substantial portion of our

operating cash flow may be dedicated to the payment of principal and interest on such indebtedness, and the terms of the debt securities issued could impose significant restrictions on our operations. If we raise additional funds through collaborations and licensing arrangements, we might be required to relinquish significant rights to our technologies or products, or grant licenses on terms that are not favorable to us. If our current operating plan including forecasted sales in 2009 does not materialize or if adequate additional funds are not available to us when required, we will be required to further delay, reduce or eliminate research and development programs, reduce or eliminate commercialization efforts, obtain funds through arrangements with collaborators or others on terms unfavorable to us, or pursue merger or divestiture strategies.

We have a history of operating losses, expect to continue to incur substantial losses, and might never achieve or maintain profitability.

We are a development-stage company with limited operating history. We have incurred significant losses in each fiscal year since our inception, including net losses attributable to common stockholders of $54.9 million and $45.7 million in the years ended December 31, 2007 and 2008, respectively. As of December 31, 2008, we had an accumulated deficit of $139.7 million. These losses have resulted principally from costs incurred in our research and development programs and from our selling, general and administrative expenses. In the year ended December 31, 2007, we used cash in operating activities of $32.8 million and had capital expenditures totaling $2.2 million. In the year ended December 31, 2008, we used cash in operating activities of $44.3 million and had capital expenditures totaling $2.9 million. As of December 31, 2008, we had $19.7 million in cash.

We will need to generate significant revenue to achieve profitability. As of December 31, 2008, we had shipped two Helicos™ Genetic Analysis Systems but had not recognized revenue from these initial shipments. Moreover, one of these two systems was returned in 2009. Because our products will be subject to various customer evaluation periods with acceptance criteria, we expect the customer evaluation period and our ability to have any recognizable revenue from additional initial sales, if any, to extend beyond the fiscal quarters in which the products are shipped. Moreover, even after we begin selling our products on a commercial scale, we expect our losses to continue for at least the next two years as a result of ongoing research and development expenses, as well as increased manufacturing, sales and marketing expenses. These losses, among other things, have had and will continue to have an adverse effect on our working capital, total assets and stockholders' equity. Because of the numerous risks and uncertainties associated with our product development and commercialization efforts, we are unable to predict when we will become profitable, and we may never become profitable. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. If we are unable to achieve and then maintain profitability, the market value of our common stock will decline.

Although we began shipping Helicos™ Genetic Analysis Systems to our initial customers during 2008, we may not be able to successfully scale the manufacturing process necessary to build and test multiple Helicos Genetic Analysis Systems on a full commercial basis, in which event our business would be materially harmed.

To ship multiple Helicos Genetic Analysis Systems on a full production scale, we need to continue the testing and performance validation of the system. In order to sustain our commercial launch involving multiple shipments of the Helicos Systems, we need to take other steps to scale the manufacturing process of the system, including improvements to our manufacturing yields and cycle times, manufacturing documentation and quality assurance and quality control procedures. We also need to scale our manufacturing process of the proprietary reagents and disposable supplies that are part of the system. If we are unable to successfully complete these tasks, we may not be able to ship multiple Helicos Systems on a full production scale which would materially harm our business. In

addition, although we believe that we have already incurred the substantial majority of the costs related to the development of the initial version of our Helicos System, if we experience unanticipated problems with our initial system placements, these costs could substantially increase, which would materially harm our business.

If our technology fails to achieve and sustain sufficient market acceptance, we will not generate expected revenue.

Our success depends, in part, on our ability to develop products that displace current technology, as well as expand the market for genetic analysis to include new applications that are not practical with current technology. To accomplish this, we must develop and successfully commercialize our Helicos™ Genetic Analysis System for use in a variety of life science applications. In particular, while our early market focus is on DNA sequencing and gene expression applications, there can be no assurances that we will be successful at inducing potential customers to purchase our Helicos System. Furthermore, we cannot guarantee that the design of the Helicos System, including the initial specifications and any enhancements or improvements to those specifications, will be satisfactory to potential customers in the markets we seek to reach. These markets are new and emerging and there can be no assurances that they will develop as quickly as we expect or that they will reach their full potential. As a result, we may be required to refocus our marketing efforts from time to time and we may have to make changes to the specifications of our system to enhance our ability to more quickly enter particular markets. There is no guarantee, even if our technology is able to successfully reduce the cost and improve the performance of genetic analysis relative to existing products, that we will be able to induce customers with installed bases of conventional genetic analysis instruments to purchase our systems or to expand the market for genetic analysis to include new applications. Even if we are able to successfully implement our technology, we may fail to achieve or sustain market acceptance of our Helicos System by academic and government research laboratories and pharmaceutical, biotechnology and agriculture companies, among others, across the full range of our intended life science applications. Any such failure would materially harm our future sales and revenue. The price of the HeliScope™ instrument is significantly greater than the instrument cost of current market-leading sequencers, which may adversely affect our ability to penetrate or grow the market for genetic analysis. In addition, if our products are only utilized as a replacement for existing DNA sequencing technology, we may face a much smaller market than we currently anticipate.

We are aware of other companies that have developed, or are developing, emerging sequencing technologies. Even if our product demonstrates dramatic cost and throughput improvements over current market-leading technologies, we may fail to achieve market acceptance due to adoption of those emerging technologies by our potential customers, thereby reducing our market opportunity.

We have limited experience in selling and marketing and, as a result, may be unable to successfully commercialize our Helicos™ Genetic Analysis System.

We have limited sales experience and limited marketing experience. Our ability to achieve profitability depends on attracting customers for our Helicos System. Although members of our sales and marketing team have considerable industry experience and have engaged in marketing activities for our Helicos System, in the future we must expand our sales, marketing, distribution and customer support capabilities with the appropriate technical expertise to effectively market our Helicos System. To successfully perform sales, marketing, distribution and customer support functions ourselves, we will face a number of risks, including:

- the ability of our remaining limited sales and marketing team to achieve our near term goals following our December 2008 workforce reduction;

- our ability to attract, retain and manage the specialized sales, marketing and service force necessary to commercialize and gain market acceptance for our technology;
- the time and cost of establishing a specialized sales, marketing and service force for a particular application, which might not be justifiable by the revenues generated by our technology; and
- the ability of our specialized sales, marketing and service force to initiate and execute successful commercialization activities.

We may seek to enlist one or more third parties to assist with sales, distribution and customer support globally or in certain regions of the world. There is no guarantee, if we do seek to enter into such arrangements, that we will be successful in attracting desirable sales and distribution partners, or that we will be able to enter into such arrangements on favorable terms. If our sales and marketing efforts, or those of any third-party sales and distribution partners, are not successful, our technologies and products may not gain market acceptance, which could materially impact our business operations.

If we are unable to timely establish manufacturing capacity by ourselves or with partners, commercialization of our products would be delayed, which would result in lost revenues and harm our business.

To commercialize our Helicos™ Genetic Analysis System, we need to either build internal manufacturing capacity or contract with one or more manufacturing partners, or both. We currently manufacture our products using a combination of internal manufacturing resources and outsourced components and subassemblies. Although we began to manufacture our instruments, reagents and disposable supplies on a commercial scale during 2008, we have limited the expansion of these capabilities following our December 2008 decision to reduce our operating expenses and conserve cash. We may encounter difficulties in manufacturing our products and, due to the complexity of our technology and our manufacturing process, we cannot be sure we fully understand all of the factors that affect our manufacturing processes or product performance. There is no assurance that we will be able to continue to build manufacturing capacity internally or find one or more suitable manufacturing partners, or both, to meet the volume and quality requirements necessary to be successful in the market. Manufacturing and product quality issues may arise as we increase production rates of our Helicos System and associated proprietary reagents and disposable supplies. If our products do not consistently meet our customers' performance expectations, we may be unable to generate sufficient revenues to become profitable. Any delay in establishing or inability to expand our manufacturing capacity could diminish our ability to develop or sell our products, which could result in lost revenue and seriously harm our business, financial condition and results of operations.

Future product sales will depend, in part, on research and development spending levels of academic, clinical and governmental research institutions and pharmaceutical, biotechnology and agriculture companies, and any reduction in such spending levels could limit our ability to sell our products.

We expect that our revenues in the foreseeable future will be derived primarily from sales of instruments, reagents and disposable supplies to a relatively small number of academic, clinical, governmental and other research institutions and pharmaceutical, biotechnology and agriculture companies that conduct large-scale genetic analyses. Our success will depend upon their demand for and use of our products. Accordingly, the spending policies of these customers could have a significant effect on the demand for our technology. These policies are based on a wide variety of factors, including the resources available to make purchases, the spending priorities among various types of equipment, policies regarding spending during recessionary periods and changes in the political climate. In addition, especially given recent weakness in the global economy and changing market conditions of our target customers, the academic, governmental and other research institutions that fund research and development activities may be subject to stringent budgetary constraints that could result in

spending reductions, reduced allocations or budget cutbacks, which could jeopardize the ability of these customers to purchase our Helicos System. Our operating results may fluctuate substantially due to reductions and delays in research and development expenditures by these customers. For example, reductions in capital expenditures by these customers may result in lower than expected instrument sales and similarly, reductions in operating expenditures by these customers could result in lower than expected sales of reagents and disposable supplies. These reductions and delays may result from factors that are not within our control, such as:

- changes in economic conditions;
- changes in government programs that provide funding to research institutions and companies;
- changes in the regulatory environment affecting life sciences companies and life sciences research;
- market-driven pressures on companies to consolidate and reduce costs; and
- other factors affecting research and development spending.

Any decrease in our customers' budgets or expenditures or in the size, scope or frequency of capital or operating expenditures as a result of the foregoing or other factors could materially adversely affect our operations or financial condition.

If the suppliers we rely on fail to supply the materials we use in the manufacturing of our products, we would be unable to satisfy product demand, which would negatively affect our business.

Some components used in the manufacturing of our Helicos™ Genetic Analysis System and certain raw materials used in the manufacturing of our reagents and disposable supplies are available from only a few suppliers. We acquire some of these components and raw materials on a purchase-order basis, which means that the supplier is not required to supply us with specified quantities of these components or raw materials over a certain period of time or to set aside part of its inventory for our anticipated requirements. If supplies from these vendors were delayed or interrupted for any reason, we may not be able to manufacture and sell our Helicos System and associated reagents and disposable supplies in a timely fashion or in sufficient quantities or under acceptable terms. Additionally, for certain of these components and raw materials, we currently purchase from sole-source suppliers and have not yet arranged for alternative suppliers. It might be difficult to find alternative suppliers in a timely manner and on terms acceptable to us. Consequently, as we begin our commercialization efforts, if we do not forecast properly, or if our suppliers are unable or unwilling to supply us in sufficient quantities or on commercially acceptable terms, we might not have access to sufficient quantities of these materials on a timely basis and might not be able to satisfy product demand. Additionally, if there is concern among potential and existing suppliers about our financial viability, these suppliers may be hesitant to supply components and raw materials under acceptable terms, if at all. Moreover, if any of these components and raw materials becomes unavailable in the marketplace, we will be forced to further develop our technologies to incorporate alternate components or raw materials.

Our inability to continually enhance our product performance, including our planned improvements to the Helicos™ Genetic Analysis System, to keep pace with rapidly changing technology and customer requirements, would adversely affect our ability to compete effectively.

The success of any products utilizing our True Single Molecule Sequencing (tSMS)™ technology will depend on our ability to continue to increase the performance and decrease the price of sequencing using this technology. New technologies, techniques or products could emerge which might allow the analysis of genomic information with similar or better price-performance than our Helicos Genetic Analysis System and could exert pricing pressures on or take market share from our products. It is critical to our success for us to anticipate changes in technology and customer requirements and to

successfully introduce new, enhanced and competitive technology to meet our customers' and prospective customers' needs on a timely basis. While we have planned substantial improvements to the Helicos System, including enhancing the performance of the system's reagents and disposable supplies and image processing subsystem and reducing the consumption of reagents, we may not be able to successfully implement these improvements. Even if we successfully implement some or all of these planned improvements, we could incur substantial development costs. We may not have adequate resources available to develop new technologies or be able to successfully introduce enhancements to our system. There can be no guarantee that we will be able to maintain technological advantages over emerging technologies in the future, and we will need to respond to technological innovation in a rapidly changing industry. If we fail to keep pace with emerging technologies, our system will become uncompetitive, our market share will decline and our business, revenue, financial condition and operating results could suffer materially.

We operate in a highly competitive industry and if we are not able to compete effectively, our business and operating results will likely be harmed.

Some of our current competitors, as well as many of our potential competitors, have greater name recognition, more substantial intellectual property portfolios, longer operating histories, significantly greater resources to invest in new technologies and more substantial experience in new product development, regulatory expertise, manufacturing capabilities and the distribution channels to deliver products to customers than we do. For example, companies such as Affymetrix, Inc., Agilent Technologies, Life Technologies Corporation, the Life Sciences Division of GE Healthcare, Illumina, Inc., and Roche Applied Science have products for genetic analysis which compete in certain segments of the market in which we plan to sell our Helicos™ Genetic Analysis System. Pharmaceutical and biotechnology companies have significant needs for genomic information and may also choose to develop or acquire competing technologies to meet these needs. In addition, a number of other companies and academic groups are in the process of developing novel techniques for genetic analysis, many of which have also received grants from the National Human Genome Research Institute, a branch of the National Institutes of Health, for the development of technologies that can achieve substantially lower costs, referred to as a "$100,000 genome" or a "$1,000 genome." These competitors may be able to respond more quickly and effectively than we can to new or changing opportunities, technologies, standards or customer requirements. Further, in light of these advantages, even if our technology is more effective than the product or service offerings of our competitors, current or potential customers might accept competitive products and services in lieu of purchasing our technology. We may not be able to compete effectively against these organizations. Increased competition is likely to result in pricing pressures, which could harm our sales, profitability or market share. Our failure to compete effectively could materially adversely affect our business, financial condition or results of operations.

In addition, to the extent that, in the long term, we commercialize any products utilizing our tSMS technology for use in future life science applications, such as clinical diagnostic or protein analysis applications, we will face additional competition. In the event that we develop new technology and products that compete with existing technology and products of well established companies, the marketplace might not adopt our technology and products.

Inability to expand our commercial and research and development capabilities would harm our business.

Our December 2008 decision to reduce the Company's operating costs that included, among other strategies, a reduction in the Company's workforce of 30%, will limit our ability to add additional personnel and expand our capabilities to successfully pursue our commercialization strategy for our Helicos™ Genetic Analysis System as well as our research and development efforts. We may not have

adequate resources to enhance our manufacturing capabilities and operations, information technology infrastructure, and financial and accounting systems and controls. For instance, certain aspects of our operations, such as our manufacturing capabilities, require additional resources to be scaled up to increase the number of Helicos Systems we could manufacture per quarter. We also must attract, train and retain qualified sales, marketing and service personnel, engineers, scientists and other technical personnel and management personnel but may not have adequate resources to do so in the future. Our inability to expand our capabilities, retain existing personnel, attract new personnel and grow our business could have a material adverse effect on our business, operating results or financial condition. Future growth would require significant capital expenditures and may divert financial resources from other projects, such as the development of new products or enhancements. If our management is unable to effectively manage our limited resources, our revenue could grow more slowly than expected and we may not be able to achieve our research and development and commercialization goals.

Our business would be harmed if we are not successful in entering into large contracts for the sale and installation of our Helicos™ Genetic Analysis Systems.

Our business may depend upon securing and maintaining large contracts for the sale and installation of our Helicos Genetic Analysis Systems to a limited number of customers each year. We expect the sales cycle for these large contracts to be longer than for other contracts because we will need to educate potential customers regarding the benefits of our system to a variety of constituencies within such customer organizations. Moreover, even after a purchase decision is made, these contracts may be delayed by factors outside our control, including financial and budget constraints of the customers purchasing our product. Accordingly, we may expend substantial funds and management effort with no assurance that an agreement will be reached with a potential customer. Our business, results of operations and financial condition could be materially adversely affected if we are unable to obtain major contracts for the sale and installation of our Helicos Systems, or if we experience delays in the performance of such contracts.

We expect that our sales cycle will be lengthy and unpredictable, which will make it difficult for us to forecast revenue and increase the magnitude of quarterly fluctuations in our operating results.

Potential customers for our Helicos™ Genetic Analysis System typically commit significant resources to evaluate genetic analysis technologies. The complexity of our product will require us to spend substantial time and effort to assist potential customers in evaluating our Helicos System and in benchmarking it against available technologies. Because our Helicos System requires a significant investment of time and cost by our customers, we must target those senior managers within the customer's organization who are able to make these decisions on behalf of such organizations. We may face difficulty identifying and establishing contact with such decision makers. Even after initial acceptance, the negotiation and documentation processes can be lengthy. Additionally, our customers may have stricter limitations on spending given the current economic climate. We expect our sales cycle to typically range between six and twelve months, but it may be longer. Any delay in completing sales in a particular quarter could cause our operating results to fall below expectations.

Our customers may purchase replacements for the reagents and disposable supplies that are a part of our Helicos™ Genetic Analysis System from third parties or discover a method that allows them to use less than the expected amounts of such products, which would materially and adversely affect our revenues.

The success of our business depends, in part, on the recurring sales of the proprietary reagents and disposable supplies for our system. Because we have not yet commercialized our Helicos Genetic Analysis System, we do not have the experience to predict the percentage of our revenues that we will derive from sales of proprietary reagents and disposable supplies. Nevertheless, we expect such sales to

represent a material source of our future revenues. Our customers or competitors could potentially produce reagents and disposable supplies that are compatible with our Helicos System at a lower cost, which could exert pricing pressures on, or take market share from, our reagents and disposable supplies. Similarly, our customers or competitors may discover a method of utilizing smaller quantities of our proprietary reagents and disposable supplies while achieving satisfactory results, which could reduce the amount of reagents and supplies we are able to sell. In either case, there could be a material adverse effect on our revenues and harm to our business, financial condition and results of operations.

If we are unable to recruit and retain key executives and scientists, we may be unable to achieve our goals.

We are substantially dependent on the performance of our senior management and key scientific and technical personnel. We do not maintain employment contracts with any of our employees. In 2008 we implemented a workforce reduction that was designed to reduce our operating costs, conserve cash and direct our resources to continue advancing towards the Company's near term goals. Depending on our circumstances, we may need to implement additional workforce reductions in the future. The loss of the services of any member of our senior management or our scientific or technical staff may significantly delay or prevent the development of our products and other business objectives by diverting management's attention to transition matters and identification of suitable replacements, if any, and could have a material adverse effect on our business, operating results and financial condition.

In addition, our product development and marketing efforts could be delayed or curtailed if we are unable to hire, train and retain highly skilled employees and scientific advisors, particularly our management team, senior scientists and engineers and sales, marketing and service personnel. To expand our research, product development and sales efforts we need additional people skilled in areas such as bioinformatics, manufacturing, sales, marketing and technical support. Because of the complex and technical nature of our Helicos System and the dynamic market in which we compete, any failure to attract and retain a sufficient number of qualified employees could materially harm our ability to develop and commercialize our technology. Competition for these people is intense. Further, our inability to hire, train and retain sales, marketing and service personnel could have a material adverse affect on our ability to generate sales or successfully commercialize our technology. Each of our executive officers and other key employees could terminate his or her relationship with us at any time. These persons' expertise would be difficult to replace and could have a material adverse effect on our ability to achieve our business goals. There can be no assurance that we will have the financial resources or otherwise be successful in hiring or retaining qualified personnel and our failure to do so could have a material adverse effect on our business, financial condition and results of operations.

Ethical, legal and social concerns surrounding the use of genetic information could reduce demand for our technology.

One of the potential uses for our product is genetic testing for predisposition to certain conditions. Genetic testing has raised ethical, legal and social issues regarding privacy and the appropriate uses of the resulting information. Governmental authorities could, for social or other purposes, call for limits on or regulation of the use of genetic testing or prohibit testing for genetic predisposition to certain conditions, particularly for those that have no known cure. Similarly, such concerns may lead individuals to refuse to use genetics tests even if permissible. These and other ethical, legal and social concerns about genetic testing may limit market acceptance of our technology for certain applications or reduce the potential markets for our technology, either of which could have a material adverse effect on our business, financial condition and results of operations.

Our products could in the future be subject to regulation by the U.S. Food and Drug Administration or other regulatory agencies, which could increase our costs and delay our commercialization efforts, thereby materially and adversely affecting our business and results of operations.

Our products are not currently subject to U.S. Food and Drug Administration ("FDA") clearance or approval if they are not used for the diagnosis or treatment of disease. However, in the future, certain of our products or related applications could be subject to FDA regulation; the FDA's regulatory jurisdiction could be expanded to include our products, or both. Even where a product is exempted from FDA clearance or approval, the FDA may impose restrictions as to the types of customers to which we can market and sell our products. Such regulation and restrictions may materially and adversely affect our business, financial condition and results of operations.

Laws and regulations are also in effect in many countries that could affect our products. The number and scope of these requirements are increasing. We may not be able to obtain regulatory approvals in such countries or may incur significant costs in obtaining or maintaining our foreign regulatory approvals. In addition, the export by us of certain of our products which have not yet been cleared for domestic commercial distribution may be subject to FDA or other export restrictions.

Our products could have unknown defects or errors, which may give rise to claims against us or divert application of our resources from other purposes.

Any product utilizing our True Single Molecule Sequencing (tSMS)™ technology will be complex and may develop or contain undetected defects or errors. We cannot assure you that a material performance problem will not arise. Despite testing, defects or errors may arise in our system, which could result in a failure to achieve market acceptance or expansion, diversion of development resources, injury to our reputation and increased service and maintenance costs. Defects or errors in our products might also discourage customers from purchasing our system. The costs incurred in correcting any defects or errors may be substantial and could adversely affect our operating margins. In addition, such defects or errors could lead to the filing of product liability claims, which could be costly and time-consuming to defend and result in substantial damages. Although we plan to obtain product liability insurance, any future product liability insurance that we procure may not protect our assets from the financial impact of a product liability claim. Moreover, we may not be able to obtain adequate insurance coverage on acceptable terms. Any insurance that we do obtain will be subject to deductibles and coverage limits. A product liability claim could have a serious adverse effect on our business, financial condition and results of operations.

We have incurred, and will continue to incur significant increased costs as a result of operating as a public company, and our management is and will continue to be required to devote substantial time to new compliance initiatives.

The Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the Securities and Exchange Commission and the NASDAQ Stock Market, Inc. have imposed various new requirements on public companies, including requiring changes in corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

In addition, the Sarbanes-Oxley Act requires, among other things, that we maintain effective internal control over financial reporting and disclosure controls and procedures. In particular, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting, as required by Section 404(a) of the Sarbanes-Oxley Act. However, our testing may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses. Our compliance with Section 404 will require that we incur substantial accounting expense and expend significant management time on compliance-related issues. We currently do not have an internal audit group and we will evaluate the need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. Moreover, if we are not able to comply with the requirements of Section 404 in a timely manner, or if we identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by the NASDAQ Stock Market, Inc., the Securities and Exchange Commission or other regulatory authorities, which would require additional financial and management resources.

We use hazardous chemicals and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.

Our research and development processes involve the controlled use of hazardous materials, including chemicals and biological materials. Our operations produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials. We do not currently maintain separate environmental liability coverage. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

Because we are subject to existing and potential additional governmental regulation, we may become subject to burdens on our operations, and the markets for our products may be narrowed.

We are subject, both directly and indirectly, to the adverse impact of existing and potential future government regulation of our operations and markets. For example, export of our instruments is subject to strict regulatory control in a number of jurisdictions. The failure to satisfy export control criteria or obtain necessary clearances could delay or prevent shipment of products, which could adversely affect our revenues and profitability. Moreover, the life sciences industry, which is the market for our technology, has historically been heavily regulated. There are, for example, laws in several jurisdictions restricting research in genetic engineering, which can operate to narrow our markets. Given the evolving nature of this industry, legislative bodies or regulatory authorities may adopt additional regulation that adversely affects our market opportunities. Additionally, if ethical and other concerns surrounding the use of genetic information, diagnostics or therapies become widespread, we may have less demand for our products. Our business is also directly affected by a wide variety of government regulations applicable to business enterprises generally and to companies operating in the life science industry in particular. Failure to comply with these regulations or obtain or maintain necessary permits and licenses could result in a variety of fines or other censures or an interruption in our business operations which may have a negative impact on our ability to generate revenues and could increase the cost of operating our business.

