NANOGEN INC
Form 10-K
April 02, 2001

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

[X] ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

FOR THE FISCAL PERIOD ENDED DECEMBER 31, 2000

OR

[ ] 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 000-23541

NANOGEN, INC.

(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

DELAWARE	33-0489621
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
10398 PACIFIC CENTER COURT, SAN DIEGO, CA	92121
(Address of principal executive offices)	(Zip code)

REGISTRANT'S TELEPHONE NUMBER, INCLUDING AREA CODE: (858) 410-4600

Securities registered pursuant to Section 12(b) of the Act:
NONE

Securities registered pursuant to Section 12(g) of the Act:
Common Stock $.001 par value
Preferred Stock Purchase Rights
(Title of Class)

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 /X/ NO / /

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (Section 229.405 of this chapter) 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. [ ]

The aggregate market value of the voting stock held by non-affiliates of the registrant based upon the closing sale price of the Common Stock on March 23, 2001, as reported on the Nasdaq National Market was approximately $112,465,223. Shares of Common Stock held by each executive officer and director and by each person who owns 10 percent or more of the outstanding Common Stock have been excluded in such calculation as such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares outstanding of the registrant's common stock was 20,981,900 as of March 23, 2001.

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PART I

PART I

ITEM 1. BUSINESS

OVERVIEW

We launched our first commercial product during the second quarter of the year 2000, beginning our transformation from a research and development company to a customer-oriented company. The NanoChip(TM) Molecular Biology Workstation has been targeted toward clinical researchers performing genetic-based analyses, particularly those involving single nucleotide polymorphisms ("SNPs"), short tandem repeats ("STRs"), single point mutations ("PMs") and other genetic variations. Our first product launch marks a point of entry from which we hope to expand our product line and served markets.

Our primary differentiation stems from our ability to integrate advanced microelectronics and molecular biology into a core technology platform with potential commercial applications in the fields of genomics and biomedical research, medical diagnostics, drug discovery, forensics, agriculture, environmental testing and potentially the electronics and telecommunications industries. The first application we have developed is an integrated bioassay system, the NanoChip(TM) Molecular Biology Workstation, comprised of two automated instruments and a consumable cartridge. The NanoChip(TM) Cartridge incorporates a proprietary microchip, providing a flexible tool for the rapid identification and precision analysis of biological test samples containing charged molecules.

Through the use of microelectronics, our technology enables the active movement and concentration of charged molecules, such as DNA, to and from designated microlocations, or test sites, on our microchips. This electronic concentration of molecules greatly accelerates molecular binding at each microlocation. In addition, our technology allows the simultaneous analysis of multiple test results, or "multiplexing," from a single sample. The potential future applications for our system include microchips with preloaded arrays designed for specific applications or with arrays that can be customized by the end user. We believe that our technology platform provides an accurate, versatile and highly efficient integrated system that may shift bioassay analysis from manual and mechanical methods to microelectronic systems, thereby significantly improving the quality and reducing the overall cost of research

and healthcare.

During the year 2000, we accomplished the following:

- finalized the beta test results for our NanoChip(TM) System, reporting extremely high accuracy and flexibility in hard to score mutations;

- raised over $76.5 million in a secondary offering;

- commercially launched the NanoChip(TM) System as our first product and shipped a total of 23 NanoChip(TM) Systems to the research laboratories of hospitals, universities, government organizations and pharmaceutical companies;

- significantly expanded our sales, marketing and field support staff and expanded our international sales and marketing efforts by opening our European office in The Netherlands;

- signed a long-term collaboration agreement with Hitachi expanding our earlier agreement and providing for the joint development of future technology;

- realigned our joint venture with Becton Dickinson to expand our licensing rights to the joint venture's proprietary amplification technique;

- received two additional government grants that provide for a total of $2.7 million of continued funding for the development of our core technologies; and

- expanded our intellectual property portfolio by adding ten U.S. patents and seven foreign patents.

YEAR 2000 ACCOMPLISHMENTS

SUCCESSFUL BETA SITE TESTS

In February 2000, we announced the completion of our third and final beta site testing results for the NanoChip(TM) Molecular Biology Workstation. These tests were conducted at three commercial and academic centers: the Mayo Clinic, the University of Texas Southwestern Medical Center and the Bode Technology Group. In each case, the results indicated very high levels of accuracy for the NanoChip(TM) System. The SNP studies performed at the Mayo Clinic and the University of Texas Southwestern Medical Center both reported 100% accuracy, exceeding the performance of their current "gold standard" techniques. The STR analysis results from the Bode Technology Group showed greater than 99.5% concordance with current techniques, results which have been further improved by subsequent software upgrades.