If we make acquisitions in the future, we may encounter a range of problems that could harm our business.

We may acquire technologies, products or companies that we feel could accelerate our ability to compete in our core markets. Acquisitions involve numerous risks, including:

- difficulties in integrating operations, technologies, accounting and personnel;
- difficulties in supporting and transitioning customers of our acquired companies;
- diversion of financial and management resources from existing operations;
- risks of entering new markets;
- potential loss of key employees; and
- inability to generate sufficient revenue to offset acquisition costs.

Acquisitions also frequently result in the recording of goodwill and other intangible assets which are subject to potential impairments in the future that could harm our financial results. In addition, if we finance acquisitions by issuing convertible debt or equity securities, our existing stockholders may be diluted, which could affect the market price of our stock. As a result, if we fail to properly evaluate acquisitions or investments, we may not achieve the anticipated benefits of any such acquisitions, and we may incur costs in excess of what we anticipate.

RISKS RELATED TO OUR INTELLECTUAL PROPERTY

Our failure to establish a strong intellectual property position and enforce our intellectual property rights against others would enable competitors to develop similar or alternative technologies.

Our success depends in part on our ability to obtain and maintain intellectual property protection for our products, processes and technologies. Our policy is to seek to protect our intellectual property by, among other methods, filing U.S. patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business.

Our patent portfolio relating to our proprietary technology is comprised of issued patents and pending patent applications which, in either case, we own directly or for which we are the exclusive or semi-exclusive licensee. Some of these patents and patent applications are foreign counterparts of U.S. patents or patent applications. We may not be able to maintain and enforce existing patents or obtain further patents for our products, processes and technologies. Even if we are able to maintain our existing patents or obtain further patents, these patents may not provide us with substantial protection or be commercially beneficial. The issuance of a patent is not conclusive as to its validity or enforceability, nor does it provide the patent holder with freedom to operate unimpeded by the patent rights of others. Patent law relating to the scope of claims in the technology fields in which we operate is still evolving and the extent of future protection is highly uncertain, so there can be no assurance that the patent rights that we have or may obtain will be valuable. Others have filed patent applications that are similar in scope to ours, and in the future are likely to file patent applications that are similar or identical in scope to ours or those of our licensors. We cannot predict whether any of our competitors' pending patent applications will result in the issuance of valid patents. Moreover, we cannot assure investors that any such patent applications will not have priority or dominate over our patents or patent applications. The invalidation of key patents owned by or licensed to us or non-approval of pending patent applications could increase competition, and materially adversely affect our business, financial condition and results of operations. Furthermore, there can be no assurance that others will not independently develop similar or alternative technologies, duplicate any of our technologies, or, if patents are issued to us, design around the patented technologies developed by us.

We may be involved in lawsuits and administrative proceedings to protect or enforce our patents and proprietary rights and to determine the scope and validity of others' proprietary rights, which could result in substantial costs and diversion of resources and which, if unsuccessful, could harm our competitive position and our results of operations.

Litigation and administrative proceedings may be necessary to enforce our patent and proprietary rights and/or to determine the scope and validity of others' proprietary rights. Litigation on these matters has been prevalent in our industry and we expect that this will continue. To determine the priority of inventions, we may have to initiate and participate in interference proceedings declared by the U.S. Patent and Trademark Office that could result in substantial costs in legal fees and could substantially affect the scope of our patent protection. Also, our intellectual property may be subject to significant administrative and litigation proceedings such as invalidity, opposition, reexamination, or reissue proceedings against our patents. The outcome of any litigation or administrative proceeding might not be favorable to us, and, in that case, we might be required to develop alternative technological approaches that we may not be able to complete successfully or require licenses from others that we may not be able to obtain. Even if such licenses are obtainable, they may not be available at a reasonable cost. We may also be held liable for money damages to third parties and could be enjoined from manufacturing or selling our products or technologies. In addition, if we resort to legal proceedings to enforce our intellectual property rights or to determine the validity and scope of the intellectual property or other proprietary rights of others, the proceedings could be burdensome and expensive, even if we were to prevail. These types of administrative proceedings and any litigation that may be necessary in the future could result in our patent protection being significantly modified or reduced, and could result in substantial costs and diversion of resources and could have a material adverse effect on our business, operating results or financial condition. In August 2006, we filed an opposition against EP 1 105 529 B1 in the European Patent Office, with respect to which we received a preliminary non-binding opinion upholding the patent. In October 2008, EP 1 105 529 B1 was maintained in amended form and in January 2009 we filed a notice of appeal of the European Patent Office's decision.

We depend upon our ability to license technologies, and the failure to license or otherwise acquire necessary technologies could harm our ability to commercialize our products or defend our intellectual property position.

We hold various licenses to use certain technologies that we consider to be material to our business. Each of these licenses imposes a range of obligations on us and may be terminated if we breach the terms of any of the respective agreements. We may also be required to enter into additional licenses with third parties for other technologies that we consider to be necessary for our business. If we are unable to maintain our existing licenses or obtain additional technologies on acceptable terms, we could be required to develop alternative technologies, either alone or with others, in order to avoid infringing the intellectual property to which we no longer hold a license. This could require our product to be re-configured which could negatively impact its availability for commercial sale and increase our development costs. Failure to license or otherwise acquire necessary technologies would harm our ability to commercialize our products, which could materially adversely affect our business, financial condition and results of operations. In addition, any licenses we obtain from federally-funded institutions are subject to the march-in rights of the U.S. government.

We may be the subject of costly and time-consuming lawsuits brought by third parties for alleged infringement of their proprietary rights, which could limit our ability to use certain technologies in the future, force us to redesign or discontinue our products, or pay royalties to continue to sell our products.

Our success depends, in part, on us neither infringing patents or other proprietary rights of third parties nor breaching any licenses to which we are a party. We may be the subject of legal claims by third-parties that we infringe their patents or otherwise violate their intellectual property rights. In addition, the technology that we license from third parties for use in our Helicos System could become subject to similar infringement claims. Infringement claims asserted against us or our licensors may have a material adverse effect on our business, results of operations or financial condition. Any claims, either with or without merit, could be time-consuming and expensive to defend, and could divert our management's attention away from the execution of our business plan. Moreover, any settlement or adverse judgment resulting from the claim could require us to pay substantial amounts of money or obtain a license to continue to use the technology that is the subject of the claim, or otherwise restrict or prohibit our use of the technology. There can be no assurance that we would be able to obtain a license on commercially reasonable terms, if at all, from third parties asserting an infringement claim; that we would be able to develop alternative technology on a timely basis, if at all; or that we would be able to obtain a license to use a suitable alternative technology to permit us to continue offering, and our customers to continue using, our affected products. Accordingly, an adverse determination could prevent us from offering our instruments, reagents or disposable supplies to others. In addition, we may be required to indemnify our customers for third-party intellectual property infringement claims, which would increase the cost to us of an adverse ruling for such a claim. We believe that there may be significant litigation in the industry regarding patent and other intellectual property rights. If we become involved in such litigation, it could consume a substantial portion of our managerial and financial resources.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

The measures that we use to protect the security of our intellectual property and other proprietary rights may not be adequate, which could result in the loss of legal protection for, and thereby diminish the value of, such intellectual property and other rights.

Our success depends in part on our ability to protect our intellectual property and other proprietary rights. In addition to patent protection, we also rely upon a combination of trademark, trade secret, copyright and unfair competition laws, as well as license agreements and other contractual provisions, to protect our intellectual property and other proprietary rights. In addition, we attempt to protect our intellectual property and proprietary information by requiring our employees, consultants and certain academic collaborators to enter into confidentiality and assignment of inventions agreements. There can be no assurance, however, that such measures will provide adequate protection for our patents, copyrights, trade secrets or other proprietary information. In addition, there can be no assurance that trade secrets and other proprietary information will not be disclosed, that others will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to or disclose our trade secrets and other proprietary information. To the extent that our intellectual property and other proprietary rights are not adequately protected, third parties might gain access to our proprietary information, develop and market genetic analysis systems similar to our tSMS technology, or use trademarks similar to ours, each of which could materially harm our business.

Existing U.S. federal and state intellectual property laws offer only limited protection. Moreover, the laws of other countries in which we may market our technology may afford little or no effective protection of our intellectual property. The failure to adequately protect our intellectual property and other proprietary rights could materially harm our business.

RISKS RELATED TO OWNERSHIP OF OUR COMMON STOCK

Our directors and management will exercise significant control over our company, which will limit your ability to influence corporate matters.

Certain of our directors and executive officers and their affiliates collectively control approximately 79.9% of our outstanding common stock as of December 31, 2008. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might negatively affect the market price of our common stock.

The market price of our common stock may be volatile, which could result in substantial losses for our stockholders and subject us to securities class action litigation.

Market prices of technology and healthcare companies have been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- fluctuations in our quarterly operating results or the operating results of companies perceived to be similar to us;
- changes in estimates of our financial results or recommendations by securities analysts;
- failure of our technology to achieve or maintain market acceptance or commercial success;
- changes in market valuations of similar companies;
- success of competitive products and services;
- changes in our capital structure, such as future issuances of securities or the incurrence of additional debt;
- announcements by us or our competitors of significant products, contracts, acquisitions or strategic alliances;
- regulatory developments in the United States, foreign countries or both;
- litigation involving our company, our general industry or both;
- additions or departures of key personnel;
- investors' general perception of us; and
- changes in general economic, industry and market conditions.

In addition, if the market for biotechnology and life sciences stocks or the stock market in general experiences a loss of investor confidence, the trading price of our common stock could decline for reasons unrelated to our business, financial condition or results of operations. If any of the foregoing occurs, it could cause our stock price to fall and may expose us to class action lawsuits that, even if unsuccessful, could be costly to defend and a distraction to management.

If equity research analysts do not publish research reports about our business or if they issue unfavorable commentary or downgrade our common stock, the price of our common stock could decline.

The trading market for our common stock may rely in part on the research and reports that equity research analysts publish about us and our business. We do not control the opinions of these analysts. The price of our stock could decline if one or more equity analysts downgrade our stock or if those analysts issue other unfavorable commentary or cease publishing reports about us or our business.

A significant portion of our total outstanding shares may be sold into the public market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Approximately 76.5% of the shares of our common stock outstanding as of December 31, 2008 may be offered and sold by selling stockholders pursuant to a Registration Statement on Form S-3 (File No. 333-156885) once it is declared effective. In addition, up to 25,652,333 additional shares of our common stock may be offered and sold pursuant to a Registration Statement on Form S-3 (File No. 333-156885) once it is declared effective by selling stockholders upon exercise of warrants issued to them on December 31, 2008. In addition, a majority of the other outstanding shares of our common stock and other warrants are eligible for resale by the holders of those shares pursuant to other effective registration statements or in exempt private transactions.

If our existing stockholders sell substantial amounts of our common stock in the public market, the market price of our common stock could decrease significantly. The perception in the public market that our stockholders might sell shares of common stock could also depress the market price of our common stock. A decline in the price of shares of our common stock might impede our ability to raise capital through the issuance of additional shares of our common stock or other equity securities, and may cause you to lose part or all of your investment in our shares of common stock.

We have registered the issuance of all shares of common stock that we have issued and may issue under our employee option plans. Having registered the issuance of these shares, they can be freely sold in the public market upon issuance. In addition, as of December 31, 2008, there were 277,777 shares of common stock reserved for future issuance as charitable contribution to the Broad Institute of MIT and Harvard that will become eligible for sale in the public market to the extent permitted by Rule 144 under the Securities Act of 1933, as amended.

Due to these factors, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

Provisions in our certificate of incorporation and by-laws or Delaware law might discourage, delay or prevent a change of control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions of our certificate of incorporation and by-laws and Delaware law may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. These provisions include:

- a staggered board of directors;
- limitations on the removal of directors;
- advance notice requirements for stockholder proposals and nominations;

- the inability of stockholders to act by written consent or to call special meetings; and
- the ability of our board of directors to make, alter or repeal our by-laws.

The affirmative vote of the holders of at least 75% of our shares of capital stock entitled to vote is necessary to amend or repeal the above provisions of our certificate of incorporation. In addition, our board of directors has the ability to designate the terms of and issue new series of preferred stock without stockholder approval. Also, absent approval of our board of directors, our by-laws may only be amended or repealed by the affirmative vote of the holders of at least 75% of our shares of capital stock entitled to vote. Accordingly, given that our executive officers, directors and their affiliates collectively own approximately 79.9% of our outstanding common stock, certain of these persons acting together will have the ability to block any such amendment.

In addition, Section 203 of the Delaware General Corporation Law prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

The existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that you could receive a premium for your common stock in an acquisition.

We do not currently intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We have never declared or paid any cash dividends on our common stock and do not currently intend to do so for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future and the success of an investment in shares of our common stock will depend upon any future appreciation in its value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which our stockholders have purchased their shares.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our principal U.S. facilities that we lease consist of a global headquarters, research and development facility and manufacturing plant in Cambridge, Massachusetts, comprising 56,461 square feet. The lease for our Cambridge facility expires in August 2009 with respect to 27,298 square feet of our facility and in March 2010 with respect to the remaining 29,163 square feet.

For additional information regarding obligations under operating leases see Note 7 to the Consolidated Financial Statements contained in this Form 10-K.

ITEM 3. LEGAL PROCEEDINGS

We are not party to any material pending or threatened litigation.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

None.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock has traded publicly under the symbol "HLCS" since our initial public offering in May 2007 on the NASDAQ Global Market. The following table sets forth the range of quarterly high and low sales prices for our common stock.

	2007		2008	
	High	Low	High	Low
First quarter	NA	NA	$18.60	$4.75
Second quarter	$ 9.82	$8.01	$ 9.00	$4.25
Third quarter	$ 9.21	$7.45	$ 5.48	$1.45
Fourth quarter	$15.00	$8.28	$ 1.85	$0.21

Holders

As of March 20, 2009, there were approximately 131 holders of record of our common stock, one of which is Cede & Co., a nominee for Depository Trust Company ("DTC"). All of the shares of common stock held by brokerage firms, banks and other financial institutions as nominees for beneficial owners are deposited into participant accounts at DTC and therefore are considered to be held of record by Cede & Co. as one shareholder.

Dividends

We have never declared or paid any cash dividends on our capital stock and do not expect to pay any cash dividends for the foreseeable future. We intend to use future earnings, if any, in the operation and expansion of our business. Any future determination relating to our dividend policy will be made at the discretion of our board of directors, based on our financial condition, results of operations, contractual restrictions, capital requirements, business properties, restrictions imposed by applicable law and other factors our board of directors may deem relevant.

Issuer Purchases of Equity Securities

During 2008, we purchased 3,544 restricted shares from employees to cover withholding taxes due from the employees at the time the shares vested. The following table provides information about these purchases of restricted shares for the year ended December 31, 2008:

Period	Total Number of Shares Purchased	Average Price Paid Per Share ($)
January 1 to 31, 2008	—	—
February 1 to 29, 2008	—	—
March 1 to 31, 2008	—	—
April 1 to 30, 2008	—	—
May 1 to 31, 2008	—	—
June 1 to 30, 2008	—	—
July 1 to 31, 2008	2,488	$4.79
August 1 to 31, 2008	397	$4.46
September 1 to 30, 2008	—	—
October 1 to 31, 2008	659	$1.76
November 1 to 30, 2008	—	—
December 1 to 31, 2008	—	—
Total	3,544	

Upon the termination of employees during the year ended December 31, 2008, 138,533 unvested restricted shares were forfeited. The following table provides information about our forfeited restricted shares for the quarter ended December 31, 2008:

Period	Total Number of Shares Forfeited	Average Price Per Share ($)
January 1 to 31, 2008	—	—
February 1 to 29, 2008	—	—
March 1 to 31, 2008	69,445	$5.90
April 1 to 30, 2008	—	—
May 1 to 31, 2008	—	—
June 1 to 30, 2008	—	—
July 1 to 31, 2008	4,000	$4.53
August 1 to 31, 2008	13,831	$4.03
September 1 to 30, 2008	383	$3.63
October 1 to 31, 2008	2,298	$0.70
November 1 to 30, 2008	47,893	$0.57
December 1 to 31, 2008	683	$0.55
Total	138,533	

Use of Proceeds from Initial Public Offering of Common Stock

On May 24, 2007, we completed our initial public offering of 5,400,000 shares of our common stock at a price to the public of $9.00 per share for an aggregate offering price of $48.6 million. We received aggregate net proceeds of approximately $43.9 million, after deducting underwriting discounts and commissions of $2.9 million, and $1.8 million of additional expenses, including legal, accounting and printing costs and various other fees associated with the registration and listing of our common stock. None of the underwriting discounts and commissions or offering expenses were incurred or paid,

directly or indirectly, to directors or officers of ours or their associates or to persons owning 10% or more of our common stock or to any affiliates of ours. The offer and sale of all of the shares in the initial public offering were registered under the Securities Act of 1933, as amended, pursuant to a registration statement on Form S-1 (File No. 333-140973), which was declared effective by the Securities and Exchange Commission on May 24, 2007. UBS Investment Bank, JP Morgan, Leerink Swann & Company, and Pacific Growth Equities, LLC were the underwriters of the initial public offering. The offering commenced on May 24, 2007 and did not terminate until after the sale of all of the securities registered in the registration statement.

On June 27, 2007, we sold an additional 397,000 shares of our common stock at $9.00 per share pursuant to the over-allotment option granted to the underwriters of our initial public offering. The net proceeds after deducting underwriters' discounts and commission related to the offering were $3.3 million. UBS Securities, J.P. Morgan Securities, Inc., Leerink Swann & Co., Inc. and Pacific Growth Equities, LLC acted as representatives of the underwriters.

Of the $52.2 million of gross proceeds we received in our initial public offering, including the exercise of the over-allotment options, through December 31, 2008, we have spent approximately $3.2 million on underwriting discounts and commissions and approximately $1.8 million for payment of expenses related to our initial public offering. Additionally, we have spent $16.6 million on pre-production research and development expenses and $10.9 million on inventory. None of these expenses were incurred or paid, directly or indirectly, to directors or officers of ours or their associates or to persons owning 10% or more of our common stock or to any affiliates of ours.

The proceeds remaining after paying the costs noted above are invested in interest bearing bank accounts. Through the first quarter of 2009, we used the remaining proceeds from our initial public offering for general corporate purposes which include ongoing research and development activities, funding the additional recruitment of our specialized sales, marketing and services force and marketing initiatives and funding manufacturing expenses associated with the commercial version of our HeliScope system. Our management has broad discretion as to the use of the net proceeds. As required by the Securities Commission regulations, we will provide further detail on our use of the net proceeds from our initial public offering in future periodic reports.

Use of Proceeds from Private Placement in Public Equity Offering

On December 19, 2008, we announced that we had entered into a securities purchase agreement with certain investors pursuant to which it has agreed to sell a total of 42,753,869 units (the "Units"), each Unit consisting of (i) one share of common stock (collectively, the "Shares") and (ii) one warrant (collectively, the "Warrants") to purchase 0.6 shares of common stock at an exercise price of $0.45 per share, for a purchase price of $0.435 per unit (representing the closing bid price plus an additional amount for the warrants) (the "Offering") for gross proceeds of $18.6 million. We paid $0.8 million in placement agent fees and offering expenses and expect to use the remaining net proceeds of $17.8 million for general corporate purposes, which include ongoing research and development activities, funding marketing initiatives and funding manufacturing expenses associated with the commercial version of our Helicos System. The Shares and Warrants were immediately separable and were issued separately. The Warrants have a five year term and became exercisable immediately following the closing of the transaction. The closing of the transaction occurred on December 23, 2008.

Under NASDAQ Marketplace Rule 4350(i)(1)(B), stockholder approval is required for issuances of securities that will result in a change of control of the issuer. In order to comply with Rule 4350(i)(1)(B), until the Offering has been approved by the stockholders, the Warrants prohibit holders from exercising the Warrants for any number of shares which would cause that holder to hold more than 19.9% of our common stock following the exercise. We expect to seek approval of the Offering at our next annual meeting of stockholders.

In connection with the Offering, we have entered into a registration rights agreement (the "Registration Rights Agreement") with each of the investors. The Registration Rights Agreement provides that we file a "resale" registration statement (the "Registration Statement") covering all of the Shares and the shares issuable upon exercise of the Warrants (the "Warrant Shares"), up to the maximum number of shares able to be registered pursuant to applicable Securities and Exchange Commission ("SEC") regulations, within 30 days of the closing of the Offering. We filed the Registration Statement with the SEC on January 22, 2009 (File No. 333-156885), which was amended on February 13, 2009. Under the terms of the Registration Rights Agreement, we are obligated to maintain the effectiveness of the "resale" registration statement until all securities therein are sold or are otherwise can be sold pursuant to Rule 144, without any restrictions. A cash penalty at the rate of 2% per month will be triggered for any filing or effectiveness failures or if, at any time after six months following the closing of the Offering, we cease to be current in periodic reports with the SEC. The aggregate penalty accrued with respect to each investor may not exceed 12% of the original purchase price paid by that investor.

ITEM 6. SELECTED FINANCIAL DATA

Smaller reporting companies are not required to provide disclosure pursuant to this Item.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following "Management's Discussion and Analysis of Financial Condition and Results of Operations", as well as disclosures included elsewhere in this Form 10-K, include "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. This Act provides a safe harbor for forward-looking statements to encourage companies to provide prospective information about themselves so long as they identify these statements as forward-looking and provide meaningful cautionary statements identifying important factors that could cause actual results to differ from the projected results. All statements other than statements of historical fact we make in this Form 10-K are forward-looking. In particular, the statements herein regarding future sales and operating results; our ability to raise capital or finance our operations; Company and industry growth and trends; growth of the markets in which the Company participates; international events; product performance; the generation, protection and acquisition of intellectual property, and litigation related to such intellectual property; new product introductions; development of new products, technologies and markets; the acquisition of or investment in other entities; the construction of new or refurbishment of existing facilities by the Company; and statements preceded by, followed by or that include the words "intends", "estimates", "plans", "believes", "expects", "anticipates", "should", "could" or similar expressions, are forward-looking statements. Forward-looking statements reflect our current expectations and are inherently uncertain. Our actual results may differ significantly from our expectations. We assume no obligation to update this forward-looking information. The section entitled "Risk Factors" describes some, but not all, of the factors that could cause these differences.

The following discussion and analysis should be read in conjunction with our historical financial statements and the notes to those financial statements which are included in Item 8 of Part II of this Form 10-K.

BUSINESS OVERVIEW

Helicos BioSciences Corporation is a life sciences company focused on innovative genetic analysis technologies for the research, drug discovery and clinical diagnostics markets. Our products are based on our proprietary True Single Molecule Sequencing (tSMS)™ technology which enables rapid analysis of large quantities of genetic material by directly sequencing single molecules of DNA or single DNA copies of RNA. This approach differs from current methods of sequencing DNA because it analyzes

individual molecules of DNA directly instead of analyzing a large number of copies of the molecule produced through complex sample preparation techniques. Our tSMS technology eliminates the need for costly, labor-intensive and time-consuming sample preparation techniques, such as amplification or cloning, which are required by other methods to produce a sufficient quantity of genetic material for analysis.

We believe that our tSMS technology will represent the first comprehensive and universal solution for single molecule genetic analysis and that its adoption can expand the market for genetic analysis while substantially lowering the cost of individual analyses. Our goal is to enable production-level genetic analysis on an unprecedented scale by providing scientists and clinicians with the ability to compare genes and genomes from thousands of individuals. If our tSMS-based products are successful, the information generated from using these products may lead to improved drug therapies, personalized medical treatments and more accurate diagnostics for cancer and other diseases.

Our Helicos™ Genetic Analysis Platform is designed to obtain sequencing information by repetitively performing a cycle of biochemical reactions on individual DNA molecules and imaging the results after each cycle. The platform consists of an instrument called the HeliScope™ Single Molecule Sequencer, an image analysis computer tower called the HeliScope™ Analysis Engine, associated reagents, which are chemicals used in the sequencing process, and disposable supplies.

The imaging capability of the HeliScope Sequencer is designed to accommodate performance beyond what is needed to meet the platform's initial goals, providing the flexibility to introduce substantial throughput and cost improvements in the future without major changes to or replacement of the instrument. We believe that the Helicos Genetic Analysis Platform will ultimately enable the automated, parallel sequencing of billions of individual DNA molecules at orders of magnitude of greater speed and lower cost than other sequencing systems.

We shipped our first two Helicos Systems in 2008, one of which was ultimately returned. We believe that we have incurred the substantial majority of the costs related to the development of the initial version of our Helicos System. In anticipation of future orders, shipments and placements, we are assembling and are testing multiple production units of our Helicos System. These future shipments of the Helicos Systems will be subject to various customer evaluation periods with acceptance criteria, and we expect the customer evaluation period to extend beyond the fiscal quarters in which commercial units are shipped. We continue to secure orders for the Helicos System and expect to recognize revenue from one of our initial 2008 instrument shipments in 2009. Future revenues from sales of our instruments, proprietary reagents and disposable supplies will depend on individual customer agreements, timing of the installation and turnover to customer, customers' use of the system and our ability to maintain our proprietary position on the reagents and disposable supplies. Because we have limited experience in the commercialization of our Helicos System, we cannot predict the percentage of our revenues that we will derive from sales of proprietary reagents and disposable supplies. However, over time we would expect the sales of the reagents and disposable supplies to increase as our installed base of instruments grows and usage of these instruments increases.

In December 2008, we raised approximately $17.8 million, after deducting placement agent fees and estimated offering expenses, through the issuance of 42,753,869 units, each unit consisting of (i) one share of common stock and (ii) one warrant to purchase 0.6 shares of common stock at an exercise price of $0.45 per share, for a purchase price of $0.435 per unit. As of December 31, 2008, we had $19.7 million in cash. We believe that our existing cash and interest income we expect to earn on invested cash balances will be sufficient to fund our operations into the first quarter of 2010. We expect to continue to incur operating losses for at least the next two years, and will need additional financing to support our activities. We will seek to fund our operations through public or private equity or debt financings or other sources, such as collaborations and licensing arrangements or partnerships. The worldwide financial markets are currently experiencing turmoil. These events have materially and

adversely impacted the availability of financing to a wide variety of companies, particularly early-stage companies such as Helicos. We do not know whether the additional capital which we will require will be available when and as needed, on favorable terms if at all, or that our actual cash requirements will not be greater than anticipated. In addition, if we raise additional funds through the issuance of equity or convertible debt securities, the percentage ownership of our stockholders could be significantly diluted, and these newly-issued securities may have rights, preferences or privileges senior to those of existing stockholders. If we obtain additional debt financing, a substantial portion of our operating cash flow may be dedicated to the payment of principal and interest on such indebtedness, and the terms of the debt securities issued could impose significant restrictions on our operations. If we raise additional funds through collaborations and licensing arrangements, we might be required to relinquish significant rights to our technologies or products, or grant licenses on terms that are not favorable to us. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue business strategies. In December 2008, we implemented a 30% reduction in the Company's workforce and took other measures to reduce our future operating costs. If our current operating plan including forecasted sales in 2009 does not materialize or if adequate additional funds are not available to us when required, we will be required to further delay, reduce or eliminate research and development programs, reduce or eliminate commercialization efforts, obtain funds through arrangements with collaborators or others on terms unfavorable to us, or pursue merger or divestiture strategies.

We were incorporated in Delaware in May 2003 under the name RareEvent Medical Corporation, renamed Newco LS6, Inc. in September 2003 and ultimately renamed Helicos BioSciences Corporation in November 2003. Our activities to date have consisted primarily of conducting research and development. Accordingly, we are considered to be in the development stage at December 31, 2008, as defined by the Financial Accounting Standards Board ("FASB") in Statement of Financial Accounting Standards ("SFAS") No. 7, "Accounting and Reporting by Development Stage Enterprises." Our fiscal year ends on December 31, and we operate as one reportable segment. Our corporate offices are located at One Kendall Square, Building 700, Cambridge, Massachusetts 02139.

FINANCIAL OVERVIEW

Grant revenue

In September 2006, we were awarded a grant from the National Human Genome Research Institute, a branch of the National Institutes of Health, pursuant to which we are eligible to receive reimbursement of our research expenses of up to $2.0 million through August 2009. We recognized revenue during the years ended December 31, 2007 and 2008 of $582,000 and $772,000, respectively, in connection with this award. We will continue to recognize revenue under this grant as the related expenses are incurred.

Research and development expenses

Research and development expenses consist of costs associated with scientific research activities, and engineering development efforts. Such costs primarily include salaries, benefits and stock-based compensation; lab and engineering supplies; investment in equipment; consulting fees; and facility related costs, including rent and depreciation. During the year ended December 31, 2008, research and development expenses also included labor and overhead costs associated with the under-utilization of the manufacturing facility, as well as a write-off of excess and obsolete inventory.

During 2007, we were focused on preparing for the launch of the initial version of the Helicos™ Genetic Analysis System. Substantially all research and development expenses since our inception have been in connection with this project and we believe that we have incurred the substantial majority of the development costs associated with the commercial launch of the first generation of the Helicos

System through December 2007. However, additional costs were incurred during 2008 to both maintain and enhance the initial version of the Helicos System in addition to development of new and different genetic analysis assays which will extend the capability of the initial version.

Research and development expenses for the years ended December 31, 2007 and 2008 were $24.8 million and $24.6 million, respectively. While research and development expenses decreased only slightly from 2007 to 2008, we experienced a shift in the focus of our activities during 2008 to manufacturing activities.

In addition to our ongoing research and development efforts, we have incurred start-up manufacturing costs related to the assembly, testing and performance validation of the Helicos System. These costs were accounted for as research and development expenses in our pre-commercialization phase as we prepared to ship the first Helicos System, which occurred on March 5, 2008. We reached technological feasibility of the Helicos System in December 2007 and, as a result, we began to record the cost of the Helicos System in inventory.

We believe that the Helicos System can potentially access a wide range of genetic analysis tests useful to the basic, pharmaceutical, and biomedical research and diagnostic markets. In addition, we have envisioned a series of performance enhancements to the chemistries and consumables used on the initial Helicos System which potentially serve to greatly enhance the sequencing throughput. Each of these research and development projects is dependent upon achieving technical objectives, which are inherently uncertain. As a result of these uncertainties, we are unable to predict to what extent we will receive additional cash inflows from the commercialization and sale of these future tests or from the future enhanced throughput. Our inability to complete these new research and development projects in a timely manner would significantly increase our capital requirements and could adversely impact our liquidity. These uncertainties could force us to seek additional, external sources of financing from time to time in order to continue with our strategy. Our inability to raise additional capital, or to do so on terms reasonably acceptable to us, would jeopardize the future success of our business.

Selling, general and administrative expenses

Selling, general and administrative expenses consist principally of salaries, benefits and stock-based compensation, consulting and professional fees, including patent related costs, general corporate costs and facility costs not otherwise included in research and development expenses or cost of product revenue.

Selling, general and administrative expenses for the years ended December 31, 2007 and 2008 were $14.3 million and $20.1 million, respectively. Prior to the reduction in force, we expanded our sales and marketing functions during 2008 and incurred additional expenses for the costs associated with ERP system enhancements, public company expenses, investor relations programs, and Sarbanes-Oxley compliance.

Restructuring

In December 2008, we implemented a work force reduction plan that resulted in the reduction of approximately 30% of our workforce (the "Reduction in Force Plan"). The Reduction in Force Plan was designed to reduce our operating costs and direct our resources to continue advancing towards our near term goals. Employees directly affected by the Reduction in Force Plan were provided with severance payments and outplacement assistance.

We incurred restructuring charges relating to one-time termination benefits of approximately $433,000 in the fourth quarter of 2008. These charges represent employee severance and termination costs which were paid out during the fourth quarter of 2008 and will continue into the first quarter of 2009.

We estimate that this restructuring will result in annual cost savings of approximately $3.8 million, including salaries and benefits.

A summary of restructuring activity at December 31, 2008 is as follows:

($ in thousands)	Year ended December 31, 2008 Charge	Payments/ Settlements	Current Liability at December 31, 2008
Employee severance, benefits and related costs:			
Research and development	$212	$(143)	$ 69
Selling, general and administrative	221	(157)	64
Total	$433	$(300)	$133

RESULTS OF OPERATIONS

Year ended December 31, 2007 compared to year ended December 31, 2008

Grant revenue. We recognized $582,000 of grant revenue during the year ended December 31, 2007, and $772,000 of grant revenue during the year ended December 31, 2008. Grant revenue recognized during the years ended December 31, 2007 and 2008 related to the reimbursement of expenses in connection with our government research grant.

Product revenue. We recognized $36,000 of product revenue during the year ended December 31, 2008. Product revenue recognized during the year ended December 31, 2008 related to the sale of proprietary reagents to a customer.

Research and development expenses. Research and development expenses during the years ended December 31, 2007 and 2008 were as follows:

($ in thousands)	Year ended December 31, 2007	2008	Change	
Research and development	$24,758	$24,615	$(143)	−1%

Research and development expenses decreased by $143,000 from the year ended December 31, 2007 to the year ended December 31, 2008. The decrease was primarily due to the $9.6 million decrease in product development costs, which included lab expenses, materials, supplies, temporary help and prototype expenses. Our product development costs decreased as we moved toward manufacturing and production activities.

Prior to reaching technological feasibility, our start-up manufacturing costs, such as those relating to the assembly, testing and performance validation of the Helicos System, were expensed to research and development expense as the costs were incurred. When management determined that the Helicos System was ready for commercial launch in December 2007, we began capitalizing our manufacturing costs to inventory.

The overall decrease was offset by a $4.4 million charge for labor and overhead costs associated with the under-utilization of the manufacturing facility, as well as a $1.6 million write-off for excess and obsolete inventory. In addition, our salary and benefit expenses increased by $1.7 million and our stock-based compensation expense increased by $296,000 due primarily to the hiring of additional personnel to support the manufacturing and production activity. The salary and benefit expense increase includes $212,000 related to the Reduction in Force Plan implemented in December 2008. Additionally,

occupancy costs increased by $1.2 million due to the build out of our reagents/consumables manufacturing infrastructure and a data center for our bioinformatics and computational biology efforts.

After implementing the Reduction in Force Plan, we expect our research and development expenses to decline in 2009. However, as we gain commercial traction we will need to invest in future versions of our system.

Selling, general and administrative expenses. Selling, general and administrative expenses during the years ended December 31, 2007 and 2008 were as follows:

	Year ended December 31,			
($ in thousands)	**2007**	**2008**	**Change**	
Selling, general and administrative	$14,312	$20,139	$5,827	41%

The increase in selling, general and administrative expenses of $5.8 million from the year ended December 31, 2007 to the year ended December 31, 2008 was primarily due to the hiring of additional personnel, which led to a $2.2 million increase in our salary and benefit expenses and an $845,000 increase in our stock based compensation expense. The salary increase includes $221,000 related to the Reduction in Force Plan implemented in December 2008. Certain legal expenses increased by $745,000 from the year ended December 31, 2007 to the year ended December 31, 2008 primarily as a result of an increase in costs associated with our intellectual property portfolio. The increase also included an additional $721,000 related to public company activities, including investor relations expenses, business insurance and consulting fees. In addition, increased headcount prior to the Reduction in Force Plan led to additional space requirements which raised our occupancy costs by $600,000 from the year ended December 31, 2007 compared to the year ended December 31, 2008.

After our Reduction in Force Plan, we expect our selling, general and administrative expenses to decrease. However, as we gain commercial traction we will need to expand our sales and marketing functions.

Interest income. Interest income for the years ended December 31, 2007 and 2008 was as follows:

	Year ended December 31,			
($ in thousands)	**2007**	**2008**	**Change**	
Interest income	$1,960	$670	$(1,290)	−66%

The decrease in interest income from the year ended December 31, 2007 compared to the year ended December 31, 2008 was due primarily to higher cash balances during the year ended December 31, 2007 in connection with the receipt of proceeds from the initial public offering ("IPO"). Decreased interest rates also contributed to the decline in interest earned during the year ended December 31, 2008 compared to the year ended December 31, 2007.

Interest expense. Interest expense for the years ended December 31, 2007 and 2008 was as follows:

	Year ended December 31,			
($ in thousands)	**2007**	**2008**	**Change**	
Interest expense	$277	$2,365	$2,088	754%

The increase in interest expense from the year ended December 31, 2007 compared to the year ended December 31, 2008 is attributable to the $10.0 million term loan entered into in December 2007, as well as the $10.0 million subsequent term loan entered into in June 2008.

Year ended December 31, 2006 compared to year ended December 31, 2007

Grant revenue. We recognized $159,000 of grant revenue during the year ended December 31, 2006, and $582,000 of grant revenue during the year ended December 31, 2007. Grant revenue recognized during the years ended December 31, 2006 and 2007 related to the reimbursement of expenses in connection with our government research grant.

Research and development expenses. Research and development expenses during the years ended December 31, 2006 and 2007 were as follows:

	Year ended December 31,			
($ in thousands)	2006	2007	Change	
Research and development	$14,382	$24,758	$10,376	72%

Research and development expenses increased by $10.4 million from the year ended December 31, 2006 to the year ended December 31, 2007. The increase was primarily due to a $4.9 million increase in product development costs in support of pre-production activity, which included lab expenses, materials, supplies, temporary help and prototype expenses. Our salary and benefit expenses increased by $3.5 million and our stock-based compensation expense increased by $925,000 due primarily to the hiring of additional personnel to support the pre-production activity. Increased headcount and pre-production activity required additional space, raising occupancy costs by $856,000.

Prior to reaching technological feasibility, our start-up manufacturing costs, such as those relating to the assembly, testing and performance validation of the Helicos System, were expensed to research and development expense as the costs were incurred. When management determined that the Helicos System was ready for commercial launch in December 2007, we began capitalizing our manufacturing costs to inventory.

Selling, general and administrative expenses. Selling, general and administrative expenses during the years ended December 31, 2006 and 2007 were as follows:

	Year ended December 31,			
($ in thousands)	2006	2007	Change	
Selling, general and administrative	$6,917	$14,312	$7,395	107%

The increase in selling, general and administrative expenses of $7.4 million from the year ended December 31, 2006 to the year ended December 31, 2007 was primarily due to an increase of $2.9 million related to becoming a public company, including legal expenses, investor relations expenses, accounting fees, dues and fees and consulting fees. In addition, our salary and benefit expenses increased by $1.7 million and our stock-based compensation expense increased by $1.2 million. These increases were primarily due to the hiring of additional personnel. The increase also included $289,000 related to initiating a marketing program and $174,000 for patent filings.

Interest income. Interest income for the years ended December 31, 2006 and 2007 was as follows:

	Year ended December 31,			
($ in thousands)	2006	2007	Change	
Interest income	$766	$1,960	$1,194	156%

The increase in interest income from the year ended December 31, 2006 compared to the year ended December 31, 2007 was due primarily to higher cash and cash equivalents during the year ended December 31, 2007 in connection with the receipt of proceeds from the IPO.

Interest expense. Interest expense was $206,000 for the year ended December 31, 2006, compared to $277,000 during the year ended December 31, 2007, respectively. The interest expense was related to interest paid on a term loan under a line of credit facility and security agreement entered into in June 2006, and interest expense related to the Series B redeemable convertible preferred stock warrants that were issued in connection with the line of credit facility.

LIQUIDITY AND CAPITAL RESOURCES

We have incurred losses since our inception in May 2003 and, as of December 31, 2008 we had an accumulated deficit of $139.7 million. We have financed our operations to date principally through the sale of preferred stock and common stock, including our IPO and a private placement of common stock and warrants, debt financing and interest earned on investments. Through December 31, 2008, we have received net proceeds of $66.8 million from the issuance of preferred stock, $65.3 million through the issuance of common stock, including our IPO and a private placement of common stock and warrants, $2.5 million in debt financing from a lender to finance equipment purchases, and $19.6 million in debt financing from a lender for working capital, capital expenditures and general corporate purposes. Working capital as of December 31, 2007 was $50.4 million, consisting of $55.1 million in current assets and $4.7 million in current liabilities. Working capital as of December 31, 2008 was $20.8 million, consisting of $27.2 million in current assets and $6.4 million in current liabilities. Our cash and cash equivalents are held in interest-bearing cash accounts. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily to achieve liquidity and capital preservation.

The following table summarizes our net increase in cash and cash equivalents for the years ended December 31, 2006, 2007, 2008 and for the period from May 9, 2003 (date of inception) through December 31, 2008:

($ in thousands)	Year ended December 31, 2006	2007	2008	Period from May 9, 2003 (date of inception) through December 31, 2008
Net cash provided by (used in):				
Operating activities	$(16,532)	$(32,803)	$(44,301)	$(110,386)
Investing activities	(3,998)	(1,388)	(2,664)	(9,717)
Financing activities	22,553	76,285	13,995	139,816
Net increase (decrease) in cash and cash equivalents	$ 2,023	$ 42,094	$(32,970)	$ 19,713

Net cash used in operating activities. Net cash used in operating activities was $32.8 million for the year ended December 31, 2007 compared to $44.3 million for the year ended December 31, 2008. The $11.5 million increase was primarily due to an increase in the net loss of $8.8 million and an increase in inventory purchases of $5.4 million, partially offset by an increase in non-cash stock-based compensation expense of $1.1 million and an increase in non-cash depreciation and amortization expense of $940,000.

Net cash used in operating activities was $16.5 million for the year ended December 31, 2006 compared to $32.8 million for the year ended December 31, 2007. The $16.3 million increase was primarily due to an increase in the net loss of $16.2 million and an increase in inventory purchases of $1.6 million, partially offset by an increase in non-cash stock-based compensation expense of $2.1 million and an increase in non-cash depreciation and amortization expense of $635,000.

Net cash used in investing activities. Net cash used in investing activities was $1.4 million for the year ended December 31, 2007 compared to $2.7 million for the year ended December 31, 2008. The

$1.3 million increase was primarily due to a $706,000 increase in purchases of property and equipment and a $795,000 decrease in cash provided by maturities of short-term investments, offset by a $225,000 decrease in restricted cash.

Net cash used in investing activities was $4.0 million for the year ended December 31, 2006 compared to $1.4 million for the year ended December 31, 2007. The $2.6 million decrease was primarily due to a $7.4 million decrease in the cash used in the purchases of short-term investments, a $570,000 decrease in purchases of property and equipment, and the increase in restricted cash of $450,000 during the year ended December 31, 2006, partially offset by a $5.8 million decrease in cash provided by maturities of short-term investments.

Net cash provided by financing activities. Net cash provided by financing activities was $76.3 million for the year ended December 31, 2007 compared to $14.0 million for the year ended December 31, 2008. The $62.3 million decrease was primarily due to the receipt of $49.0 million of cash proceeds from the initial public offering and the $20.0 million of cash proceeds from the issuance of redeemable convertible preferred stock, net of issuance costs during the year ended December 31, 2007. Also contributing to the decrease was the $12.9 million increase in payments on debt during the year ended December 31, 2008. The decrease was offset with the receipt of $17.8 million of net cash proceeds from the issuance of common stock, net of issuance costs, in December 2008.

Net cash provided by financing activities was $22.6 million for the year ended December 31, 2006 compared to $76.3 million for the year ended December 31, 2007. The $53.7 million increase was primarily due to $49.0 million of cash proceeds from the initial public offering and a $7.5 million increase of cash proceeds from the issuance of debt, partially offset by a $1.7 million increase of IPO costs and a $685,000 increase of cash payments on debt.

Operating Capital and Capital Expenditure Requirements

To date, we have shipped two Helicos™ Genetic Analysis Systems, one of which was returned, and have not achieved profitability. We anticipate that we will continue to incur substantial net losses for at least two years as we continue our efforts in commercializing the Helicos System and develop the corporate infrastructure required to manufacture and sell our products. We continue to secure orders for the Helicos System, and we expect to generate instrument revenue in 2009.

As of December 31, 2008, we had $19.7 million in cash. We believe that our existing cash and interest income we expect to earn on invested cash balances will be sufficient to fund our operations into the first quarter of 2010. At some point prior to the end of the first quarter of 2010, we expect that we will need additional financing to support our activities. We will seek to fund our operations through public or private equity or debt financings or other sources, such as collaborations and licensing arrangements or partnerships. If we raise additional funds through the issuance of preferred or debt securities, these securities would have rights senior to those of our common stock and could contain covenants that would restrict our operations. We may require additional capital beyond our currently anticipated amounts. Any such required additional capital may not be available on reasonable terms, if at all, given the current economic turmoil and restricted access to capital markets. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue business strategies. In December 2008, we implemented a 30% reduction in the Company's workforce and took other measures to reduce our future operating costs. If our current operating plan including forecasted sales in 2009 does not materialize or if adequate additional funds are not available to us when required, we will be required to further delay, reduce or eliminate research and development programs, reduce or eliminate commercialization efforts, obtain funds through arrangements with collaborators or others on terms unfavorable to us, or pursue merger or divestiture strategies.

Our forecast of the period of time through which our financial resources will be adequate to support our operations, the costs to complete development of products and the cost to commercialize our future products are forward-looking statements and involve risks and uncertainties, and actual results could vary materially and negatively as a result of a number of factors, including the factors discussed in the "Risk Factors" section of this report. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

Because of the numerous risks and uncertainties associated with the development of our product, we are unable to estimate the exact amounts of capital outlays and operating expenditures necessary to complete the development of our future products and successfully deliver any such products to the market. Our future capital requirements will depend on many factors, including, but not limited to, the following:

- the rate of progress and cost of our commercialization activities;
- the success of our research and development efforts;
- the expenses we incur in marketing and selling our products;
- the revenue generated by future sales of our products;
- the timeliness of payments from our customers;
- the emergence of competing or complementary technological developments;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the terms and timing of any collaborative, licensing or other arrangements that we may establish; and
- the acquisition of businesses, products and technologies, although we currently have no commitments or agreements relating to any of these types of transactions.

Working capital as of December 31, 2008 was $20.8 million, consisting of $27.2 million in current assets and $6.4 million in current liabilities. Working capital as of December 31, 2007 was $50.4 million, consisting of $55.1 million in current assets and $4.7 million in current liabilities.

Contractual Obligations

The following table summarizes our outstanding obligations as of December 31, 2008 and the effect those obligations are expected to have on our liquidity and cash flows in future periods:

Contractual obligations	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
			($ in thousands)		
Operating leases	$ 1,444	$1,280	$ 164	$ —	$ —
Long-term debt (including interest)	9,629	4,038	5,591	—	—
License agreements(1)	1,664	181	362	347	774
Total	$12,737	$5,499	$6,117	$347	$774

(1) Consists of fixed payments that we believe we are reasonably likely to make under the license agreements over the lives of the underlying existing patents.

The table above does not include possible royalties payable under our license agreements. Our commitments for operating leases relate to the lease for our corporate headquarters in Cambridge, Massachusetts.

License agreements and patents

We have fixed annual costs associated with license agreements into which we have entered. In addition, we may have to make contingent payments in the future upon realization of certain milestones or royalties payable under these agreements.

Line of credit facility and security agreement

In June 2006, we entered into a line of credit facility and security agreement with General Electric Capital Corporation ("GE Capital"). The credit facility provided that we may borrow up to $8.0 million at an interest rate based on the Federal Reserve's three year Treasury Constant Maturities Rate. The advance period ended on December 31, 2007. The proceeds of the credit facility may be used for the purchase of equipment and are collateralized by specific equipment assets. Payments are required to be made on a monthly basis. For the first six months interest-only payments were required. Thereafter, for the following 30 months, payments of principal and interest will be due for each advance. The outstanding balance is collateralized by the equipment purchased with the proceeds from each equipment advance. As of December 31, 2008, advances on the credit facility were $2.5 million at a weighted-average interest rate of 10.1%.