$76.5 MILLION SECONDARY OFFERING

In March 2000, we completed a secondary public offering of common stock that generated net proceeds of approximately $76.5 million. As of December 31, 2000, our cash, cash equivalents and short-term investment balance was in excess of $95 million.

COMMERCIAL LAUNCH OF THE NANOCHIP(TM) SYSTEM AND SHIPMENT OF 23 SYSTEMS

We began commercialization of our NanoChip(TM) Molecular Biology Workstation during the second quarter of 2000 in the genomics and biomedical research fields. The initial application for the technology is the analysis of SNPs including those that are hard to score, insertions and deletions, STRs, PMs and other genetic variations. We anticipate adding the analysis of gene expression as an additional application during 2001. Because of the importance of the genomics and biomedical research markets for the development and sales of future applications for the NanoChip(TM) System and for other products related to our technology, we chose to build a commercial infrastructure that would allow us to be directly involved in marketing and selling our first product. Additionally, we set up a distribution capability for our products in Japan through the distribution arm of Hitachi, Ltd., our manufacturing partner.

As of December 31, 2000, we shipped a total of 23 NanoChip(TM) Systems to customers in three countries, including the research laboratories of hospitals, universities, government organizations and pharmaceutical companies. Such customers include the National Cancer Institute, the Mayo Clinic, the Children's Research Hospital of Tokyo, Aventis, Stanford University and Beth Israel Deaconess Medical Center at Harvard. Our NanoChip(TM) System is designed to assist research in the fields of genetics, cancer and infectious and cardiovascular disease.

These 23 shipments include two sales recorded as sponsored research revenue and funded by corporate alliances, seven title transfer transactions representing sales and recorded as product revenue, and 14 non-title transfer transactions. Of the non-title transfers, one was a shipment made to a corporate collaborator pursuant to an expanded relationship. The other 13 were strategic placements made pursuant to our development site agreements. Non-title transferring transactions may include development site agreements, leases and reagent rentals. Title transferring transactions normally result in recording of full instrument revenue at the time of the transaction, while non-title transferring transactions may spread instrument revenue associated with the transaction, if any, over the life of the instrument or the agreement. We believe that the non-title transferring transactions help us establish awareness and credibility in our target markets.

EXPANDED SALES, MARKETING AND FIELD SUPPORT EFFORTS

We increased the number of employees in our sales and marketing group from three at December 31, 1999 to twenty-six at December 31, 2000. In addition, in August 2000, we incorporated a subsidiary, Nanogen Europe B.V. in The Netherlands as our European sales office. At December 31, 2000, this office employed four European-based sales executives in the United Kingdom, Germany, The Netherlands and Denmark.

EXPANDED HITACHI COLLABORATION

In July 2000, we executed a ten-year agreement with Hitachi, Ltd., Nissei Sangyo Co. Ltd. and Hitachi Instruments Service Co. Ltd. of Japan (collectively, "Hitachi") to develop, manufacture and distribute products based on the parties' proprietary technologies, potentially including, among other things, reduced-size instruments for genetic testing, integrated amplification and point-of-care detection. The agreement expands on the agreement executed by the Company and Hitachi in January 2000. The agreement provides that the parties will jointly determine which projects to prioritize over the term of the agreement. The agreement may be terminated before its expiration by either party, subject to certain restrictions. Pursuant to the terms of the agreement,

we and Hitachi each may contribute up to $28.5 million in cash over the ten-year period. In addition, Hitachi made an equity investment in us by purchasing 74,590 shares of our common stock worth approximately $2.0 million pursuant to a private sale by us based on a per share price of $26.813 (the fair market value as of the signing date of the Hitachi agreement). Hitachi has the right to be the exclusive distributor of collaboration products in Japan and, based upon the attainment of minimum sales targets to be mutually agreed upon, in other Asian countries. We retain the exclusive right to distribute collaboration products outside of these countries. The agreement is non-exclusive and excludes some clinical markets.