Loan and security agreement

In December 2007, we entered into a loan and security agreement with two lenders including GE Capital Corporation, which is serving as agent. The loan agreement provided that we may borrow up to $20.0 million at an interest rate equal to the sum of (i) the greater of (A) an interest rate based on the Federal Reserve's three year Treasury Constant Maturities Rate and (B) 3.84% plus (ii) 6.11%. The initial term loan was made on the closing date in an aggregate principal amount equal to $10.0 million.

In June 2008, we entered into an amendment to the loan and security agreement with two lenders including GE Capital Corporation. A subsequent term loan was made upon execution of the amendment in an aggregate principal amount equal to $10.0 million. The loan amendment provided that the interest rate for the subsequent term loan is equal to the sum of (i) the greater of (A) an interest rate based on the Federal Reserve's three year Treasury Constant Maturities Rate and (B) 3.17% plus (ii) 8.33%. The loan agreement, as amended, contained affirmative and negative covenants to which we and our subsidiaries were required to adhere. Pursuant to the amendment, we were required to maintain, at all times, unrestricted cash in our bank account equal to at least $10.0 million. The borrowings under the loan agreement were collateralized by essentially all of our assets. Payments are required to be made on a monthly basis. For the initial term loan, interest-only payments were required for the first five months. Thereafter, for the following 31 months, payments of principal and interest will be due. For the subsequent term loan, principal and interest payments are required for the 36 month term of the loan.

In connection with the execution of the June 2008 amendment to the loan and security agreement with two lenders including GE Capital Corporation, we issued warrants to the two lenders to purchase an aggregate of 110,000 shares of common stock. The warrants have an exercise price of $4.80 per share and expire in June 2014. The fair value of the warrants was estimated at $337,000 using a Black-Scholes model with the following assumptions: expected volatility of 65.4%, risk free interest rate of 3.4%, expected life of six years and no dividends. Expected volatility was based on the volatility of similar entities in the life sciences industry of comparable size of market capitalization and financial

position that completed initial public offerings within the last ten years. The fair value of the warrants was recorded as equity and a debt discount and will be amortized to interest expense over the term of the loan.

In December 2008, we entered into an additional amendment to the loan and security agreement with certain lenders including GE Capital Corporation. The amendment amended the prepayment provisions of the loan and security agreement to allow us to make a prepayment of $10.0 million (the "Pay Down Amount") without incurring any prepayment penalties. Pursuant to the amendment, we made a prepayment, equal to the Pay Down Amount, before December 31, 2008. In connection with such prepayment, and in lieu of the 4% final payment fee with respect to the Pay Down Amount, the amendment provides that we will pay a fee equal to 2% of the initial $10.0 million term loan, payable on the earlier of (a) January 31, 2011 and (b) the maturity date for the subsequent term loan.

The amendment further provides that our obligations under the loan agreement, as amended, are no longer secured by a cash amount of $10.0 million. As such, this amount in no longer classified as restricted cash as of December 31, 2008. Such obligations continue to be secured under various collateral documents by interests in substantially all of our personal property, including the pledge of the stock of our wholly-owned subsidiary, and proceeds of any intellectual property, but not by our intellectual property.

As of December 31, 2008, advances on the loan agreement, as amended, were $20.0 million at an interest rate of 11.5%. As of December 31, 2007 and 2008, the outstanding balance on the loan agreement was $10.0 million and $7.1 million, respectively.

Private Placement in Public Equity Offering

In December 2008, we entered into a securities purchase agreement with certain investors pursuant to which we sold a total of 42,753,869 units (the "Units"), each Unit consisting of (i) one share of common stock (collectively, the "Shares") and (ii) one warrant (collectively, the "Warrants") to purchase 0.6 shares of common stock at an exercise price of $0.45 per share, for a purchase price of $0.435 per unit (representing the closing bid price plus an additional amount for the warrants) (the "Offering"). The Warrants have a five year term and became exercisable immediately following the closing of the transaction. The closing of the transaction occurred on December 23, 2008. In connection with the Offering, we raised approximately $18.6 million in gross proceeds. We paid $813,000 in placement agent fees and offering expenses and expect to use the remaining net proceeds of $17.8 million for general corporate purposes.

OFF-BALANCE SHEET ARRANGEMENTS

We currently do not have any special purpose entities or off-balance sheet financing arrangements.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

Our management's discussion and analysis of our financial condition and results of operations is based upon our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements as well as the reported expenses during the reporting periods. We evaluate our estimates and judgments on an ongoing basis. Actual results may differ materially from these estimates under different assumptions or conditions.

Inventory

Prior to reaching technological feasibility, our start-up manufacturing costs, such as those relating to the assembly, testing and performance validation of the Helicos™ Genetic Analysis System, were expensed to research and development as the costs were incurred. When management determined that the Helicos System was ready for commercial launch during December 2007, we began capitalizing our manufacturing costs to inventory.

We value our inventory at the lower of cost or market on a first-in, first-out basis. Our policy is to capitalize inventory costs associated with our products when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Included in inventory are raw materials, work in process and finished goods used in the production of our first commercial product, the HeliScope system and related reagents.

We periodically review our inventories for excess or obsolete inventory and write-down obsolete or otherwise unmarketable inventory to its estimated net realizable value. If the actual net realizable value is less than that estimated by us, or if there are any further determinations that inventory will not be marketable based on estimates of demand, additional inventory write-downs will be required.

We value inventory in accordance with SFAS No. 151, "Inventory Costs, an Amendment of ARB 43, Chapter 4," or SFAS No. 151. SFAS No. 151 amends the guidance in ARB No. 43, Chapter 4, "Inventory Pricing," to clarify that abnormal amounts of idle facility expense, freight, handling costs, and wasted material (spoilage) should be recognized as current-period charges regardless of whether they meet the criterion of "so abnormal." In addition, SFAS No. 151 requires that allocation of fixed production overheads to the costs of conversion be based on the normal capacity of the production facilities.

We have concluded that because we are not yet functioning under normal capacity, our production level is abnormally low. As such, abnormal costs such as the unfavorable labor, overhead and absorption variances were recognized as current period charges, rather than as a portion of the inventory cost, during the year ended December 31, 2008.

Revenue recognition

We recognize revenue in accordance with Staff Accounting Bulletin No. 104, "Revenue Recognition in Financial Statements," or SAB No. 104 and Emerging Issues Task Force No. 00-21, "Accounting for Multiple Element Revenue Arrangements." SAB No. 104 requires that persuasive evidence of a sales arrangement exists; delivery of goods occurs through transfer of title and risk and rewards of ownership, the selling price is fixed or determinable and collectibility is reasonably assured. EITF No. 00-21 provides guidance on how to account for arrangements that involve the delivery or performance of multiple products, services and/or rights to use assets.

In instances where we sell instruments with a related installation obligation, we will allocate the revenue between the instrument and the installation based on relative fair value at the time of the sale. The instrument revenue will be recognized when title and risk of loss passes. The installation revenue will be recognized when the installation is performed. If fair value is not available for any undelivered element, revenue for all elements is deferred until delivery and installation are complete.

In instances where we sell an instrument with specified acceptance criteria, we will defer revenue recognition until such acceptance has been obtained.

The customer may also purchase a service contract. Revenue from service contracts will be recognized ratably over the service period.

Impairment of long-lived assets

Long-lived assets primarily include property and equipment. In accordance with SFAS No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets," we periodically review long-lived assets for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable or that the useful lives are no longer appropriate. Each impairment test is based on a comparison of the undiscounted cash flows expected to result from the use and eventual disposition of the asset to the carrying amount of the asset. If an impairment is indicated, the asset is written down to its estimated fair value based on a discounted cash flow analysis. Determining the fair value of long-lived assets includes significant judgment by management, and different judgments could yield different results.

Allowance for doubtful accounts

We plan to perform ongoing evaluations of our customers and continuously monitor collections and payments to estimate an allowance for doubtful accounts based on the aging of the underlying receivables and our experiences of specific collection issues.

Stock-based compensation

Effective January 1, 2006, we adopted the fair value recognition provisions of SFAS No. 123(R), "Share-Based Payment," ("SFAS No. 123(R)"), using the modified prospective transition method. Under the modified prospective transition method, compensation cost recognized in the year ended December 31, 2006 included: (a) the pro rata compensation cost for all share-based compensation granted prior to, but not yet vested as of December 31, 2005, based on the grant-date fair value estimated in accordance with the original provisions of SFAS No. 123, and (b) the pro rata compensation cost for all share-based payments granted on or subsequent to January 1, 2006, based on the grant-date fair value estimated in accordance with the provisions of SFAS No. 123(R). In accordance with the modified prospective transition method of SFAS No. 123(R), results for prior periods have not been restated, and the impact of adopting SFAS No. 123(R) was not material to the net loss or cash flows. For all grants, share-based payment expense is adjusted for actual forfeitures as they occur.

We account for stock-based compensation issued to non-employees in accordance with SFAS 123(R) and EITF No. 96-18, "Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with, Selling Goods or Services." We record the expense of such services based on the estimated fair value of the equity instrument using the Black-Scholes option pricing model. The value of the equity instrument is charged to earnings over the term of the service agreement.

For stock-based compensation awards granted to both employees and non-employees, we use the fair value method of calculating stock-based compensation in accordance with SFAS No. 123 for awards prior to January 1, 2006 and SFAS No. 123(R) for awards after December 31, 2005. Calculating the fair value of stock-based awards requires the input of highly subjective assumptions. We use the Black-Scholes option pricing model to value our stock option awards. Stock-based compensation expense is significant to our financial statements and is calculated using our best estimates which involve inherent uncertainties and the application of management's judgment. Significant estimates include the expected life of the stock option, stock price volatility, risk-free interest rate and forfeiture rates.

During the year ended December 31, 2008, we recognized approximately $4.5 million of stock-based compensation expense related to equity awards granted to employees and non-employees. Total unrecognized stock-based compensation expense for all stock-based awards was approximately $8.0 million at December 31, 2008, of which $3.4 million will be recognized in 2009, $2.8 million in

2010, $1.5 million in 2011 and $277,000 thereafter. This results in these amounts being recognized over a weighted-average period of 1.3 years.

Net operating losses and tax credit carryforwards

We record income taxes using the asset and liability method. Deferred income tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective income tax bases and operating loss and tax credit carryforwards. Our consolidated financial statements contain certain deferred tax assets, which have arisen primarily as a result of operating losses, as well as other temporary differences between financial and tax accounting. SFAS No. 109 "Accounting for Income Taxes," requires us to establish a valuation allowance if the likelihood of realization of the deferred tax assets is reduced based on an evaluation of objective verifiable evidence. Significant management judgment is required in determining our provision for income taxes, deferred tax assets and liabilities and any valuation allowance recorded against those net deferred tax assets. We evaluate the weight of all available evidence to determine whether it is more likely than not that some portion or all of the net deferred income tax assets will not be realized.

RECENT ACCOUNTING PRONOUNCEMENTS

In February 2007, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standards No. 159, "The Fair Value Option for Financial Assets and Financial Liabilities—Including an amendment of FASB Statement No. 115" ("SFAS No. 159"). SFAS No. 159 permits an entity to choose to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings. We did not elect to re-measure any of our existing financial assets or liabilities under the provisions of SFAS No. 159.

In June 2007, the Emerging Issues Task Force ("EITF") issued EITF Issue No. 07-03, "Accounting for Nonrefundable Advance Payment for Goods and Services Received for Use in Future Research and Development Activities," ("EITF 07-03"). EITF 07-03 provides guidance on whether nonrefundable advance payments for goods and services that will be used in research and development activities should be expensed when the advance payment is made or when the research and development activity has been performed. EITF 07-03 is effective for fiscal years beginning after December 15, 2007. The adoption of EITF 07-03 did not have a material impact on our financial position, results of operations or cash flows.

In November 2007, the EITF issued EITF Issue 07-01 "Accounting for Collaborative Arrangements" ("EITF No. 07-01"). EITF No. 07-01 requires collaborators to present the results of activities for which they act as the principal on a gross basis and report any payments received from (made to) other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational, and consistently applied accounting policy election. Further, EITF No. 07-01 clarified that the determination of whether transactions within a collaborative arrangement are part of a vendor-customer (or analogous) relationship subject to Issue 01-9, "Accounting for Consideration Given by a Vendor to a Customer". EITF No. 07-01 is effective for fiscal years beginning after December 15, 2008, and interim periods within those years. We are currently evaluating the impact, if any, that the adoption of EITF No. 07-01 will have on our financial position, results of operations or cash flows.

In December 2007, the FASB issued SFAS No. 160, "Non-controlling Interests in Consolidated Financial Statements, an Amendment of ARB No. 51". This statement establishes accounting and reporting standards for the non-controlling interest in a subsidiary and for the deconsolidation of a subsidiary. This statement is effective for fiscal years beginning on or after December 15, 2008.

Adoption of this statement is not expected to have a material impact on our consolidated financial position, results of operations or cash flows when it becomes effective, but may affect the accounting for non-controlling (or minority) interests from that date forward.

In December 2007, the FASB issues SFAS No. 141(R), "Business Combinations", ("SFAS 141(R)"). This Standard will require an acquiring company to measure all assets acquired and liabilities assumed, including contingent considerations and all contractual contingencies, at fair value as of the acquisition date. In addition, an acquiring company is required to capitalize IPR&D and either amortize it over the life of the product, or write it off if the project is abandoned or impaired. The Standard is effective for transactions occurring on or after January 1, 2009. We have not determined the effect that the adoption of SFAS 141(R) will have on our consolidated financial statements, but the effect will generally be limited to future acquisitions in 2009, except for certain tax treatment of previous acquisitions.

Effective January 1, 2008, we implemented Statement of Financial Accounting Standards No. 157, "Fair Value Measurement" ("SFAS No. 157") for our financial assets and liabilities that are re-measured and reported at fair value at each reporting period, and non-financial assets and liabilities that are re-measured and reported at fair value at least annually. In accordance with the provisions of FSP No. FAS 157-2, "Effective Date of FASB Statement No. 157", we have elected to defer implementation of SFAS No. 157 as it relates to our non-financial assets and non-financial liabilities that are recognized and disclosed at fair value in the financial statements on a nonrecurring basis until January 1, 2009. We are currently evaluating the impact, if any, that FSP No. FAS 157-2 will have on our non-financial assets and liabilities. The adoption of SFAS No. 157 to our financial assets and liabilities and non-financial assets and liabilities that are re-measured and reported at fair value at least annually did not have an impact on our financial results in any period.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES OF MARKET RISK

Our exposure to market risk is limited to our cash. The goals of our investment policy are preservation of capital, fulfillment of liquidity needs and fiduciary control of cash and investments. We also seek to maximize income from our investments without assuming significant risk. To achieve our goals, we maintain our cash in interest-bearing cash accounts. As all of our investments are cash deposits in a global bank, it is subject to minimal interest rate risk.

EFFECT OF CURRENCY EXCHANGE RATES AND EXCHANGE RATE RISK MANAGEMENT

We conduct business operations outside of the United States primarily in Canada. These business operations are not material at this time and therefore, any currency fluctuations will not have a material impact on our financial position, results of operations or cash flows.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Helicos BioSciences Corporation (A development stage company)
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of
Helicos BioSciences Corporation:

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, of redeemable convertible preferred stock and stockholders' equity (deficit) and of cash flows present fairly, in all material respects, the financial position of Helicos BioSciences Corporation and its subsidiary (a development stage enterprise) at December 31, 2007 and December 31, 2008, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2008 and, cumulatively, for the period from May 9, 2003 (date of inception) to December 31, 2008, in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

As discussed in Note 3 to the consolidated financial statements, the Company changed the manner in which it accounts for uncertain tax positions effective January 1, 2007.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 30, 2009

Helicos BioSciences Corporation (a development stage company)

CONSOLIDATED BALANCE SHEETS

(in thousands, except share and per share data)

	December 31, 2007	December 31, 2008
ASSETS		
Current assets		
Cash	$ 52,683	$ 19,713
Accounts receivable	—	223
Unbilled government grant receivable	117	205
Inventory	1,612	6,830
Prepaid expenses and other current assets	706	235
Total current assets	55,118	27,206
Property and equipment, net	3,400	4,016
Restricted cash	450	225
Other assets	241	13
Total assets	$ 59,209	$ 31,460
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 1,691	$ 789
Accrued expenses and other current liabilities	1,993	1,652
Deferred revenue	—	623
Current portion of long-term debt	988	3,323
Total current liabilities	4,672	6,387
Long-term debt, net of current portion	10,786	4,535
Other long-term liabilities	312	35
Total liabilities	15,770	10,957
Commitments and contingencies (Notes 7, 8, and 9)		
Stockholders' equity		
Preferred stock: par value $0.001 per share; 5,000,000 shares authorized at December 31, 2007 and 2008; no shares issued and outstanding at December 31, 2007 and 2008	—	—
Common stock: par value $0.001 per share; 120,000,000 shares authorized at December 31, 2007 and 2008; 20,983,638 and 63,808,282 shares issued and outstanding at December 31, 2007 and December 31, 2008, respectively	21	64
Additional paid-in capital	137,472	160,144
Deficit accumulated during the development stage	(94,054)	(139,705)
Total stockholders' equity	43,439	20,503
Total liabilities and stockholders' equity	$ 59,209	$ 31,460

The accompanying notes are an integral part of these consolidated financial statements

Helicos BioSciences Corporation (a development stage company)

CONSOLIDATED STATEMENTS OF OPERATIONS

(in thousands, except share and per share data)

	Year Ended December 31,			Period from May 9, 2003 (date of inception) through December 31, 2008
	2006	2007	2008	
Grant revenue	$ 159	$ 582	$ 772	$ 1,513
Product revenue	—	—	36	36
Total revenue	159	582	808	1,549
Costs and expenses				
Cost of product revenue	—	—	10	10
Research and development	14,382	24,758	24,615	76,360
Selling, general and administrative	6,917	14,312	20,139	47,955
Total costs and expenses	21,299	39,070	44,764	124,325
Operating loss	(21,140)	(38,488)	(43,956)	(122,776)
Interest income	766	1,960	670	4,059
Interest expense	(206)	(277)	(2,365)	(2,848)
Net loss	(20,580)	(36,805)	(45,651)	(121,565)
Beneficial conversion feature related to Series B redeemable convertible preferred stock	—	(18,140)	—	(18,140)
Net loss attributable to common stockholders	$ (20,580)	$ (54,945)	$ (45,651)	$(139,705)
Net loss attributable to common stockholders per share—basic and diluted	$ (16.35)	$ (4.23)	$ (2.10)	
Weighted average number of common shares used in computation—basic and diluted	1,258,438	12,989,889	21,773,394	

The accompanying notes are an integral part of these consolidated financial statements

Helicos BioSciences Corporation (a development stage company)
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
Period from May 9, 2003 (date of inception) to December 31, 2008
(in thousands, except share and per share data)

	Series A redeemable convertible preferred stock		Series B redeemable convertible preferred stock		Common stock		Additional paid-in capital	Subscription receivable	Deficit accumulated during development stage	Other accumulated income (loss)	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount	Shares	Amount					
Balance at inception	—	$ —	—	$ —	—	$—	$ —	$—	$ —	$ —	$ —
Issuance of Series A redeemable convertible preferred stock in December 2003 for cash at $0.9555 per share, net of issuance costs of $59	27,815,946	26,469	—	—	—	—	—	—	—	—	—
Conversion of promissory note for shares of Series A redeemable convertible preferred stock in December 2003 at $0.9555 per share	366,300	350	—	—	—	—	—	—	—	—	—
Issuance of restricted common stock in October 2003 to a founder for cash	—	—	—	—	444,444		2	—	—	—	2
Issuance of restricted common stock in November and December 2003 to nonemployees	—	—	—	—	618,126	1	2	(3)	—	—	—
Issuance of common stock in December 2003 at $0.45 per share in exchange for intellectual property	—	—	—	—	46,514	—	20	—	—	—	20
Stock-based compensation expense	—	—	—	—	—	—	23	—	—	—	23
Net loss	—	—	—	—	—	—	—	—	(547)	—	(547)
Balance at December 31, 2003	28,182,246	26,819	—	—	1,109,084	1	47	(3)	(547)	—	(502)
Exercise of a stock warrant to purchase shares of common stock in January 2004	—	—	—	—	120,123	—	—	—	—	—	—
Cash received from investors in January 2004 for previously issued shares of Series A redeemable convertible preferred stock	—	50	—	—	—	—	—	—	—	—	—
Cash received fron nonemployee in January 2004 for previously issued shares of restricted common stock	—	—	—	—	—	—	—	3	—	—	3
Issuance of restricted common stock in February, March and April 2004 to employees for cash at $0.45 per share	—	—	—	—	155,555		1	—	—	—	1
Issuance of restricted common stock in September 2004 to nonemployees for cash at $0.45 per share	—	—	—	—	11,888	—	—	—	—	—	—
Exercise of nonemployee stock options in December 2004 for cash of $0.45 per share	—	—	—	—	15,200		6	—	—	—	6
Stock-based compensation expense	—	—	—	—	—	—	138	—	—	—	138
Unrealized short-term loss	—	—	—	—	—	—	—	—	—	(17)	(17)
Net loss	—	—	—	—	—	—	—	—	(7,064)	—	(7,064)
Balance at December 31, 2004	28,182,246	26,869	—	—	1,411,850	1	192	—	(7,611)	(17)	(7,435)

The accompanying notes are an integral part of these consolidated financial statements

Helicos BioSciences Corporation (a development stage company)
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) (Continued)
Period from May 9, 2003 (date of inception) to December 31, 2008
(in thousands, except share and per share data)

	Series A redeemable convertible preferred stock		Series B redeemable convertible preferred stock		Common stock		Additional paid-in capital	Subscription receivable	Deficit accumulated during development stage	Other accumulated income (loss)	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount	Shares	Amount					
Balance at December 31, 2004	28,182,246	26,869	—	—	1,411,850	1	192	—	(7,611)	(17)	(7,435)
Issuance of restricted common stock in March 2005 in exchange for intellectual property	—	—	—	—	88,888	—	—	—	—	—	—
Issuance of restricted common stock in July 2005 to employees for cash at $0.45 per share	—	—	—	—	55,555	1	—	—	—	—	1
Issuance of restricted common stock in April and December 2005 to nonemployees for cash at $0.45 per share	—	—	—	—	1,666	—	1	—	—	—	1
Exercise of employee stock options in June 2005 for cash at $0.45 per share	—	—	—	—	277	—	—	—	—	—	—
Exercise of nonemployee stock options in September 2005 for cash at $0.45 per share	—	—	—	—	444	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	55	—	—	—	55
Vesting of previously issued shares of restricted common stock	—	—	—	—	—	—	36	—	—	—	36
Change in unrealized short-term loss	—	—	—	—	—	—	—	—	—	17	17
Net loss	—	—	—	—	—	—	—	—	(10,918)	—	(10,918)
Balance at December 31, 2005	28,182,246	26,869	—	—	1,558,680	2	284	—	(18,529)	—	(18,243)
Issuance of restricted common stock in January 2006 to nonemployees for cash at $0.45 per share	—	—	—	—	1,111	—	—	—	—	—	—
Issuances of Series B redeemable convertible preferred stock in March 2006 for cash at $1.29 per share, net of issuance costs of $108	—	—	15,503,876	19,892	—	—	—	—	—	—	—
Issuance of common stock in July 2006 to employees for cash at $0.585 per share	—	—	—	—	44,444	—	247	—	—	—	247
Issuance of restricted common stock in September, November and December 2006 to employees for cash at $0.585 per share	—	—	—	—	394,444	—	2	(4)	—	—	(2)
Exercise of nonemployee stock options in November 2006 for cash at $0.585 per share	—	—	—	—	4,444	—	2	—	—	—	2
Exercise of employee stock options in January and December 2006 for cash at $0.45 per share	—	—	—	—	48,146	—	22	—	—	—	22
Stock-based compensation expense	—	—	—	—	—	—	1,058	—	—	—	1,058
Vesting of previously issued shares of restricted common stock	—	—	—	—	—	—	157	—	—	—	157
Net loss	—	—	—	—	—	—	—	—	(20,580)	—	(20,580)
Balance at December 31, 2006	28,182,246	26,869	15,503,876	19,892	2,051,269	2	1,772	(4)	(39,109)	—	(37,339)