REALIGNED JOINT VENTURE WITH BECTON DICKINSON

In September 2000, we and Becton Dickinson modified our joint venture to permit each of us the opportunity to commercialize certain of the joint venture's technology and allow collaborations with third parties to develop and commercialize certain products in the field of infectious diseases. Pursuant to amendments to the Master Agreement, the General Partnership Agreement and the Collaborative Research and Development and License Agreement, the Partnership exclusively licensed Partnership technology developed up to that date to Becton Dickinson and Becton Dickinson exclusively sublicensed the Partnership technology to us to commercialize products in the field of infectious diseases. Becton Dickinson also agreed to non-exclusively license SDA technology to us for use and for sublicensing purposes in the field of infectious diseases. Becton Dickinson also expanded the field of use for our SDA license outside of the Partnership to not only include IN VITRO human genetic testing and IN VITRO cancer diagnostics, but also IN VITRO testing of environmental, agricultural and veterinary samples. Pursuant to the amendments, Becton Dickinson paid us $300,000.

RECEIVED ADDITIONAL GOVERNMENT GRANTS

In August 2000, we were awarded a contract by the Space and Naval Warfare Systems Center San Diego for the Defense Advanced Research Projects Agency in an amount totaling approximately $1.6 million over a two year period. The goal of the contract is to develop and refine electronically driven sample preparation protocols on specifically designed microelectronic chips. In October 2000, we entered into a cooperative agreement with the U.S. Army Medical Research Acquisition Activity ("USAMRAA") in an amount totaling approximately $1.1 million over a two year period. The objective of the USAMRAA agreement is to develop an arrayable electronic system for the identification of biological warfare or infectious disease agents.

EXPANDED OUR INTELLECTUAL PROPERTY PORTFOLIO

During 2000, we expanded our intellectual property portfolio adding ten additional U.S. patents and seven additional foreign patents. As of December 31, 2000, we had a total of 20 U.S. patents and 13 foreign patents.

OUR TECHNOLOGY AND RELEVANT MARKETS

LIMITATIONS OF CURRENT ASSAY TECHNOLOGIES

Many bioassay techniques have been developed from a wide variety of different scientific disciplines for molecular biology and clinical diagnostic laboratories. Many of these techniques are technically demanding, difficult to perform, expensive or inflexible and may lack acceptable clinical accuracy. In addition, technologies well suited or targeted to one market, such as the biomedical research or drug discovery markets, often are unable to bridge the gap to serve downstream markets such as clinical diagnostics.

Despite recent advances in technology, many bioassays are too specialized or inflexible to be used throughout the various departments of a life sciences laboratory. Current bioassay tools were designed for large scale data generation, the automation of repetitious tasks such as very high throughput discovery and the narrowing of genetic targets from thousands of genes to a small set of perhaps 1 to 20 genes that function in a selected biological process. In addition, many of these systems are not useful in molecular, protein, enzyme, cell biology, and forensics laboratories. These tools fall primarily into three categories: high-density arrays; high throughput sequencing and SNP discovery tools; and gel-based methods. While these technologies each have certain advantages, they also have significant drawbacks that inhibit their broad applicability across the life sciences market.

THE NANOGEN SOLUTION

We believe that our initial product, the NanoChip(TM) Molecular Biology Workstation, or the NanoChip(TM) System, provides the accuracy, flexibility, versatility and ease-of-use features required to serve a wide range of genomic and biomedical as well as many other applications. We are promoting the NanoChip(TM) System as the research laboratory standard for molecular biologists, and eventually the industry standard for accurate, targeted genomics in both laboratory and non-laboratory settings. The NanoChip(TM) System provides the following advantages:

ACCURACY

Accuracy is critical in laboratory analysis. The NanoChip(TM) Molecular Biology Workstation, with its precision electronic addressing and high degree of stringency, exceeded the accuracy of the current "gold standard" techniques in the SNP studies conducted at the Mayo Clinic and the University of Texas Southwestern Medical Center. Nanogen's technology may have the ability to expand a customer's range of testing to include important, difficult to score mutations such as genetic deletions.

FLEXIBILITY

Nanogen's technology is highly flexible. The NanoChip(TM) System is centered around an electronics microarray containing 100 individually controllable and programmable electronic test sites. Each of the major bioassay formats, the "dot blot" and the "reverse dot blot" are conveniently handled by the NanoChip(TM) System and customers can design arrays in several different formats to meet their specific needs. Customers can combine several types of assays on one chip and multiple Loaders can be controlled by one Reader.