The accompanying notes are an integral part of these consolidated financial statements

Helicos BioSciences Corporation (a development stage company)

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) (Continued)

Period from May 9, 2003 (date of inception) to December 31, 2008

(in thousands, except share and per share data)

	Series A redeemable convertible preferred stock		Series B redeemable convertible preferred stock		Common stock		Additional paid-in capital	Subscription receivable	Deficit accumulated during development stage	Other accumulated income (loss)	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount	Shares	Amount					
Balance at December 31, 2006	28,182,246	26,869	15,503,876	19,892	2,051,269	2	1,772	(4)	(39,109)	—	(37,339)
Issuances of Series B redeemable convertible preferred stock in January 2007 for cash at $1.29 per share, net of issuance costs of $6	—	—	15,503,876	19,994	—	—	—	—	—	—	—
Exercise of employee stock options in January 2007 for cash at $0.585 per share	—	—	—	—	4,311	—	3	—	—	—	3
Exercise of employee stock options in June, August and December 2007 for cash at $0.45 per share	—	—	—	—	1,866	—	—	—	—	—	—
Exercise of employee stock options in June, July and November 2007 for cash at $1.80 per share	—	—	—	—	1,079	—	2	—	—	—	2
Exercise of non-employee stock options in June, October and November 2007 for cash at $0.45 per share	—	—	—	—	6,500	—	3	—	—	—	3
Issuance of restricted common stock in July and August 2007 to employees	—	—	—	—	56,757	—	—	—	—	—	—
Issuance of restricted common stock in April 2007 to a non-employee	—	—	—	—	2,222	—	—	—	—	—	—
Cash received from employee in January 2007 for previously issued shares of restricted common stock	—	—	—	—	—	—	—	4	—	—	4
Cancellation of shares of restricted common stock	—	—	—	—	(88,888)	—	—	—	—	—	—
Forfeiture of shares of unvested restricted common stock	—	—	—	—	(11,111)	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	3,396	—	—	—	3,396
Vesting of previously issued shares of restricted common stock	—	—	—	—	—	—	85	—	—	—	85
Beneficial conversion feature related to Series B redeemable convertible preferred stock	—	—	—	—	—	—	18,140	—	(18,140)	—	—
Reclassification of amounts due to stockholders for fractional shares upon reverse stock split	—	—	—	—	(10)	—	—	—	—	—	—
Issuance of common stock in initial public offering ("IPO"), net of discounts, commissions and issuance costs of $4,750	—	—	—	—	5,400,000	5	43,845	—	—	—	43,850
Issuance of common stock in over-allotment to underwriters, net of discounts and commissions of $250	—	—	—	—	397,000	1	3,322				3,323
Conversion of preferred stock	(28,182,246)	(26,869)	(31,007,752)	(39,886)	13,153,293	13	66,742	—	—	—	66,755
Exercise of warrants to purchase common stock	—	—	—	—	9,350	—	162	—	—	—	162
Net loss	—	—	—	—					(36,805)		(36,805)
Balance at December 31, 2007	—	$ —	—	$ —	20,983,638	$21	$137,472	$—	$ (94,054)	$ —	$43,439

The accompanying notes are an integral part of these consolidated financial statements

Helicos BioSciences Corporation (a development stage company)
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) (Continued)
Period from May 9, 2003 (date of inception) to December 31, 2008
(in thousands, except share and per share data)

	Series A redeemable convertible preferred stock		Series B redeemable convertible preferred stock		Common stock		Additional paid-in capital	Subscription receivable	Deficit accumulated during development stage	Other accumulated income (loss)	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount	Shares	Amount					
Balance at December 31, 2007	—	—	—	—	20,983,638	21	137,472	—	(94,054)	—	43,439
Exercise of employee stock options in January, February and July 2008 for cash at $0.45 per share	—	—	—	—	15,861	—	7	—	—	—	7
Exercise of employee stock options in January, July and August 2008 for cash at $1.80 per share	—	—	—	—	1,201	—	2	—	—	—	2
Exercise of non-employee stock options in January and April 2008 for cash at $0.45 per share	—	—	—	—	5,790	—	3	—	—	—	3
Issuance of restricted common stock in June and July 2008 to employees	—	—	—	—	190,000	—	—	—	—	—	—
Forfeiture of shares of unvested restricted common stock	—	—	—	—	(142,077)	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	4,538	—	—	—	4,538
Vesting of previously issued shares of restricted common stock	—	—	—	—	—	—	43	—	—	—	43
Issuance of common stock warrants in June 2008 in connection with debt issuance	—	—	—	—	—	—	337	—	—	—	337
Issuance of common stock and common stock warrants in securities offering, net of discounts, commissions and issuance costs of $813	—	—	—	—	42,753,869	43	17,742				17,785
Net loss	—	—	—	—					(45,651)		(45,651)
Balance at December 31, 2008	—	$ —	—	$ —	63,808,282	$64	$160,144	$—	$(139,705)	$ —	$ 20,503

The accompanying notes are an integral part of these consolidated financial statements

Helicos BioSciences Corporation (a development stage company)

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)

	Year Ended December 31,			Period from May 9, 2003 (date of inception) through December 31, 2008
	2006	2007	2008	
Cash flows from operating activities:				
Net loss	$(20,580)	$(36,805)	$(45,651)	$(121,565)
Adjustments to reconcile net loss to cash used in operating activities:				
Depreciation and amortization	953	1,588	2,528	5,731
Amortization of lease incentive	(70)	(146)	(149)	(365)
Common stock issued for licenses	127	—	—	147
Stock-based compensation expense	1,279	3,396	4,538	9,429
Noncash interest expense related to debt and warrants	137	11	404	552
Provisions on inventory	—	—	1,577	1,577
Changes in operating assets and liabilities:				
Accounts receivable	—	—	(223)	(223)
Unbilled government grant receivable	(159)	42	(88)	(205)
Inventory	—	(1,612)	(7,050)	(8,662)
Prepaid expenses and other current assets	(274)	(338)	471	(235)
Deferred revenue	—	—	623	623
Accounts payable	825	222	(902)	789
Accrued expenses and other current liabilities	819	886	(207)	1,829
Other long-term liabilities	411	(47)	(172)	192
Net cash used in operating activities	(16,532)	(32,803)	(44,301)	(110,386)
Cash flows from investing activities:				
Purchases of property and equipment	(2,753)	(2,183)	(2,889)	(9,492)
(Increase) decrease in restricted cash	(450)	—	225	(225)
Purchases of short-term investments	(7,433)	—	—	(34,709)
Maturities of short-term investments	6,638	795	—	34,709
Net cash used in investing activities	(3,998)	(1,388)	(2,664)	(9,717)
Cash flows from financing activities:				
Proceeds from debt issuances	2,473	9,933	9,850	22,256
Payments on debt	—	(685)	(13,585)	(14,270)
Payments of debt issuance costs	—	(174)	(20)	(194)
Proceeds from initial public offering	—	49,011	—	49,011
Deferred initial public offering costs	(89)	(1,749)	—	(1,838)
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	19,892	19,994	—	66,405
Proceeds from bridge loan	—	—	—	350
Proceeds from issuance of common stock	26	—	17,785	17,811
Proceeds from issuance of restricted common stock	227	4	—	339
Payments to employees for cancelled restricted common stock	—	(57)	(47)	(104)
Proceeds from exercise of stock options	24	8	12	50
Net cash provided by financing activities	22,553	76,285	13,995	139,816
Net increase in cash and cash equivalents	2,023	42,094	(32,970)	19,713
Cash and cash equivalents, beginning of period	8,566	10,589	52,683	—
Cash and cash equivalents, end of period	$ 10,589	$ 52,683	$ 19,713	$ 19,713
Supplemental disclosure of cash flow information				
Cash paid during the year for interest	$ 69	$ 234	$ 1,478	$ 1,781
Transfers from inventory to property and equipment	—	—	255	255
Noncash financing activities:				
Issuance of redeemable convertible preferred stock warrants	$ 95	$ —	$ —	$ 95
Issuance of common stock warrants	$ —	$ —	$ 6,021	$ 6,021
Conversion of bridge loan to equity	$ —	$ —	$ —	$ 350
Beneficial conversion feature related to Series B redeemable convertible preferred stock	$ —	$ 18,140	$ —	$ 18,140
Conversion of preferred stock to common stock	$ —	$ 66,755	$ —	$ 66,755
Reclassification of preferred stock warrants to common stock warrants	$ —	$ 162	$ —	$ 162

The accompanying notes are an integral part of these consolidated financial statements

Helicos BioSciences Corporation (a development stage company)
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Business Description

Helicos BioSciences Corporation ("Helicos" or the "Company") is a life sciences company focused on innovative genetic analysis technologies for the research, drug discovery and clinical diagnostics markets. Helicos has developed a proprietary technology to enable the rapid analysis of large volumes of genetic material by directly sequencing single molecules of DNA or single DNA copies of RNA. Helicos is a Delaware corporation and was incorporated on May 9, 2003.

The Company has had limited operations to date and its activities have consisted primarily of raising capital, conducting research and development and recruiting personnel. Accordingly, the Company is considered to be in the development stage at December 31, 2008, as defined by the Financial Accounting Standards Board ("FASB") in Statement of Financial Accounting Standards ("SFAS") No. 7, "Accounting and Reporting by Development Stage Enterprises." The Company's fiscal year ends on December 31. The Company operates as one reportable segment.

Since inception, the Company has incurred losses and has not generated positive cash flows from operations. The Company expects such losses to continue for at least two years as it continues to develop and commercialize its products. As of December 31, 2008, the Company had $19.7 million in cash. The Company believes that its existing cash and interest income it expects to earn on invested cash balances will be sufficient to fund its operations into the first quarter of 2010. At some point prior to the end of the first quarter of 2010, the Company expects that it will need additional financing to support its activities. The Company will seek to fund its operations through public or private equity or debt financings or other sources, such as collaborations and licensing arrangements or partnerships. The worldwide financial markets are currently experiencing turmoil. These events have materially and adversely impacted the availability of financing to a wide variety of companies, particularly early-stage companies such as Helicos. Adequate additional funding may not be available to the Company on acceptable terms, or at all. The Company's failure to raise capital as and when needed would have a negative impact on its financial condition and its ability to pursue its business strategies. In December 2008, the Company implemented a 30% reduction in its workforce and took other measures to reduce its future operating costs. If the Company's current operating plan including forecasted sales in 2009 does not materialize or if adequate additional funds are not available when required, the Company will be required to further delay, reduce or eliminate research and development programs, reduce or eliminate commercialization efforts, obtain funds through arrangements with collaborators or others on terms unfavorable to the Company, or pursue merger or divestiture strategies.

On May 7, 2007, a 1 for 4.5 reverse split of the Company's common stock was made effective by the filing of a Certificate of Amendment of the Company's Second Amended and Restated Certificate of Incorporation. The split had been approved by the Company's Board of Directors and shareholders. All share and per share amounts have been retroactively adjusted to reflect the reverse stock split for all periods presented.

Certain amounts reported in previous periods have been reclassified to conform to the current presentation.

2. Initial Public Offering

On May 24, 2007, the Company completed its initial public offering ("IPO") of 5,400,000 shares of common stock at an initial public offering price of $9.00 per share. Net proceeds were approximately $43.9 million after deducting underwriting discounts and commissions and offering expenses paid by the Company. Total fees and expenses paid by the Company, excluding underwriting discounts and

2. Initial Public Offering (Continued)

commissions were approximately $1.8 million which includes legal, accounting and printing costs and various other fees associated with registration and listing of the Company's common stock.

On May 24, 2007, upon completion of the Company's IPO, all of the Company's 59,189,998 shares of redeemable convertible preferred stock outstanding on that date were automatically converted into 13,153,293 shares of common stock. In addition, the outstanding warrants to purchase 81,184 shares of Series B redeemable convertible preferred stock were converted into warrants to purchase 18,040 shares of common stock. During the period January 1, 2007 through the date of the Company's IPO, the estimated fair value of the warrants to purchase 81,184 shares of Series B redeemable convertible preferred stock decreased by $42,000 to $162,000. Upon conversion on the date of the Company's IPO, the warrants to purchase 18,040 shares of the Company's common stock were reclassified to additional paid-in capital.

On June 27, 2007, the underwriters exercised their over-allotment option and purchased an additional 397,000 shares of the Company's common stock, and the net proceeds after deducting underwriters' discounts and commissions related to the offering were approximately $3.3 million.

3. Summary of Significant Accounting Policies

Basis of presentation and consolidation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America. The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary. All intercompany accounts and transactions have been eliminated. It is management's opinion that the accompanying consolidated financial statements reflect all adjustments (which are normal and recurring) that are necessary to present fairly the Company's financial position at December 31, 2007 and 2008 and results of operations and cash flows for the years ended December 31, 2006, 2007, 2008 and the period from May 9, 2003 (date of inception) through December 31, 2008.

Use of estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. On an ongoing basis, the Company evaluates its estimates, including those related to revenue recognition, inventory valuation, income taxes, contingencies, and stock-based compensation. The Company bases its estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual amounts may differ from these estimates under different assumptions or conditions. Changes in estimates are recorded in the period in which they become known.

3. Summary of Significant Accounting Policies (Continued)

Cash and cash equivalents

The Company considers all highly liquid investments with original maturities of generally three months or less at the time of acquisition to be cash equivalents. Cash equivalents are stated at cost, which approximates fair market value.

Short-term investments

The Company classifies marketable securities as available-for-sale in accordance with the provisions of SFAS No. 115, "Accounting for Certain Investments in Debt and Equity Securities." These securities are carried at fair market value with unrealized gains and losses reported, if material, as a component of other comprehensive gain or loss in stockholders' equity (deficit). There were no gross unrealized gains and losses at December 31, 2007 or 2008. Gains or losses on securities sold are based on the specific identification method.

Concentration of credit risk

The Company has no significant off-balance sheet concentrations of credit risk such as foreign currency exchange contracts, option contracts or other hedging arrangements. Financial instruments that subject the Company to credit risk consist primarily of cash, cash equivalents and short-term investments. The Company maintains all of its cash in one accredited financial institution. Although the risk is concentrated in one financial institution, management believes these accounts are subject to minimal credit and market risk and are of high credit quality.

Fair value of financial instruments

Effective January 1, 2008, the Company implemented Statement of Financial Accounting Standards No. 157, "Fair Value Measurement" ("SFAS No. 157") for its financial assets and liabilities that are re-measured and reported at fair value at each reporting period, and non-financial assets and liabilities that are re-measured and reported at fair value at least annually. In accordance with the provisions of FSP No. FAS 157-2, "Effective Date of FASB Statement No. 157", the Company has elected to defer implementation of SFAS No. 157 as it relates to the Company's non-financial assets and non-financial liabilities that are recognized and disclosed at fair value in the financial statements on a nonrecurring basis until January 1, 2009. The Company is currently evaluating the impact, if any, that FSP No. FAS 157-2 will have on its non-financial assets and liabilities. The adoption of SFAS No. 157 to the Company's financial assets and liabilities and non-financial assets and liabilities that are re-measured and reported at fair value at least annually did not have an impact on the Company's financial results in any period. The carrying amounts of the Company's financial instruments, which include cash and cash equivalents, accounts payable, accrued expenses, debt, redeemable convertible preferred stock warrants and common stock warrants approximate their fair value at December 31, 2007 and 2008.

Inventory

Prior to reaching technological feasibility, start-up manufacturing costs, such as those relating to the assembly, testing and performance validation of the Helicos™ Genetic Analysis System, were expensed to research and development as the costs were incurred. When management determined that the Helicos System was ready for commercial launch during December 2007, the Company began capitalizing its manufacturing costs to inventory.

3. Summary of Significant Accounting Policies (Continued)

The Company values its inventory at the lower of cost or market on a first-in, first-out basis. The Company's policy is to capitalize inventory costs associated with its products when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Included in inventory are raw materials, work in process and finished goods used in the production of the Company's first commercial product, the HeliScope system and related reagents.

The Company periodically reviews its inventories for excess or obsolete inventory and writes-down obsolete or otherwise unmarketable inventory to its estimated net realizable value. If the actual net realizable value is less than that estimated by the Company, or if there are any further determinations that inventory will not be marketable based on estimates of demand, additional inventory write-downs will be required.

The Company values inventory in accordance with SFAS No. 151, "Inventory Costs, an Amendment of ARB 43, Chapter 4," or SFAS No. 151. SFAS No. 151 amends the guidance in ARB No. 43, Chapter 4, "Inventory Pricing," to clarify that abnormal amounts of idle facility expense, freight, handling costs, and wasted material (spoilage) should be recognized as current-period charges regardless of whether they meet the criterion of "so abnormal." In addition, SFAS No. 151 requires that allocation of fixed production overheads to the costs of conversion be based on the normal capacity of the production facilities.

The Company concluded that because it is not yet functioning under normal capacity, its production level is abnormally low. As such, abnormal costs such as the unfavorable labor, overhead and absorption variances were recognized as current period charges, rather than as a portion of the inventory cost, during the year ended December 31, 2008.

Property and equipment

Property and equipment are recorded at cost. Expenditures for maintenance and repairs are charged to expense while the costs of significant improvements are capitalized. Depreciation is provided using the straight-line method over the following estimated useful lives: Machinery and equipment—three to five years, office furniture and equipment—three years, leasehold improvements—the shorter of three years or the life of lease. Upon retirement or sale, the cost of the assets disposed of and the related accumulated depreciation are eliminated from the consolidated balance sheets and related gains or losses are reflected in the consolidated statements of operations. There have been no material retirements or sale of assets since May 9, 2003 (date of inception).

Long-lived assets

In accordance with SFAS No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets," the Company reviews the carrying values of its long-lived assets for possible impairment whenever events or changes in circumstances indicate that the carrying amounts of the assets may not be recoverable. Any long-lived assets held for disposal are reported at the lower of their carrying amounts or fair values less costs to sell.

3. Summary of Significant Accounting Policies (Continued)

Redeemable convertible preferred stock warrant

Freestanding warrants and other similar instruments related to shares that are redeemable are accounted for in accordance with SFAS No. 150, "Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity" and FASB Staff Position ("FSP") FAS 150-5, "Issuer's Accounting under FASB Statement No. 150 for Freestanding Warrants and Other Similar Instruments on Shares that are Redeemable." Under FSP FAS 150-5, the freestanding warrant that was related to the Company's redeemable convertible preferred stock was classified as a liability on the balance sheet as of January 1, 2006. The warrant was subject to re-measurement at each balance sheet date and any change in fair value was recognized as a component of interest expense. Fair value was measured using the Black-Scholes option pricing model. The Company continued to adjust the liability for changes in fair value until the completion of its initial public offering on May 24, 2007, at which time all redeemable convertible preferred stock warrants were converted into warrants to purchase common stock and, accordingly, the liability was reclassified to equity.

Revenue recognition

Government research grants that provide for payments to the Company for work performed are recognized as revenue when the related expenses are incurred.

The Company recognizes revenue in accordance with Staff Accounting Bulletin No. 104, "Revenue Recognition in Financial Statements," or SAB No. 104 and Emerging Issues Task Force No. 00-21, "Accounting for Multiple Element Revenue Arrangements." SAB No. 104 requires that persuasive evidence of a sales arrangement exists; delivery of goods occurs through transfer of title and risk and rewards of ownership, the selling price is fixed or determinable and collectibility is reasonably assured. EITF No. 00-21 provides guidance on how to account for arrangements that involve the delivery or performance of multiple products, services and/or rights to use assets.

In instances where the Company sells instruments with a related installation obligation, the Company will allocate the revenue between the instrument and the installation based on relative fair value at the time of the sale. The instrument revenue will be recognized when title and risk of loss passes. The installation revenue will be recognized when the installation is performed. If fair value is not available for any undelivered element, revenue for all elements is deferred until delivery and installation are complete.

In instances where the Company sells an instrument with specified acceptance criteria, the Company will defer revenue recognition until such acceptance has been obtained.

The customer may also purchase a service contract. Revenue from service contracts will be recognized ratably over the service period.

Research and development

Research and development expenditures are charged to the consolidated statement of operations as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries and benefits, facilities costs, clinical trial and related supply costs, contract services, depreciation and amortization expense and other related costs. During the year ended December 31, 2008, research and development expenses also included labor and

3. Summary of Significant Accounting Policies (Continued)

overhead costs associated with the under-utilization of the manufacturing facility, as well as a reserve for excess and obsolete inventory.

Income taxes

The Company records income taxes using the asset and liability method. Deferred income tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective income tax bases, and operating loss and tax credit carryforwards. The Company's consolidated financial statements contain certain deferred tax assets, which have arisen primarily as a result of operating losses, as well as other temporary differences between financial and tax accounting. SFAS No. 109 "Accounting for Income Taxes," requires the Company to establish a valuation allowance if the likelihood of realization of the deferred tax assets is reduced based on an evaluation of objective verifiable evidence. Significant management judgment is required in determining the Company's provision for income taxes, the Company's deferred tax assets and liabilities and any valuation allowance recorded against those net deferred tax assets. The Company evaluates the weight of all available evidence to determine whether it is more likely than not that some portion or all of the net deferred income tax assets will not be realized.

Effective January 1, 2007, the Company adopted FASB Interpretation ("FIN") No. 48, "Accounting for Uncertainty in Income Taxes—an Interpretation of FASB Statement No. 109." This Interpretation prescribes the methodology by which a company must measure, report, present and disclose in its financial statements the effects of any uncertain tax return reporting positions that a company has taken or expects to take. See Note 11, "Income Taxes" for additional disclosure.

Stock-based compensation

Prior to January 1, 2006, the Company accounted for employee stock-based compensation arrangements in accordance with the provisions of SFAS No. 123 "Accounting for Stock-Based Compensation." Under the fair value recognition provisions of SFAS No. 123, stock-based compensation cost is measured at the grant date based on the fair value of the award and is recognized as expense over the vesting period.

Effective January 1, 2006, the Company adopted the fair value recognition provisions of SFAS No. 123(R), "Share-Based Payment," using the modified prospective transition method. Under the modified prospective transition method, compensation cost recognized in the year ended December 31, 2006 included: (a) the pro rata compensation cost for all share-based compensation granted prior to, but not yet vested as of December 31, 2005, based on the grant-date fair value estimated in accordance with the original provisions of SFAS No. 123, and (b) the pro rata compensation cost for all share-based payments granted on or subsequent to January 1, 2006, based on the grant-date fair value estimated in accordance with the provisions of SFAS No. 123(R). In accordance with the modified prospective transition method of SFAS No. 123(R), results for prior periods have not been restated, and the impact of adopting SFAS No. 123(R) was not material to the net loss or cash flows. For all grants, the amount of share-based compensation expense recognized has been adjusted for estimated forfeitures of awards for which the requisite service is not expected to be provided. Estimated forfeiture rates are developed based on the Company's analysis of historical forfeiture data. Prior to the adoption of the fair value recognition provisions of SFAS No. 123(R), share-based payment expense was adjusted

3. Summary of Significant Accounting Policies (Continued)

for actual forfeitures as they occurred. The cumulative effect of the change in accounting for forfeitures is immaterial.

The Company accounts for stock-based compensation issued to non-employees in accordance with SFAS No. 123(R) and EITF No. 96-18, "Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with, Selling Goods or Services." The Company records the expense of such services based on the estimated fair value of the equity instrument using the Black-Scholes option pricing model. The value of the equity instrument is charged to earnings over the term of the service agreement.