VERSATILITY

The NanoChip(TM) System is designed to analyze SNP's, including those that are hard to score, insertions, deletions, STRs, single point mutations and other genetic variations. Our electronic-based technology is potentially applicable to biological analyses beyond genomics and biomedical research including immunoassays, enzyme assays, cell separation and cell receptor studies.

FAST ARRAY DESIGN

Experimental design of arrays on the NanoChip(TM) Cartridge is straightforward. Customers can program NanoChip(TM) arrays in their own laboratories, allowing for faster turnaround times and higher levels of confidentiality.

EASE OF USE

Nanogen assays are easy to perform. Our fully automated Loader allows the simultaneous programming of up to four NanoChip(TM) arrays. A loaded cartridge is inserted and then analyzed on the Nanogen Reader. The NanoChip(TM) System includes proprietary software to automate assay operation and provide results in "real time." Data interpretation is clear-cut and presented in a user-friendly format.

THROUGHPUT

Our system's ability to program as many as 100 test sites at a time allows for higher throughput than is achievable with some competitive technologies. This throughput capacity permits highly efficient workflow for many biomedical applications in a variety of laboratory settings.

COST EFFECTIVENESS

We have designed the NanoChip(TM) System to be a cost-effective solution for most molecular biology assays. Moreover, the custom features of the system allow users to employ their own reagents in designing arrays for specific purposes. Since the NanoChip(TM) System consumes small quantities of reagents, generally at low concentration, bioassay reagent costs (such as DNA) per result are relatively low. Walk-away automation conserves direct labor, while improving the overall effectiveness of the laboratory operation. In addition, user definability allows important experiments to be done quickly, both accelerating the discovery process and simplifying the validation of important targets.

COMMERCIALIZATION STRATEGY

Our primary commercialization strategy is to research, develop, manufacture and market instruments and components, independently and in conjunction with highly regarded corporate and government partners, to facilitate breakthrough genetic analyses. Our NanoChip(TM) System is designed eventually to bridge the gap between scientific research and clinical practice. Our strategy is to make our proprietary bioassay technology platform a standard for molecular identification and analysis across a broad range of applications. Our initial commercial product is a bench-top system for use in biomedical research and genomic applications. The capabilities that are incorporated into this system are the core technology platform that will serve as the basis for expanding into other biological and non-biological areas. In addition, we believe we have the core technology that will enable us to design and deliver products incorporating molecular biology and electronics in additional formats, beyond the microchip format. These new product forms may broaden the markets we serve.

CONTINUE TO PURSUE GENOMICS AND BIOMEDICAL RESEARCH APPLICATIONS

While researchers want to use high throughput devices to discover genes and genetic mutations, they will want to explore the function and impact of these genes and mutations with a more targeted technology. Nanogen seeks to position the NanoChip(TM) System as such a technology. We intend to pursue the genomics and biomedical research markets by taking advantage of the open architecture design of our technology that allows end users to customize microchips to meet their individual research needs and help drive development of novel applications.

PURSUE MULTIPLE APPLICATIONS

We intend to use substantially the same core hardware and consumable cartridge platform across a spectrum of applications. By doing this, we believe we can establish our platform as an industry standard and also reduce development costs for follow-on applications. This approach should also allow us to achieve manufacturing economies of scale that may help reduce our per unit cost of goods sold over time. For our initial commercial market, the biomedical research market, we do not anticipate the need for Food and Drug Administration or FDA or other regulatory approval. Over time, we expect that additional features, such as genetic content-based kits, sample-to-answer capabilities and portability at reduced cost, may broaden the market potential from the research market to larger markets that include drug discovery, diagnostics, forensics, agriculture and environmental applications. Some of these applications would require FDA or other regulatory approval.

DEVELOP RECURRING REVENUE STREAM THROUGH BENCH-TOP AND CONSUMABLE PRODUCT SALES

We are selling bench-top instruments that we anticipate will lead to a recurring stream of revenue from consumable cartridge sales. We believe that widespread market penetration of our instruments and the open architecture of the system will promote sustained demand for our cartridges.

CONTINUE TO ESTABLISH STRATEGIC COLLABORATIONS

We intend to continue to enter into collaborations to expand applications of our technology platform and to accelerate the commercialization of our products. By partnering with multinational healthcare and technology companies, we believe that we can gain broader access to global markets without shifting our resources from the development of our core technology platform. In addition, as part of these arrangements, we believe we can better focus our efforts on tailoring our technology to expanding markets while our collaborative partners contribute their technology and expertise in areas such as sales, marketing and regulatory approvals.