Net loss per share

Basic net loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding during the period. The Company's potential dilutive shares, which include outstanding common stock options, unvested restricted stock, redeemable convertible preferred stock and warrants, have not been included in the computation of diluted net loss per share for all periods as the result would be antidilutive. Such potentially dilutive shares are excluded when the effect would be to reduce a net loss per share.

Other comprehensive income (loss)

SFAS No. 130, "Reporting Comprehensive Income," establishes standards for reporting and displaying comprehensive income and its components in a full set of general-purpose financial statements. For each of the years ended December 31, 2006, 2007 and 2008, and the period from May 9, 2003 (date of inception) to December 31, 2008, there was no material difference between the net loss and comprehensive loss.

Segment reporting

SFAS No. 131, "Disclosure about Segments of an Enterprise and Related Information," establishes standards for reporting information about operating segments in annual financial statement and in interim financial reports issued to stockholders. Operating segments are defined as components of an enterprise about which separate financial information is available that is evaluated on a regular basis by the chief operating decision-maker, or decision making group, in deciding how to allocate resources to an individual segment and in assessing performance of the segment. The Company believes that it operates in one segment.

Recent accounting pronouncements

In February 2007, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standards No. 159, "The Fair Value Option for Financial Assets and Financial Liabilities—Including an amendment of FASB Statement No. 115" ("SFAS No. 159"). SFAS No. 159 permits an entity to choose to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings. The Company did not elect to re-measure any of its existing financial assets or liabilities under the provisions of SFAS No. 159.

3. Summary of Significant Accounting Policies (Continued)

In June 2007, the Emerging Issues Task Force ("EITF") issued EITF Issue No. 07-03, "Accounting for Nonrefundable Advance Payment for Goods and Services Received for Use in Future Research and Development Activities," ("EITF 07-03"). EITF 07-03 provides guidance on whether nonrefundable advance payments for goods and services that will be used in research and development activities should be expensed when the advance payment is made or when the research and development activity has been performed. EITF 07-03 is effective for fiscal years beginning after December 15, 2007. The adoption of EITF 07-03 did not have a material impact on the Company's financial position, results of operations or cash flows.

In November 2007, the EITF issued EITF Issue 07-01 "Accounting for Collaborative Arrangements" ("EITF No. 07-01"). EITF No. 07-01 requires collaborators to present the results of activities for which they act as the principal on a gross basis and report any payments received from (made to) other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational, and consistently applied accounting policy election. Further, EITF No. 07-01 clarified that the determination of whether transactions within a collaborative arrangement are part of a vendor-customer (or analogous) relationship subject to Issue 01-9, "Accounting for Consideration Given by a Vendor to a Customer". EITF No. 07-01 is effective for fiscal years beginning after December 15, 2008, and interim periods within those years. The Company is currently evaluating the impact, if any, that the adoption of EITF No. 07-01 will have on its financial position, results of operations or cash flows.

In December 2007, the FASB issued SFAS No. 160, "Non-controlling Interests in Consolidated Financial Statements, an Amendment of ARB No. 51". This statement establishes accounting and reporting standards for the non-controlling interest in a subsidiary and for the deconsolidation of a subsidiary. This statement is effective for fiscal years beginning on or after December 15, 2008. Adoption of this statement is not expected to have a material impact on the Company's consolidated financial position, results of operations or cash flows when it becomes effective, but may affect the accounting for non-controlling (or minority) interests from that date forward.

In December 2007, the FASB issues SFAS No. 141(R), "Business Combinations", ("SFAS 141(R)"). This Standard will require an acquiring company to measure all assets acquired and liabilities assumed, including contingent considerations and all contractual contingencies, at fair value as of the acquisition date. In addition, an acquiring company is required to capitalize IPR&D and either amortize it over the life of the product, or write it off if the project is abandoned or impaired. The Standard is effective for transactions occurring on or after January 1, 2009. The Company has not determined the effect that the adoption of SFAS 141(R) will have on its consolidated financial statements, but the effect will generally be limited to future acquisitions in 2009, except for certain tax treatment of previous acquisitions.

Effective January 1, 2008, the Company implemented Statement of Financial Accounting Standards No. 157, "Fair Value Measurement" ("SFAS No. 157") for its financial assets and liabilities that are re-measured and reported at fair value at each reporting period, and non-financial assets and liabilities that are re-measured and reported at fair value at least annually. In accordance with the provisions of FSP No. FAS 157-2, "Effective Date of FASB Statement No. 157", the Company has elected to defer implementation of SFAS No. 157 as it relates to the Company's non-financial assets and non-financial liabilities that are recognized and disclosed at fair value in the financial statements on a nonrecurring basis until January 1, 2009. The Company is currently evaluating the impact, if any, that FSP No.

3. Summary of Significant Accounting Policies (Continued)

FAS 157-2 will have on its non-financial assets and liabilities. The adoption of SFAS No. 157 to the Company's financial assets and liabilities and non-financial assets and liabilities that are re-measured and reported at fair value at least annually did not have an impact on the Company's financial results in any period.

4. Inventory

The components of inventory are as follows (in thousands):

	December 31,	
	2007	2008
Raw materials	$ 799	$1,277
Work in process	813	3,238
Finished goods	—	2,315
Inventory	$1,612	$6,830

The Company periodically reviews its inventories for excess or obsolete inventory and writes-down obsolete or otherwise unmarketable inventory to its estimated net realizable value. If the actual net realizable value is less than that estimated by the Company, or if there are any further determinations that inventory will not be marketable based on estimates of demand, additional inventory write-downs will be required. Based on management's estimates of demand, the Company determined that some of its inventory was in excess of its estimated net realizable value. During the year ended December 31, 2008, the Company recorded a $1.6 million charge to research and development expenses to write-off excess and obsolete inventory.

5. Property and Equipment, net

Property and equipment, net consist of the following (in thousands):

	December 31,	
	2007	2008
Machinery and equipment	$ 4,732	$ 6,646
Leasehold improvements	910	1,937
Software	654	820
Office furniture	243	280
	6,539	9,683
Less accumulated depreciation and amortization	(3,139)	(5,667)
Property and equipment, net	$ 3,400	$ 4,016

Depreciation and amortization charged to the consolidated statements of operations for the years ended December 31, 2006, 2007, 2008 and from May 9, 2003 (date of inception) to December 31, 2008 was $953,000, $1.6 million, $2.5 million and $5.7 million, respectively.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following (in thousands):

	December 31, 2007	December 31, 2008
Professional fees	$ 846	$ 532
Compensation and benefits	513	333
Deferred rent and lease incentives	206	245
Accrued interest	2	166
License fees	65	51
Other	361	325
Accrued expenses and other current liabilities	$1,993	$1,652

7. Commitments and Contingencies

License agreements and patents

In November 2003, the Company entered into a license agreement with California Institute of Technology (the "Caltech License Agreement") that granted the Company a worldwide, exclusive, royalty-bearing license, with the right to grant sublicenses, under specified patents and patent applications, and a worldwide, non-exclusive royalty bearing license, with the right to grant sublicenses, under specified technology outside the scope of the licensed patents. In connection with the Caltech License Agreement, the Company issued 46,514 shares of common stock, and recorded a charge of $20,000. In addition, the Company pays an annual license fee of $10,000 per year. The license fee payments are creditable against royalties based upon sales of products covered by patents licensed under the agreement. Royalties are calculated based on a percentage of defined net sales. The Company is also obligated to pay California Institute of Technology a portion of specified license and sublicense income, proceeds from sales of specified intellectual property and specified service revenue amounts that it receives based on licenses and sublicenses that the Company grants, sales of intellectual property and services that are provided to third parties. The royalty obligation with respect to any licensed product extends until the later of the expiration of the last-to-expire of the licensed patents covering the licensed product and three years after the first commercial sale of the licensed product in any country for non-patented technology covered under the agreement. Through December 31, 2008, no royalty payments have been made. In March 2007, the Company amended the Caltech License Agreement to provide rights under an additional patent application under the terms of the existing license in exchange for a one-time payment of $50,000 to the California Institute of Technology. All amounts paid to date and the value of the common stock issued have been expensed to research and development expense as technological feasibility had not been established and the technology had no alternative future use. The total expense recognized under the Caltech License Agreement for the years ended December 31, 2006, 2007 and 2008, and the period from May 9, 2003 (date of inception) through December 31, 2008 was $10,000, $60,000, $10,000 and $113,000, respectively.

In June 2004, the Company entered into a license agreement with Roche Diagnostics (the "Roche License Agreement") that granted the Company a worldwide, semi-exclusive royalty-bearing license, with the right to grant sublicenses under a patent relating to sequencing methods. In connection with the Roche License Agreement, the Company paid an upfront fee of 175,000 Euros and committed to pay an annual license fee ranging from 10,000 to 40,000 Euros. The Company has an option to convert

7. Commitments and Contingencies (Continued)

the license to non-exclusive beginning in 2008, in which case the annual license fees would be reduced to 10,000 Euros beginning in 2008. The Company has the right to terminate the Roche License Agreement at any time for convenience upon 90 days prior written notice to Roche Diagnostics. Both the Company and Roche Diagnostics have the right to terminate the Roche License Agreement upon breach by the other party, subject to notice and an opportunity to cure. The Roche License Agreement also terminates upon the occurrence of specified bankruptcy events. As part of the Roche License Agreement, the Company agrees to pay royalties based on a percentage of defined net sales. The Company also agrees to pay a portion of specified sublicense income amounts that are received based on sublicenses that the Company grants to third parties. The Company's royalty obligation, if any, extends until the expiration of the last-to-expire of the licensed patents. Through December 31, 2008, no royalty payments have been made. All amounts paid to date have been expensed to research and development expense as technological feasibility had not established and the technology had no alternative future use. The total expense recognized under the Roche License Agreement for the years ended December 31, 2006, 2007 and 2008, and the period from May 9, 2003 (date of inception) through December 31, 2008 was $23,000, $39,000, $62,000 and $367,000, respectively.

In March 2005, the Company entered into a license agreement with Arizona Technology Enterprises (the "AZTE License Agreement") that granted the Company a worldwide, exclusive, irrevocable, royalty-bearing license, with the right to grant sublicenses, under specified patents and patent applications exclusively licensed by AZTE from Arizona State University and the University of Alberta. In connection with the AZTE License Agreement, the Company paid an upfront fee of $350,000, committed to an annual license fee of $50,000, which will increase to $100,000 upon the successful issuance of a U.S. patent, committed to pay a three-year maintenance fee of $50,000, payable in equal annual installments beginning in March 2006, and issued 88,888 shares of restricted common stock, which vest in two equal installments upon the achievement of separate milestones. The Company is obligated to use reasonable commercial efforts to develop, manufacture and commercialize licensed products. In addition, if the Company fails to meet specified development and commercialization deadlines, the AZTE License Agreement converts from exclusive to non-exclusive. The AZTE License Agreement will remain in force until terminated. The Company has the right to terminate the AZTE License agreement at any time for convenience upon 60 days prior written notice to Arizona Technology Enterprises. Both the Company and Arizona Technology Enterprises have the right to terminate the agreement upon breach by the other party, subject to notice and an opportunity to cure. The AZTE License Agreement also terminates upon the occurrence of specified bankruptcy events.

As part of the AZTE License Agreement, the Company agrees to pay royalties based on a percentage of defined net sales. The Company also agrees to pay a portion of specified sublicense income amounts that are received based on sublicenses granted to third parties. The Company's royalty obligation, if any, extends until the expiration of the last-to-expire of the licensed patents. Through December 31, 2008, no royalty payments have been made. All amounts paid to date have been expensed to research and development expense as technological feasibility had not been established and the technology had no alternative future use. In May 2006, in accordance with the license agreement, due to the successful issuance of a U.S. patent, the committed annual license fee increased from $50,000 to $100,000 and 44,444 shares of the restricted common stock vested. The vesting of 44,444 shares of restricted common stock resulted in a charge to research and development expense of $127,000 based on the fair value of the Company's common stock at the time the milestone was achieved. The remaining 44,444 shares of restricted common stock will vest immediately upon the

7. Commitments and Contingencies (Continued)

successful issuance of a second U.S. patent. The total expense recognized under the AZTE License Agreement for the years ended December 31, 2006, 2007 and 2008, and the period from May 9, 2003 (date of inception) through December 31, 2008 was $229,000, $117,000, $103,000 and $849,000, respectively.

In June 2006, the Company entered into an agreement to acquire certain U.S. and foreign patents and patent applications. In connection with the agreement, the Company paid an upfront fee of $350,000, committed to a one-time payment of $250,000 once technological feasibility has been established, and committed to a one-time payment of $400,000 upon the first commercial sale of product. As part of the agreement, the Company agrees to pay royalties based on a percentage of defined net sales. Through December 31, 2008, no royalty payments have been made. All amounts paid to date have been expensed to research and development expense as technological feasibility had not established and the technology had no alternative future use. The total expense recognized under this agreement for the years ended December 31, 2006, 2007 and 2008, and the period from May 9, 2003 (date of inception) through December 31, 2008 was $350,000, $0, $0 and $350,000, respectively.

In April 2007, the Company entered into an agreement with PerkinElmer LAS, Inc. ("PerkinElmer"), in which PerkinElmer granted the Company a worldwide, non-exclusive, non-transferable, non-sublicensable, royalty bearing license under specified patents. The license from PerkinElmer grants the Company rights under certain patents to produce and commercialize certain of the reagents used in some applications on the HeliScope system, which contain chemicals purchased from PerkinElmer. In exchange for rights licensed from PerkinElmer, the Company is obligated to pay PerkinElmer a portion of the Company's net revenue from the sale of reagents that contain chemicals covered by the patents licensed under the PerkinElmer agreement. The Company has the right to terminate the agreement at any time upon 90 days written notice to PerkinElmer. Each party has the right to terminate the agreement upon breach by the other party subject to notice and an opportunity to cure. The agreement also terminates upon the occurrence of specified bankruptcy events. PerkinElmer has the sole right under the agreement to enforce the licensed patents. There has been no expense recorded for this agreement for any period from May 9, 2003 (inception) through December 31, 2008.

Operating leases

In January 2004, the Company entered into a sublease and a direct operating lease for office and laboratory space. The sublease expired on April 30, 2005. The direct lease commenced thereafter from May 1, 2005 and expired on December 31, 2005. As provided in the facility lease, the Company deposited $40,000 for the sublease and $30,000 for the direct lease in escrow for security. At December 31, 2008, the Company has no further obligations under this agreement.

In December 2005, the Company entered into an operating lease for new office and laboratory space. The lease expires in August 2009. In connection with this lease agreement, the Company entered into a letter of credit in the amount of $450,000, naming the Company's landlord as beneficiary. In October 2008, the letter of credit was decreased to $225,000 pursuant to the lease agreement which allows for a fifty percent reduction provided that the Company was not in default and that the lease was in full force and effect. As of December 31, 2008, the Company has classified the $225,000 letter of credit as restricted cash on the consolidated balance sheet. Additionally, in connection with the lease agreement, the Company received lease incentives from the landlord of certain leasehold

7. Commitments and Contingencies (Continued)

improvements. The Company recorded the lease incentives as a liability and is amortizing them over the lease term as a reduction in rent expense. For the years ended December 31, 2007 and 2008, the Company recorded $146,000 and $149,000, respectively, as a reduction in rent expense for this amortization. The Company has recorded a liability for these lease incentives at December 31, 2007 and 2008 of $258,000 and $109,000, respectively, of which $149,000 and $105,000 is recorded in accrued expenses and other current liabilities at December 31, 2007 and 2008, respectively, and $109,000 and $4,000 is recorded in other long-term liabilities at December 31, 2007 and 2008, respectively, on the accompanying consolidated balance sheet.

In February and December 2007 and July 2008, the Company amended its existing operating lease for office and laboratory space to include additional office space in the same building, which will result in additional cash payments of approximately $656,000 and $164,000 for each of the years ending December 31, 2009 and 2010.

Future minimum lease payments under operating leases as of December 31, 2008 are as follows (in thousands):

2009	$1,280
2010	164
Thereafter	—
Total minimum lease payments	$1,444

Total rent expense was $939,000, $1.3 million, $1.9 million and $4.7 million for the years ended December 31, 2006, 2007, and 2008, and the period from May 9, 2003 (date of inception) through December 31, 2008, respectively.

The Company records rent expense on a straight-line basis over the term. Accordingly, the Company has recorded a liability for deferred rent at December 31, 2007 and 2008 of $185,000 and $159,000, respectively, of which $57,000 and $140,000 is recorded in accrued expenses and other current liabilities at December 31, 2007 and 2008, respectively, and $128,000 and $19,000 is recorded in other long-term liabilities at December 31, 2007 and 2008, respectively, on the accompanying consolidated balance sheet.

8. Long-Term Debt

Line of credit facility and security agreement

In June 2006, the Company entered into a line of credit facility and security agreement (the "Credit Facility") with General Electric Capital Corporation ("GE Capital"). The Credit Facility provides that the Company may borrow up to $8.0 million at an interest rate based on the Federal Reserve's 3 year Treasury Constant Maturities Rate. The end of the advance period was December 31, 2007. The proceeds of the Credit Facility may be used for the purchase of equipment, and is collateralized by specific equipment assets. Payments are required to be made on a monthly basis, of which, the first 6 months will be interest-only payments and then 30 months of principal and interest for each advance. The outstanding balance is collateralized by the equipment purchased with the proceeds from each equipment advance. As of December 31, 2007 and 2008, advances on the Credit

8. Long-Term Debt (Continued)

Facility were $2.5 million at a weighted-average interest rate of 10.1%. As of December 31, 2007 and 2008, the outstanding balance on the Credit Facility was $1,787,000 and $799,000, respectively.

Loan and security agreement

In December 2007, the Company entered into a loan and security agreement with two lenders including GE Capital Corporation, which is serving as agent. The loan agreement provided that the Company may borrow up to $20.0 million at an interest rate equal to the sum of (i) the greater of (A) an interest rate based on the Federal Reserve's three year Treasury Constant Maturities Rate and (B) 3.84% plus (ii) 6.11%. The initial term loan was made in December 2007 in an aggregate principal amount equal to $10.0 million.

In June 2008, the Company entered into a second amendment to the loan and security agreement with two lenders including GE Capital Corporation. A subsequent term loan was made upon execution of the amendment in an aggregate principal amount equal to $10.0 million. The loan amendment provided that the interest rate for the subsequent term loan is equal to the sum of (i) the greater of (A) an interest rate based on the Federal Reserve's three year Treasury Constant Maturities Rate and (B) 3.17% plus (ii) 8.33%. The loan agreement, as amended, contained affirmative and negative covenants to which the Company and its subsidiaries must adhere. Pursuant to the amendment, the Company was required to maintain, at all times, unrestricted cash in its bank account equal to at least $10.0 million. The proceeds of the loan agreement were collateralized by essentially all of the Company's assets. Payments are required to be made on a monthly basis. For the initial term loan, interest-only payments were required for the first five months. Thereafter, for the following 31 months, payments of principal and interest will be due. For the subsequent term loan, principal and interest payments are required for the 36 month term of the loan.

In December 2008, the Company entered into an additional amendment to the loan and security agreement with certain lenders including GE Capital Corporation. The amendment amended the prepayment provisions of the loan and security agreement to allow the Company to make a prepayment of $10.0 million (the "Pay Down Amount") without incurring any prepayment penalties. Pursuant to the amendment, the Company made a prepayment, equal to the Pay Down Amount, in December 2008. In connection with such prepayment, and in lieu of the 4% final payment fee with respect to the Pay Down Amount, the amendment provides that the Company will pay a fee equal to 2% of the initial $10.0 million term loan, payable on the earlier of (a) January 31, 2011 and (b) the maturity date for the subsequent term loan.

The amendment further provides that the Company's obligations under the loan agreement, as amended, are no longer secured by a cash amount of $10.0 million. As such, this amount is no longer classified as restricted cash as of December 31, 2008. Such obligations continue to be secured under various collateral documents by interests in substantially all of the Company's personal property, including the pledge of the stock of its wholly-owned subsidiary, and proceeds of any intellectual property, but not by its intellectual property.

As of December 31, 2008, the loan agreement did not require the Company to comply with any financial covenants.

8. Long-Term Debt (Continued)

As of December 31, 2008, advances on the loan agreement, as amended, were $20.0 million at an interest rate of 11.5%. As of December 31, 2007 and 2008, the outstanding balance on the loan agreement was $10.0 million and $7.1 million, respectively.

As of December 31, 2008, loan payable payments are due as follows (in thousands):

2009	$ 4,038
2010	3,152
2011	2,439
Thereafter	—
Total future minimum payments	9,629
Less: amount representing interest	(1,768)
Less: debt discount	(567)
Add: amortization of debt discount	564
Carrying value of debt	7,858
Less: current portion	3,323
Long-term obligations	4,535

Redeemable convertible preferred stock warrant

In connection with the execution of the Credit Facility, the Company issued a warrant to GE Capital to purchase 62,016 shares of Series B redeemable convertible preferred stock. The warrants had an exercise price of $1.29 per share and expired on the earlier of (i) June 2013; or (ii) two years from the effective date of a Qualified IPO, as defined. In the event of a liquidation event, including the completion of an initial public offering, the warrants, if not exercised, will be converted into warrants to purchase common stock. The fair value of the warrants was estimated at $70,000 using the Black-Scholes valuation model with the following assumptions: expected volatility of 74%, risk free interest rate of 5.1%, expected life of seven years and no dividends. Expected volatility was based on the volatility of similar entities in the life sciences industry of comparable size of market capitalization and financial position that completed initial public offerings within the last ten years. The fair value of the warrants was recorded as a liability. Debt issuance costs of $70,000 were amortized to interest expense over the advance period of eighteen months. A total of $25,000 and $45,000 was amortized to interest expense during the years ended December 31, 2006 and 2007, respectively.

In connection with the drawdowns under the Credit Facility in June and November 2006, the Company issued warrants to purchase 19,168 shares of Series B redeemable convertible preferred stock. The warrants had an exercise price of $1.29 per share and expire on the earlier of (i) dates ranging from June 2013 to November 2013; or (ii) two years from the effective date of a Qualified IPO, as defined. In the event of a liquidation event, including the completion of an initial public offering, the warrants, if not exercised, will be converted into warrants to purchase common stock. The fair value of the warrant was estimated at an aggregate of $25,000 using the Black-Scholes valuation model with the following assumptions: expected volatility ranging from 73-74%, risk free interest rate ranging from 4.6%-5.1%, expected life of seven years and no dividends. The fair value of the warrant was recorded as a liability and a debt discount and is being amortized to interest expense using the over the loan term. A total of $4,000 and $8,000 was amortized to interest expense during the years ended December 31, 2006 and 2007, respectively.

8. Long-Term Debt (Continued)

The warrants were classified as liabilities and revalued each reporting period, with the resulting gains and losses recorded in interest expense. The change in carrying value of the warrants resulted in a charge of $109,000 for the year ended December 31, 2006 and a credit of $42,000 for the year ended December 31, 2007. The Company continued to adjust the liability for changes in fair value until the completion of its initial public offering on May 24 2007, at which time all redeemable convertible preferred stock warrants were converted into warrants to purchase common stock and, accordingly, the liability of $162,000 was reclassified to equity. All of the outstanding warrants were exercised in November 2007 resulting in the purchase of 9,350 shares of common stock.

Common stock warrants

In connection with the execution of the June 2008 amendment to the loan and security agreement with two lenders including GE Capital Corporation, the Company issued warrants to the two lenders to purchase an aggregate of 110,000 shares of common stock. The warrants have an exercise price of $4.80 per share and expire in June 2014. The fair value of the warrants was estimated at $337,000 using a Black-Scholes model with the following assumptions: expected volatility of 65.4%, risk free interest rate of 3.4%, expected life of six years and no dividends. Expected volatility was based on the volatility of similar entities in the life sciences industry of comparable size of market capitalization and financial position that completed initial public offerings within the last ten years. The fair value of the warrants was recorded as equity and a debt discount and will be amortized to interest expense over the term of the loan.

9. Redeemable Convertible Preferred Stock

As discussed at Note 2, on May 24, 2007, upon completion of the Company's IPO, 59,189,998 shares of redeemable convertible preferred stock were automatically converted into 13,153,293 shares of common stock.

As of December 31, 2006, the Company had 59,314,030 authorized shares of preferred stock, of which 28,182,246 are designated as Series A redeemable convertible preferred stock and 31,131,784 are designated as Series B redeemable convertible preferred stock. As of December 31, 2007 and 2008, the Company has 5,000,000 authorized and no shares issued or outstanding.

As of December 31, 2006, redeemable convertible preferred stock consists of:

	Number of Shares Authorized	Number of shares issued and outstanding	Carrying value (in thousands)	Liquidation preference per share
Series A	28,182,246	28,182,246	$26,869	$0.9555
Series B	31,131,784	15,503,876	19,892	$ 1.29
	59,314,030	43,686,122	$46,761	

In March 2006, the Company sold 15,503,876 shares of Series B redeemable convertible preferred stock, at a price of $1.29 per share, resulting in net proceeds of approximately $19.9 million, net of $108,000 of issuance costs.

In January 2007, the Company sold an additional 15,503,876 shares of Series B redeemable convertible preferred stock, at a price of $1.29 per share, resulting in proceeds of approximately

9. Redeemable Convertible Preferred Stock (Continued)

$20.0 million. This issuance of Series B redeemable convertible preferred stock contained a beneficial conversion feature as the estimated fair value of the Company's common stock on the date of issuance was in excess of the $1.29 per share conversion price. As the shares of Series B redeemable convertible preferred stock can be immediately converted into shares of common stock at the option of the holder, the beneficial conversion feature of $18.1 million was recorded as an immediate charge to the consolidated statement of operations and a corresponding credit to additional paid-in capital.

As of December 31, 2006, the rights, preferences and privileges of the Company's redeemable convertible preferred stock are listed below.

Conversion

Each share of redeemable convertible preferred stock was convertible, at the option of the holder, into common stock of the Company based on a defined conversion rate, adjustable for certain standard antidilution adjustments. At December 31, 2006, the conversion rate for the Series A and Series B redeemable convertible preferred stock would result in a 4.5 for 1 exchange. Each share of the redeemable convertible preferred stock would automatically convert into common stock at the then appropriate conversion rate upon the closing of an initial public offering of the Company's common stock from which aggregate net proceeds to the Company exceed $50.0 million and the per share offering price was at least $12.8993 for the Series A redeemable convertible preferred stock to automatically convert and at least $17.415 for the Series B redeemable convertible preferred stock to automatically convert. Additionally, at any time, the holders of at least two-thirds of the outstanding shares of redeemable convertible preferred stock could elect to convert all of the shares into common stock.

Dividends

The redeemable convertible preferred stockholders are entitled to receive 8% cumulative dividends. Dividends shall accrue and shall be cumulative, provided, however, that the Company shall be under no obligation to pay such dividends unless so declared by the Board of Directors or upon liquidation. Through May 24, 2007, the date of conversion, the Board of Directors did not declare a payment of dividends.

Voting rights

The redeemable convertible preferred stockholders generally voted together with all other classes and series of stock as a single class on all matters and are entitled to a number of votes equal to the number of shares of common stock into which each share of such preferred stock was convertible. With respect to the number of directors, the holders of the Series A and Series B redeemable convertible preferred stock were entitled to elect five directors of the Company.

Liquidation preferences

In the event of liquidation, dissolution, merger, sale or winding-up of the Company, the holders of the Series A and Series B redeemable convertible preferred stock were entitled to receive, prior to and in preference of the holders of common stock, an amount equal to the greater of (i) $0.9555 and $1.29 per share (subject to certain standard antidilution adjustments), respectively, plus any accrued but

9. Redeemable Convertible Preferred Stock (Continued)

unpaid dividends; or (ii) such amount per share that would have been payable had each such share been converted to common stock.

If upon any such liquidation, dissolution, merger, sale or winding-up of the Company the remaining assets of the Company available for distribution to its stockholders should be insufficient to pay the holders of shares of preferred stock the full amount to which they were entitled, the assets of the Company should be distributed ratably amongst the holders of Series A and Series B redeemable convertible preferred stock.

After the payment of all preferential amounts required to be paid to the holders of Series A and Series B redeemable convertible preferred stock upon the liquidation, dissolution, merger, sale or winding-up of the Company, the holders of Series A and Series B redeemable convertible preferred stock would have no further participation in the distribution of assets of the Company and would have no further rights of conversion to common stock. All remaining net assets of the Company available for distribution would be distributed ratably among the holders of common stock.

The Series A and Series B redeemable convertible preferred stock were not subject to mandatory redemption; however, there were circumstances outside the control of the Company that could have resulted in the holders of the Series A or Series B redeemable convertible preferred stock being redeemed upon certain deemed liquidation events in limited circumstances. Accordingly, the Series A and Series B preferred stock had been classified as redeemable convertible preferred stock. The Series A and Series B redeemable convertible preferred stock was not being accreted and the dividends were not being accrued because the conditions to cause these deemed liquidation events were not considered to be probable.

10. Common Stock

In December 2008, the Company entered into a securities purchase agreement ("Offering") with certain investors pursuant to which it sold a total of 42,753,869 units (the "Units"), each Unit consisting of (i) one share of common stock (collectively, the "Shares") and (ii) one warrant (collectively, the "Warrants") to purchase 0.6 shares of common stock at an exercise price of $0.45 per share, for a purchase price of $0.435 per unit (representing the closing bid price plus an additional amount for the warrants) (the "Offering"). The closing of the transaction occurred on December 23, 2008. In connection with the Offering, the Company raised approximately $18.6 million in gross proceeds. After paying $813,000 in placement agent fees and offering expenses, the net proceeds were $17.8 million.

In connection with the Offering, the Company issued warrants to purchase an aggregate of 25,652,333 shares of common stock which are exercisable immediately. The warrants have an exercise price of $0.45 per share and have a five year term. The relative fair value of the warrants was estimated at $4,449,397 using a Black-Scholes model with the following assumptions: expected volatility of 66.15%, risk free interest rate of 1.53%, expected life of five years and no dividends. Expected volatility was based on the volatility of similar entities in the life sciences industry of comparable size of market capitalization and financial position that completed initial public offerings within the last ten years. The relative fair value of the warrants was recorded in the equity section of the balance sheet.

In connection with the Offering, the Company entered into a registration rights agreement (the "Registration Rights Agreement") with each of the investors. The Registration Rights Agreement

10. Common Stock (Continued)

provides that the Company file a "resale" registration statement (the "Registration Statement") covering all of the Shares and the shares issuable upon exercise of the Warrants (the "Warrant Shares"), up to the maximum number of shares able to be registered pursuant to applicable Securities and Exchange Commission ("SEC") regulations, within 30 days of the closing of the Offering. The Company filed the Registration Statement with the SEC on January 22, 2009 (File No. 333-156885), which was amended on February 13, 2009. Under the terms of the Registration Rights Agreement, the Company is obligated to maintain the effectiveness of the "resale" registration statement until all securities therein are sold or are otherwise can be sold pursuant to Rule 144, without any restrictions. A cash penalty at the rate of 2% per month will be triggered for any filing or effectiveness failures or if, at any time after six months following the closing of the Offering, the Company ceases to be current in periodic reports with the SEC. The aggregate penalty accrued with respect to each investor may not exceed 12% of the original purchase price paid by that investor.

In December 2006, the FASB issued FASB Staff Position No. EITF 00-19-2, "Accounting for Registration Payment Arrangements," ("EITF 00-19-2"), which addresses an issuer's accounting for registration payment arrangements. EITF 00-19-2 specifies that the contingent obligation to make future payments or otherwise transfer consideration under a registration payment arrangement, whether issued as a separate agreement or included as a provision of a financial instrument or other agreement, should be separately recognized and measured in accordance with FASB Statement No. 5, "Accounting for Contingencies." EITF 00-19-2 further clarifies that a financial instrument subject to a registration payment arrangement should be accounted for in accordance with US GAAP without regard to the contingent obligation to transfer consideration pursuant to the registration payment arrangement. The Company applied the recognition and measurement provisions of EITF 00-19-2 to the registration rights associated with the Registration Rights Agreement. As result, the Company believes that the contingent obligation to make future payments is not probable under EITF 00-19-2 and as such has recorded no liability associated with these registration rights.

As of December 31, 2007 and 2008, the Company had 120,000,000 shares of common stock authorized. As of December 31, 2007 and 2008, the Company had 20,983,638 and 63,808,282 shares issued and outstanding, respectively. As of December 31, 2008, the Company had reserved 25,762,333 shares of common stock for issuance to common stockholders upon exercise of common stock warrants. As of December 31, 2007 and 2008, the Company has reserved 2,194,663 and 2,679,614 shares of common stock, respectively, for future issuance upon exercise of common stock options.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are not entitled to receive dividends unless declared by the Company's Board of Directors.

11. Income Taxes

There is no provision for income taxes because the Company has incurred operating losses since inception. The reported amount of income tax expense for the years differs from the amount that would result from applying domestic federal statutory tax rates to pretax losses primarily because of the changes in the valuation allowance. Significant components of the Company's deferred tax assets at December 31, 2007 and 2008 are as follows (in thousands):

	December 31,	
	2007	2008
Deferred tax assets:		
Net operating loss carryforwards	$ 24,204	$ 39,764
Research and development credit carryforwards	3,430	4,323
Depreciation and amortization	4,336	4,374
Allowances and reserves	328	1,859
	32,298	50,320
Less: Valuation allowance	(32,298)	(50,320)
Net deferred tax assets	$ —	$ —

As of December 31, 2008, the Company has federal and state net operating losses ("NOL") of approximately $97.3 million and $98.0 million, respectively, as well as federal and state research and development credits of approximately $2.9 million and $2.2 million, respectively, which may be available to reduce future taxable income and taxes. Federal NOLs and research and development credits each begin to expire in 2024. State NOLs and research and development credits begin to expire in 2009 and 2019, respectively. As required by SFAS No. 109 "Accounting for Income Taxes," the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are comprised principally of NOLs. Management has determined that is it more likely than not that the Company will not recognize the benefits of the federal and state deferred tax assets and, as a result, a valuation allowance of $32.3 million and $50.3 million has been established at December 31, 2007 and 2008, respectively.

A reconciliation of income tax expense (benefit) at the statutory federal income tax rate and income taxes as reflected in the financial statements is as follows:

	Year ended December 31,		
	2006	2007	2008
Federal income tax at statutory rate	34.0%	34.0%	34.0%
State income tax, net of federal tax benefit	6.0%	6.2%	5.9%
Research and development credits	4.4%	4.4%	1.8%
Other	(1.5)%	(2.1)%	(2.1)%
Increase in valuation allowance	(42.9)%	(42.5)%	(39.6)%
Effective tax rate	0.0%	0.0%	0.0%

On January 1, 2007, the Company adopted the provisions of FIN No. 48. The Company has no amounts recorded for any unrecognized tax benefits as of January 1, 2007, December 31, 2007 or December 31, 2008. In addition, the Company did not record any amount for the implementation of

11. Income Taxes (Continued)

FIN 48. The Company's policy is to record estimated interest and penalties related to the underpayment of income taxes as a component of its income tax provision. As of January 1, 2007, December 31, 2007, and December 31, 2008, the Company had no accrued interest or tax penalties recorded. Each of the Company's income tax return reporting periods since May 9, 2003 (date of inception) are open to income tax audit examination by the federal and state tax authorities.

Utilization of NOL and research and development credit carryforwards may be subject to a substantial annual limitation due to ownership changes that have occurred previously or that could occur in the future provided by Section 382 of the Internal Revenue Code of 1986, as well as similar state provisions. These ownership changes may limit the amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period. Since the Company's formation, the Company has raised capital through the issuance of common stock and preferred stock, which, combined with the purchasing shareholders' subsequent disposition of those shares, may have resulted in a change of control, as defined by Section 382, or could result in a change of control in the future upon subsequent disposition. The Company has not currently completed a study to assess whether a change of control has occurred or whether there have been multiple changes of control since the Company's formation due to the significant complexity and cost associated with such study and that there could be additional changes in control in the future. If we have experienced a change of control at any time since the Company's formation, utilization of NOL or research and development credit carryforwards would be subject to an annual limitation under Section 382. Any limitation may result in expiration of a portion of the NOL or research and development credit carryforwards before utilization. Further, until a study is completed and any limitation known, no amounts are being presented as an uncertain tax position under FIN No. 48.

12. Stock-Based Compensation

In 2003, the Company's Board of Directors adopted the 2003 Stock Option and Incentive Plan (the "2003 Stock Plan"). The 2003 Stock Plan provides for the granting of incentive and non-qualified stock options, restricted stock and other equity awards to employees, officers, directors, consultants and advisors of the Company. Provisions such as vesting, repurchase and exercise conditions and limitations are determined by the Board of Directors on the grant date. The Company's 2007 Stock Option and Incentive Plan ("2007 Stock Plan") was adopted by the Company's Board of Directors in April 2007 and approved by the Company's stockholders in May 2007. The 2007 Stock Plan permits the Company to make grants of incentive stock options, non-qualified stock options, stock appreciation rights, deferred stock awards, restricted stock awards, unrestricted stock awards and dividend equivalent rights. The 2007 Stock Plan provides that the number of shares reserved and available for issuance under the plan will be automatically increased each January 1, beginning in 2008, by 4.5% of the outstanding number of shares of common stock on the immediately preceding December 31 or such lower number of shares of common stock as determined by the Board of Directors. This number is subject to adjustment in the event of a stock split, stock dividend or other change in the Company's capitalization. Generally, shares that are forfeited or canceled from awards under the 2007 Option Plan also will be available for future awards. In addition, available shares under the Company's 2003 Stock Plan, including as a result of the forfeiture, expiration, cancellation, termination or net issuances of awards,

12. Stock-Based Compensation (Continued)

are automatically made available for issuance under the 2007 Option Plan. The maximum number of shares of common stock that may be issued pursuant to the 2007 Stock Plan as of December 31, 2008 is 2,384,529. As of December 31, 2008, 1,022,169 shares of common stock are available for issuance under the 2007 Stock Plan.

Effective January 1, 2006, the Company adopted the fair value recognition provisions of SFAS No. 123(R), "Share-Based Payment," using the modified prospective transition method. Under the modified prospective transition method, compensation cost recognized in the year ended December 31, 2006 included: (a) the pro rata compensation cost for all share-based compensation granted prior to, but not yet vested as of December 31, 2005, based on the grant-date fair value estimated in accordance with the original provisions of SFAS No. 123, and (b) the pro rata compensation cost for all share-based payments granted on or subsequent to January 1, 2006, based on the grant-date fair value estimated in accordance with the provisions of SFAS No. 123(R).

The Company accounts for stock-based compensation issued to non-employees in accordance with SFAS No. 123(R) and EITF No. 96-18, "Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with, Selling Goods or Services." The Company records the expense of such services based on the estimated fair value of the equity instrument using the Black-Scholes option pricing model. The value of the equity instrument is charged to earnings over the term of the service agreement.

Stock options

During the years ended December 31, 2006, 2007, 2008 and the period from May 9, 2003 (date of inception) to December 31, 2008, the Company granted 581,755, 1,572,749, 1,163,091 and 3,476,264 stock options, respectively to certain employees and directors. The vesting of these awards is time-based and the restrictions typically lapse 25% after one year and monthly thereafter for the next 36 months.

During the years ended December 31, 2006, 2007, 2008 and the period from May 9, 2003 (date of inception) to December 31, 2008, the Company granted 6,666, 13,332, 0 and 97,530 stock options, respectively to certain nonemployees in exchange for certain consulting services. Vesting on these awards is time-based and the vesting periods range from immediate vesting on grant date to a four-year period. The Company recorded a stock-based compensation charge on these awards following the guidance of EITF No. 96-18, and the accelerated vesting method as described in FIN No. 28, "Accounting for Stock Appreciation Rights and Other Variable Stock Option or Award Plans—an Interpretation of APB Opinion No. 15 and 25."

The exercise price of each stock option shall be specified by the Board of Directors at the time of grant. The vesting period for each stock option is specified by the Board of Directors at the time of grant and is generally over a four-year period. The stock options expire ten years after the grant date.

The fair value of each stock option grant was estimated on the date of grant using the Black-Scholes option-pricing model. The expected life assumption is based on the expected life assumptions of similar entities. Expected volatility is based on volatility of similar entities in the life sciences industry of comparable size of market capitalization and financial position that have completed initial public offerings within the last ten years. The risk-free interest rate is the yield currently available on U.S. Treasury zero-coupon issues with a remaining term approximating the expected term used as the input to the Black-Scholes model. SFAS No. 123(R) requires forfeitures to be estimated at the time of

12. Stock-Based Compensation (Continued)

grant and revised, if necessary, in subsequent periods as options vest, if actual forfeitures differ from those estimates. During the years ended December 31, 2007 and 2008, because substantially all of the Company's stock option grants vest monthly, stock-based employee compensation expense includes the actual impact of forfeitures. The relevant data used to determine the value of the stock option grants is as follows:

	December 31,		
	2006	2007	2008
Weighted average risk-free interest rate	4.8%	4.5%	2.7%
Expected life in years	7.0	6.2	6.0
Expected volatility	75.7%	72.1%	65.6%
Expected dividends	0.0%	0.0%	0.0%

A summary of stock option activity for the year ended December 31, 2008 is as follows:

	Number of Shares	Weighted average exercise price	Weighted average remaining contractual term (in years)	Aggregate intrinsic value as of December 31, 2008 (in thousands)
Balance at December 31, 2007	2,194,663	$7.86		
Granted	1,163,091	$5.85		
Exercised	(22,850)	$0.51		
Forfeited	(587,259)	$8.12		
Expired	(68,031)	$9.10		
Balance at December 31, 2008	2,679,614	$6.97	8.5	$—
Exercisable at December 31, 2008	1,117,019	$6.22	7.7	$—
Vested and unvested expected to vest at December 31, 2008	2,456,749	$6.97	8.5	$—

In March 2007, the Company modified 578,554 unvested stock options granted during the year ended December 31, 2006, which had an exercise price of $0.59 per share, to an exercise price of $1.80 per share with respect to 493,888 stock options granted through October 31, 2006, and to an exercise price of $8.87 per share with respect to 84,666 stock options granted in November and December 2006. This transaction was accounted for as a modification in accordance with SFAS No. 123(R) and did not have a material impact on the Company's financial position, statement of operations or cash flows.

From May 9, 2003 (date of inception) through December 31, 2008, there were 3,573,794 stock options granted, of which 105,119 were exercised, 687,814 were forfeited, and 101,246 had expired through December 31, 2008. The weighted average exercise prices of stock option grants, exercises, forfeitures, and expirations from May 9, 2003 (date of inception) through December 31, 2008 was $7.02 per share, $0.49 per share, $7.80 per share and $9.70 per share, respectively.

The aggregate intrinsic value is calculated based on the positive difference between the fair value of the Company's common stock on December 31, 2008 of $0.39 per share and the exercise price of the underlying options. Because the fair value of the Company's common stock on December 31, 2008 is lower than the exercise price of the underlying options, there is no aggregate intrinsic value.

12. Stock-Based Compensation (Continued)

The weighted-average grant-date fair value of grants of stock options was $3.06 per share, $10.57 per share, and $3.60 for the years ended December 31, 2006, 2007 and 2008, respectively.

The total intrinsic value of stock options exercised was $285,000, $83,000, and $283,000 for the years ended December 31, 2006, 2007 and 2008, respectively.

The following table summarizes information about stock options outstanding at December 31, 2008:

Options outstanding			Options exercisable		
Range of exercise prices	Number of stock options	Weighted average remaining life (years)	Number of stock options	Weighted average exercise price	Weighted average remaining life (years)
$ 0.45–$ 0.98	106,199	6.5	86,207	$ 0.45	6.1
$ 1.80–$ 4.93	1,101,401	8.6	442,006	$ 1.80	7.2
$ 5.93–$ 7.85	235,406	9.2	44,444	$ 7.85	8.6
$ 8.20–$10.85	573,098	8.6	225,689	$ 9.52	8.6
$11.07–$12.36	663,510	8.4	318,673	$11.34	8.2
	2,679,614	8.5	1,117,019	$ 6.22	7.7

Restricted stock

During the years ended December 31, 2006, 2007 and 2008, and the period from May 9, 2003 (date of inception) to December 31, 2008, the Company granted 394,444, 56,757, 190,000 and 1,296,755 shares of restricted stock, respectively to certain employees. The vesting of these awards is time-based. For restricted stock granted prior to December 31, 2007, the restrictions typically lapse 25% after one year and quarterly thereafter for the next 3 years. For restricted stock granted during 2008, the vesting periods range from quarterly vesting over six fiscal quarters to a two-year vesting period, with 50% vesting on each anniversary of the grant date.

During the years ended December 31, 2006, 2007 and 2008, and the period from May 9, 2003 (date of inception) to December 31, 2008, the Company granted 1,111, 2,222, 0 and 635,013 shares of restricted stock, respectively to certain nonemployees in exchange for certain consulting services. Vesting on these awards is time-based and the vesting periods range from immediate vesting on grant date to a four-year period. The Company recorded a stock-based compensation charge on these awards following the guidance of EITF No. 96-18, and the accelerated vesting method as described in FIN 28, "Accounting for Stock Appreciation Rights and Other Variable Stock Option or Award Plans—an Interpretation of APB Opinion No. 15 and 25."

For employee and nonemployee restricted stock awards granted before January 1, 2007, the employee or nonemployee paid the Company cash in an amount up to the fair market value of the award. If the employee ceases employment with the Company, or if the nonemployee terminates the service arrangement, the employee or nonemployee is automatically entitled to be refunded the cash paid for any unvested awards. At the time the cash is received, the Company records the cash as subscription payable in the consolidated balance sheet, and the amount is reclassified to additional paid-in capital over the vesting period. At December 31, 2007 and 2008, the Company had $127,000 and $37,000, respectively, recorded as subscription payable, of which $52,000 and $25,000 was recorded

12. Stock-Based Compensation (Continued)

to accrued expenses and other current liabilities at December 31, 2007 and 2008, respectively, and $75,000 and $12,000 was recorded to other long-term liabilities at December 31, 2007 and 2008, respectively.

A summary of restricted stock activity during the year ended December 31, 2008 is as follows:

	Number of shares	Weighted average grant date fair value	Weighted average remaining contractual term (in years)	Aggregate intrinsic value as of December 31, 2008 (in thousands)
Balance of unvested restricted stock at December 31, 2007	277,593	$6.56		
Granted	190,000	$4.84		
Vested	(100,360)	$6.04		
Forfeited	(138,533)	$6.59		
Balance of unvested restricted stock at December 31, 2008	228,700	$5.51	1.6	$—

From May 9, 2003 (date of inception) through December 31, 2008, there were 1,931,768 shares of restricted stock granted, at a weighted average grant date fair value of $1.94, of which 1,464,536 were fully vested at December 31, 2008, with a weighted average grant date fair value of $0.98.

The aggregate intrinsic value is calculated based on the positive difference between the fair value of the Company's common stock on December 31, 2008 of $0.39 per share and the estimated fair value of the Company's common stock at the date of grant. Because the fair value of the Company's common stock on December 31, 2008 is lower than the fair value of the Company's common stock at the date of grant, there is no aggregate intrinsic value.

The total intrinsic value of restricted stock vested was $1.4 million, $1.7 million and $0 for the years ended December 31, 2006. 2007 and 2008, respectively.

In March 2005, in connection with the AZTE License Agreement, the Company issued 88,888 shares of restricted common stock, which vest in two equal installments upon the achievement of separate milestones. In May 2006, due to the successful issuance of a U.S. patent, 44,444 shares of the restricted common stock vested. The vesting of 44,444 shares of restricted common stock resulted in a charge to research and development expense of $127,000 based on the fair value of the Company's common stock at the time the milestone was achieved. The remaining 44,444 shares of restricted common stock will vest immediately upon the successful issuance of a second U.S. patent. The 44,444 unvested shares are not included in the summary of restricted stock activity.

In July 2006, the Company sold 44,444 shares of fully vested common stock to an executive for cash at a price of $0.59 per share. The fair value of the Company's common stock at the time of grant was $5.58 per share, resulting in an intrinsic value of $4.99 per share. During the year ended December 31, 2006, the Company recorded a charge to selling, general and administrative expenses of $221,000 relating to the grant of these shares of common stock.

The Company recorded stock-based compensation expense to the extent that the fair value of the Company's common stock at the date of the grant exceeded the exercise price of the equity awards.

12. Stock-Based Compensation (Continued)

The Company recognized stock-based compensation expense on all employee and nonemployee awards as follows (in thousands):

	Year Ended December 31,			Period from May 9, 2003 (date of inception) through December 31, 2008
	2006	2007	2008	
Selling, general and administrative	$1,180	$2,372	$3,217	$6,971
Research and development	99	1,024	1,321	2,458
Total	$1,279	$3,396	$4,538	$9,429

Total unrecognized stock-based compensation expense for all stock-based awards was approximately $8.0 million at December 31, 2008, of which $3.4 million will be recognized in 2009, $2.8 million in 2010, $1.5 million in 2011 and $277,000 thereafter. This results in these amounts being recognized over a weighted-average period of 1.3 years.

13. Net Loss per Share

Basic net loss per share is computed by dividing net loss by the weighted average number of common shares outstanding for the period. The Company's potential dilutive shares, which include outstanding common stock options, unvested restricted stock, redeemable convertible preferred stock and warrants have not been included in the computation of diluted net loss per share for all periods as the result would be antidilutive. Such potentially dilutive shares are excluded when the effect would be to reduce net loss per share. Because the Company reported a net loss for the years ended December 31, 2006, 2007 and 2008, all potential common shares have been excluded from the computation of the dilutive net loss per share for all periods presented because the effect would have been antidilutive. Such potential common shares consist of the following:

	December 31,		
	2006	2007	2008
Stock options	711,775	2,194,663	2,679,614
Unvested restricted stock	591,480	322,037	273,144
Warrants	18,040	—	25,762,333
Redeemable convertible preferred stock	9,707,997	—	—
	11,029,292	2,516,700	28,715,091

14. Related Party Transactions

In June 2003, the Company entered into two agreements with a founder of the Company: 1) a services agreement providing for the rendering of certain administrative, management and development services and 2) a license agreement allowing for the use of a portion of leased premises. Under these agreements, the Company paid this founder $30,000 during the year ended December 31, 2004. The license agreement was terminated in February 2004.

In September 2003, the Company entered into a consulting arrangement with a board member and scientific founder of the Company. Under this agreement, the Company paid this board member and scientific founder $120,000 and $120,000 for the years ended December 31, 2004 and 2005, respectively. At December 31, 2005, this arrangement was discontinued and the board member and scientific founder resigned from the Board of Directors.

In September 2006, the Company loaned $28,000 to an officer, of which $4,000 was outstanding at December 31, 2006 and was recorded as a subscription receivable in the stockholders' equity (deficit) section of the consolidated balance sheet. The $4,000 was repaid to the Company in January 2007.

15. 401(k) Plan

The Company has a 401(k) income deferral plan (the "Plan") for employees. According to the terms of the Plan, the Company may make discretionary matching contributions to the Plan. The Company made no discretionary contributions during the years ended December 31, 2006, 2007 and 2008.

16. Unaudited Quarterly Results

The Company's unaudited quarterly results are summarized below (in thousands, except share and per share data):

	Three Months Ended							
	March 31, 2007	June 30, 2007	September 30, 2007	December 31, 2007	March 31, 2008	June 30, 2008	September 30, 2008	December 31, 2008
Grant revenue	$ 92	$ 143	$ 230	$ 117	$ 113	$ 251	$ 202	$ 206
Product revenue	—	—	—	—	—	—	—	36
Total revenue	92	143	230	117	113	251	202	242
Costs and expenses								
Cost of product revenue	—	—	—	—	—	—	—	10
Research and development	5,385	5,298	7,242	6,833	5,705	7,083	5,644	6,183
General and administrative	3,251	3,310	3,615	4,136	6,184	4,830	5,403	3,722
Total costs and expenses	8,636	8,608	10,857	10,969	11,889	11,913	11,047	9,915
Operating loss	(8,544)	(8,465)	(10,627)	(10,852)	(11,776)	(11,662)	(10,845)	(9,673)
Interest income	267	427	736	530	338	145	124	63
Interest expense	(73)	(34)	(73)	(97)	(360)	(370)	(734)	(901)
Net loss	(8,350)	(8,072)	(9,964)	(10,419)	(11,798)	(11,887)	(11,455)	(10,511)
Beneficial conversion feature related to Series B redeemable convertible preferred stock	(18,140)	—	—	—	—	—	—	—
Net loss attributable to common stockholders	$ (26,490)	$ (8,072)	$ (9,964)	$ (10,419)	$ (11,798)	$ (11,887)	$ (11,455)	$ (10,511)
Net loss attributable to common stockholders per share—basic and diluted	$ (17.90)	$ (0.87)	$ (0.48)	$ (0.50)	$ (0.57)	$ (0.57)	$ (0.55)	$ (0.42)
Weighted average number of common shares used in computation—basic and diluted	1,480,130	9,294,298	20,573,636	20,639,115	20,688,578	20,726,679	20,741,822	24,914,939

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer (PEO) and principal financial officer (PFO), has evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")), as of December 31, 2008. In designing and evaluating our disclosure controls and procedures, we and our management recognize that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and our management necessarily was required to apply its judgment in evaluating and implementing possible controls and procedures. Based on that evaluation, our PEO and PFO have concluded that our disclosure controls and procedures were effective at the reasonable level of assurance.

Management's Report on Internal Control over Financial Reporting.

The Company's management is responsible for establishing and maintaining adequate internal control over financial reporting for the Company as defined in Rule 13a-15(f) under the Securities Exchange Act of 1934. The Company's management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2008. In making this assessment, the Company's management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") in *Internal Control—Integrated Framework*. Based on this assessment, the Company's management concluded that, as of December 31, 2008, the Company's internal control over financial reporting is effective based on those criteria.

This annual report does not include an attestation report of the Company's registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by the Company's registered public accounting firm pursuant to temporary rules of the Securities and Exchange Commission that permit the Company to provide only management's report in this annual report.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the fiscal quarter ended December 31, 2008 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item concerning our directors and executive officers is incorporated by reference herein from the information to be contained in our definitive proxy statement (the "2009 Definitive Proxy Statement") for the 2009 annual meeting of stockholders to be filed with the Securities and Exchange Commission within 120 days after the year ended December 31, 2008.

The information required by this item concerning compliance with Section 16(a) of the Exchange Act is incorporated herein by reference from the information contained in our 2009 Definitive Proxy Statement.

Code of Ethics

Certain documents relating to our corporate governance, including our Code of Business Conduct and Ethics, which is applicable to our directors, officers and employees, and the charters of the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee of our Board of Directors, are available on our website at *http://www.helicosbio.com.* We intend to disclose substantive amendments to or waivers (including implicit waivers) of any provision of the Code of Business Conduct and Ethics that apply to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, by posting such information on our website available at *http://www.helicosbio.com.*

ITEM 11. EXECUTIVE COMPENSATION

The information required by Item 11 of Form 10-K is incorporated herein by reference from the information contained in our 2009 Definitive Proxy Statement.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by Item 12 of Form 10-K is incorporated herein by reference from the information contained in our 2009 Definitive Proxy Statement.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE

The information required by Item 13 of Form 10-K is incorporated herein by reference from the information contained in our 2009 Definitive Proxy Statement.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by Item 14 of Form 10-K is incorporated herein by reference from the information contained in our 2009 Definitive Proxy Statement.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this Form 10-K:

(1) *Consolidated Financial Statements:*

(2) *Financial Statement Schedules*: These Schedules have been omitted because they are not required or because the required information is given in the consolidated financial statements or notes thereto.

(3) *Exhibits:*

INDEX TO EXHIBITS

Exhibit Number	Description of Document
3.1	Form of Fourth Amended and Restated Certificate of Incorporation of the Registrant (Incorporated by reference herein to Exhibit 3.3 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007)
3.2	Amended and Restated By-laws of the Registrant (Incorporated by reference herein to Exhibit 3.2 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007)
4.1	Specimen Stock Certificate (Incorporated by reference herein to Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007)
4.2+	Form of Warrant between the Registrant and the Lenders (Incorporated by reference herein to Exhibit 10.2 to the Company's Form 8-K, filed with the Securities and Exchange Commission on June 30, 2008).
4.3	Form of Warrant (Incorporated by reference herein to Exhibit 4.1 to the Company's Current Report on Form 8-K, filed with the Securities and Exchange Commission on December 22, 2008).
10.1	Master Loan Agreement by and between the Registrant and General Electric Capital Corporation, dated June 9, 2006 (Incorporated by reference herein to Exhibit 10.3 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).

Exhibit Number	Description of Document
10.2	Lease Agreement by and between the Registrant and Lincoln Property Company, dated December 30, 2005 (Incorporated by reference herein to Exhibit 10.4 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.3	Lease Agreement by and between the Registrant and Cummings Properties, LLC, dated February 1, 2006 (Incorporated by reference herein to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.4	2003 Stock Option and Incentive Plan and forms of agreements thereunder (Incorporated by reference herein to Exhibit 10.6 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.5†	License Agreement between the Registrant and California Institute of Technology, dated November 30, 2003 (Incorporated by reference herein to Exhibit 10.7 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.6	License Agreement between the Registrant, Roche Diagnostics GMBH and Roche Diagnostics Corporation, dated June 7, 2004 (Incorporated by reference herein to Exhibit 10.8 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.7†	License Agreement between the Registrant and Arizona Technology Enterprises, dated March 16, 2005 (Incorporated by reference herein to Exhibit 10.9 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.8	Form of Indemnification Agreement (Incorporated by reference herein to Exhibit 10.10 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.9	Amended and Restated Investor Rights Agreement by and among the Registrant and the Investors named therein, dated as of March 1, 2006 (Incorporated by reference herein to Exhibit 10.11 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.10†	Amendment to License Agreement Having an Effective Date of March 7, 2007 between California Institute of Technology and the Registrant (Incorporated by reference herein to Exhibit 10.12 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.11+	Employee Offer Letter, dated as of October 15, 2003, by and between Stanley N. Lapidus and the Registrant (Incorporated by reference herein to Exhibit 10.13 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.12+*	Amended and Restated Management Incentive Bonus Plan of the Registrant as of December 11, 2008.
10.13†	License and Supply Agreement, having an effective date of April 23, 2007 between PerkinElmer LAS, Inc. and the Registrant (Incorporated by reference herein to Exhibit 10.15 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).

Exhibit Number	Description of Document
10.14	Amendment to the Amended and Restated Investor Rights Agreement dated as of May 7, 2007 (Incorporated by reference herein to Exhibit 10.16 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.15+	Change in Control Agreement, dated as of May 2, 2007, by and between Stanley N. Lapidus and the Registrant (Incorporated by reference herein to Exhibit 10.17 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.16+	Change in Control Agreement, dated as of May 7, 2007, by and between Stephen J. Lombardi and the Registrant (Incorporated by reference herein to Exhibit 10.18 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.17+	Non-Employee Director Compensation Policy (Incorporated by reference herein to Exhibit 10.20 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.18+	2007 Stock Option and Incentive Plan and forms of agreement thereunder, as amended (Incorporated by reference herein to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on August 14, 2008).
10.19+	Change in Control Agreement between the Company and J. William Efcavitch, dated August 8, 2007 (Incorporated by reference herein to Exhibit 10.1 to the Company's Current Report on Form 8-K, filed with the Securities and Exchange Commission on August 10, 2007).
10.20†	Loan and Security Agreement by and between the Registrant and General Electric Capital Corporation, dated December 31, 2007 (Incorporated by reference herein to Exhibit 10.23 to the Company's Annual Report on Form 10-K, filed with the Securities and Exchange Commission on March 17, 2008).
10.21+	Offer Letter between the Registrant and Stephen P. Hall dated April 25, 2008 (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on May 1, 2008).
10.22+	Change in Control Agreement between the Registrant and Stephen P. Hall dated April 25, 2008 (Incorporated by reference herein to Exhibit 10.2 to the Company's Form 8-K, filed with the Securities and Exchange Commission on May 1, 2008).
10.23+	Second Amendment to Loan and Security Agreement by and between the Registrant, the Lenders and General Electric Capital Corporation, dated June 27, 2008 (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on June 30, 2008).
10.24+	Offer Letter between the Registrant and Stephen J. Lombardi, dated August 19, 2008 (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on August 20, 2008).
10.25+	Amended and Restated Change in Control Agreement between the Registrant and Stephen J. Lombardi, dated August 19, 2008 (Incorporated by reference herein to Exhibit 10.2 to the Company's Form 8-K, filed with the Securities and Exchange Commission on August 20, 2008).

Exhibit Number	Description of Document
10.26+	Severance and Consulting Services Agreement, by and between the Registrant and Stanley N. Lapidus, dated as of September 12, 2008 (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on September 12, 2008).
10.27+	Consultant Agreement between the Registrant and Stanley N. Lapidus, dated as of December 5, 2008 (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on December 8, 2008).
10.28+	Corporate Officer Severance Plan (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on December 17, 2008).
10.29+	Securities Purchase Agreement between the Registrant and each of the Purchasers identified therein, dated December 19, 2008 (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on December 22, 2008).
10.30+	Registration Rights Agreement between the Registrant and each of the Purchasers identified therein, dated December 19, 2008 (Incorporated by reference herein to Exhibit 10.2 to the Company's Form 8-K, filed with the Securities and Exchange Commission on December 22, 2008).
10.31+	Third Amendment to the Loan and Security Agreement among the Registrant, the Lenders and General Electric Capital Corporation, dated as of December 29, 2008 (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on December 30, 2008).
10.32+	Change in Control Agreement by and between the Registrant and Ronald A. Lowy, dated as of January 28, 2009 (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on January 30, 2009).
21.1	Subsidiary of the Registrant (Incorporated by reference to Exhibit 21.1 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
23.1*	Consent of PricewaterhouseCoopers LLP, an independent registered public accounting firm.
31.1*	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certifications pursuant to 18 U.S.C. Section 1350.

* Filed herewith

† Confidential treatment has been requested for certain provisions of this Exhibit pursuant to Rule 406 promulgated under the Securities Act.

\+ Indicates a management contract or any compensatory plan, contract or arrangement.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Dated: March 30, 2009

/s/ RONALD A. LOWY

Ronald A. Lowy
Chief Executive Officer
(Principal Executive Officer)

Dated: March 30, 2009

/s/ STEPHEN P. HALL

Stephen P. Hall
Senior Vice President, Chief Financial Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer)

POWER OF ATTORNEY AND SIGNATURES

We, the undersigned officers and directors of Helicos BioSciences Corporation, hereby severally constitute and appoint Ronald A. Lowy and Stephen P. Hall, our true and lawful attorneys, with full power to them to sign for us and in our names in the capacities indicated below, any amendments to this Annual Report on Form 10-K, and generally to do all things in our names and on our behalf in such capacities to enable Helicos BioSciences Corporation to comply with the provisions of the Securities Exchange Act of 1934, as amended, and all the requirements of the Securities Exchange Commission.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated:

Signature	Title	Date
/s/ STANLEY N. LAPIDUS Stanley N. Lapidus	Chairman of the Board of Directors	March 30, 2009
/s/ RONALD A. LOWY Ronald A. Lowy	Chief Executive Officer, Director (Principal Executive Officer)	March 30, 2009
/s/ STEPHEN J. LOMBARDI Stephen J. Lombardi	President, Director	March 30, 2009
/s/ STEPHEN P. HALL Stephen P. Hall	Senior Vice President and Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 30, 2009

Signature	Title	Date
/s/ NOUBAR B. AFEYAN, PHD Noubar B. Afeyan, PhD	Director	March 30, 2009
/s/ ELISABETH K. ALLISON, PHD Elisabeth K. Allison, PhD	Director	March 30, 2009
/s/ BRIAN G. ATWOOD Brian G. Atwood	Director	March 30, 2009
/s/ PETER BARRETT, PHD Peter Barrett, PhD	Director	March 30, 2009
/s/ ROBERT F. HIGGINS Robert F. Higgins	Director	March 30, 2009
/s/ THEO MELAS-KYRIAZI Theo Melas-Kyriazi	Director	March 30, 2009

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10.8	Form of Indemnification Agreement (Incorporated by reference herein to Exhibit 10.10 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.9	Amended and Restated Investor Rights Agreement by and among the Registrant and the Investors named therein, dated as of March 1, 2006 (Incorporated by reference herein to Exhibit 10.11 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.10†	Amendment to License Agreement Having an Effective Date of March 7, 2007 between California Institute of Technology and the Registrant (Incorporated by reference herein to Exhibit 10.12 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
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10.17+	Non-Employee Director Compensation Policy (Incorporated by reference herein to Exhibit 10.20 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
10.18+	2007 Stock Option and Incentive Plan and forms of agreement thereunder, as amended (Incorporated by reference herein to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on August 14, 2008).

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10.19+	Change in Control Agreement between the Company and J. William Efcavitch, dated August 8, 2007 (Incorporated by reference herein to Exhibit 10.1 to the Company's Current Report on Form 8-K, filed with the Securities and Exchange Commission on August 10, 2007).
10.20†	Loan and Security Agreement by and between the Registrant and General Electric Capital Corporation, dated December 31, 2007 (Incorporated by reference herein to Exhibit 10.23 to the Company's Annual Report on Form 10-K, filed with the Securities and Exchange Commission on March 17, 2008).
10.21+	Offer Letter between the Registrant and Stephen P. Hall dated April 25, 2008 (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on May 1, 2008).
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10.26+	Severance and Consulting Services Agreement, by and between the Registrant and Stanley N. Lapidus, dated as of September 12, 2008 (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on September 12, 2008).
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Exhibit Number	Description of Document
10.31+	Third Amendment to the Loan and Security Agreement among the Registrant, the Lenders and General Electric Capital Corporation, dated as of December 29, 2008 (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on December 30, 2008).
10.32+	Change in Control Agreement by and between the Registrant and Ronald A. Lowy, dated as of January 28, 2009 (Incorporated by reference herein to Exhibit 10.1 to the Company's Form 8-K, filed with the Securities and Exchange Commission on January 30, 2009).
21.1	Subsidiary of the Registrant (Incorporated by reference to Exhibit 21.1 to the Company's Registration Statement on Form S-1 (File No. 333-140973) which became effective on May 24, 2007).
23.1*	Consent of PricewaterhouseCoopers LLP, an independent registered public accounting firm.
31.1*	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certifications pursuant to 18 U.S.C. Section 1350.

* Filed herewith

† Confidential treatment has been requested for certain provisions of this Exhibit pursuant to Rule 406 promulgated under the Securities Act.

\+ Indicates a management contract or any compensatory plan, contract or arrangement.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (File No. 333-144094) and Form S-3 (File No. 333-156885) of Helicos BioSciences Corporation of our report dated March 30, 2009 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 30, 2009

EXHIBIT 31.1

CERTIFICATION

I, Ronald A. Lowy, certify that:

1. I have reviewed this annual report on Form 10-K of Helicos BioSciences Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 30, 2009

/s/ RONALD A. LOWY

Ronald A. Lowy
Chief Executive Officer (Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATION

I, Stephen P. Hall, certify that:

1. I have reviewed this annual report on Form 10-K of Helicos BioSciences Corporation;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 30, 2009

/s/ STEPHEN P. HALL

Stephen P. Hall
Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)

EXHIBIT 32.1

CERTIFICATION

In connection with the Annual Report on Form 10-K of Helicos BioSciences Corporation (the "Company") for the year ended December 31, 2008 as filed with the Securities and Exchange Commission on the date hereof (the "Report), we Ronald A. Lowy, the Principal Executive Officer of the Company and Stephen P. Hall, the Principal Financial and Accounting Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to our knowledge that:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended, and

(2) the information in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company

Dated: March 30, 2009

/s/ RONALD A. LOWY

Ronald A. Lowy
Chief Executive Officer (Principal Executive Officer)

Dated: March 30, 2009

/s/ STEPHEN P. HALL

Stephen P. Hall
Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)

A signed original of this written statement required by Section 906 has been provided to Helicos BioSciences Corporation and will be retained by Helicos BioSciences Corporation and furnished to the Securities and Exchange Commission or its staff upon request

Corporate Information

Management

Ronald A. Lowy
Chief Executive Officer

Stephen J. Lombardi
President

Stephen P. Hall
Senior Vice President and
Chief Financial Officer

J. William Efcavitch, PhD
Senior Vice President and
Chief Technology Officer

Marc S. Levine
Senior Vice President of
Product Development

Board of Directors

Stanley N. Lapidus
Chairman of the Board

Noubar B. Afeyan, PhD[3]

Elisabeth K. Allison, PhD[2]

Brian G. Atwood[1]

Peter Barrett, PhD[1,2]

Robert F. Higgins[2,3]

Stephen J. Lombardi

Ronald A. Lowy

Theo Melas-Kyriazi[1]

[1] Audit Committee
[2] Compensation Committee
[3] Nominating and Corporate Governance Committee

Shareholder Information

Corporate Headquarters:
One Kendall Square, Building 700
Cambridge, MA 02139

Common Stock Listing:
Common stock of Helicos BioSciences Corporation is traded on the NASDAQ Global Market under the symbol "HLCS"

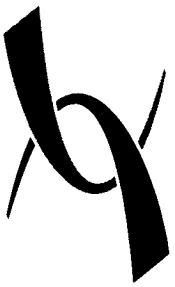
Outside Legal Counsel:
Goodwin Procter LLP
Exchange Place
53 State Street
Boston, MA 02109

Independent Registered Public Accounting Firm:
PricewaterhouseCoopers LLP
125 High Street
Boston, MA 02110

Transfer Agent:
Computershare Shareholder Services
250 Royall Street
Canton, MA 02021

Investor Relations:
Susan Shepard
617-264-1850
InvestorRelations@helicosbio.com

Certain statements made in this annual report that are not based on historical information are forward-looking statements which are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. This annual report contains express or implied forward-looking statements relating to our "expectations," "beliefs," "hopes," "intentions," "strategies," or the like. These statements are neither promises nor guarantees, but are subject to a variety of risks and uncertainties, many of which are beyond Helicos' control, which could cause actual results to differ materially from those contemplated in these forward-looking statements. In particular, the risks and uncertainties include, among other things, our ability to successfully complete and/or scale the manufacturing and commercialization process for the Helicos™ Genetic Analysis System; our history of operating losses and ability to achieve profitability; our ability to establish manufacturing capabilities; the research and development spending levels of academic, clinical and governmental research institutions and pharmaceutical, biotechnology and agriculture companies who may purchase our Helicos™ Genetic Analysis System; our reliance on third-party suppliers; competition; changing technology and customer requirements; our ability to operate in an emerging market; market acceptance of our technology; the length of our sales and implementation cycles; our dependence on large contracts for the sale and implementation of our Helicos™ Genetic Analysis System; failure of our technology and products; our ability to maintain customer relationships and contracts; ethical, legal and social concerns surrounding the use of genetic information; our ability to retain our personnel and hire additional skilled personnel; our ability to manage our growth while operating with limited resources; our ability to control our operating expenses; general economic and business conditions; our ability to obtain capital when desired on favorable terms; and the volatility of the market price of our common stock. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Helicos undertakes no obligation to update or revise the information contained in this annual report, whether as a result of new information, future events or circumstances or otherwise. For additional disclosure regarding these and other risks faced by Helicos, see the disclosure contained in Helicos' public filings with the Securities and Exchange Commission.



Helicos

BioSciences Corporation

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