OUR PLATFORM TECHNOLOGY

Our proprietary platform technology takes advantage of the fact that most biological molecules are either positively or negatively charged. Through the use of microelectronics, this technology enables the active movement and concentration of electronically charged molecules such as DNA to and from designated test sites on a semiconductor microchip or other electronics device. In the NanoChip(TM) Cartridge, these test sites are arranged in an array on our proprietary microchips. In addition, the technology allows for the simultaneous analysis of multiple test results, or "multiplexing," from a single sample. We believe these attributes make our technology well suited to unraveling complex genetic information. We have initially focused on DNA-based sample analysis in developing applications utilizing our platform.

We believe our technology may be applicable to a number of other analyses, in addition to DNA applications, including antigen-antibody, enzyme-substrate, cell-receptor, and cell separation techniques.

Our system can integrate in a single platform the following electronic operational features:

ELECTRONIC ADDRESSING

Electronic addressing is the process by which we place charged molecules at

specific test sites. Since DNA has a strong negative charge, it can be electronically moved to an area of positive charge. A group of test sites on the microchip is electronically activated with a positive charge. A solution of DNA probes is introduced onto the microchip. The negatively charged probes rapidly move to the positively charged sites, where they concentrate and are chemically bound to those sites. The microchip is then washed and another solution of distinct DNA probes can be added. Site by site, row by row, an array of specifically bound DNA probes can be addressed on the microchip. Multiplexed sites can be addressed simultaneously, allowing for speed and flexibility of array assembly. With the ability to electronically address capture probes to specific sites, the NanoChip(TM) System allows end users to build custom arrays through the placement of specific capture probes on a microchip. Alternatively, the target samples themselves can be electronically addressed to the test sites. All tests are performed using replicate probes or samples for control purposes. These microchip arrays provide research professionals with a powerful and versatile tool to process and analyze molecular information.

ELECTRONIC CONCENTRATION AND HYBRIDIZATION

Following electronic addressing, we use electronics to move and concentrate target molecules to one or more test sites on the microchip. In contrast to the passive hybridization process, the electronic concentration process has the advantage of significantly accelerating the rate of hybridization of a given target molecule with complementary capture probes. In addition, because we use buffers with low ionic strength, we improve the system's accuracy by reducing the occurrence of undesirable, non-specific hybridization. Again, the alternative method of attaching the target molecules to the test sites and then adding probes to interrogate the targets electronically is also available. All tests are performed using replicate probes or samples for control purposes.

STRINGENCY CONTROL

In addition to utilizing conventional thermal and chemical stringency techniques, the NanoChip(TM) System is capable of utilizing electronic stringency control when appropriate. Electronic stringency control can provide a means to quickly and easily remove non-complementary DNA as part of the hybridization process. Electronic stringency can provide quality control for the hybridization process and ensures that any bound pairs of DNA are truly complementary. The precision, control, and accuracy of our platform technology permits the detection of single point mutations, single base pair mismatches or other genetic mutations which have significant implications

in a number of disease states. Electronic control allows rapid and selective stringency conditions to be applied to individual test sites, which cannot be achieved with conventional methods. In contrast to conventional approaches, our technology can also accommodate both short and long single-stranded fragments of DNA on the same chip. This flexibility reduces the required number of probes or samples and related test sites on the microchip. Other currently marketed DNA arrays either are more difficult to control and/or require more uniformity in the preparation of the sample.

ELECTRONIC MULTIPLEXING

Our electronic multiplexing feature allows the simultaneous analysis of multiple tests from a single sample or multiple samples to be queried during the hybridization process. Electronic multiplexing is facilitated by the ability to control individual test sites (for addressing of capture probes and concentration of test sample molecules) which allows for the simultaneous use of

biochemically unrelated molecules on the same microchip. Sites on a conventional DNA array cannot be individually controlled, and therefore the same process steps must be performed on the entire array. The use of electronics in our technology provides increased versatility and flexibility over these conventional methods.

STRAND DISPLACEMENT AMPLIFICATION

Strand Displacement Amplification, or SDA, is a proprietary target amplification process whereby very low numbers of diagnostic targets in a test sample are enzymatically amplified to exponentially higher levels, greatly simplifying accurate detection of these targets. Because this process does not require thermal cycling, it is extremely fast, and complex instrumentation for thermal regulation is not required. The Nanogen/Becton Dickinson Partnership was granted rights to Becton Dickinson's patents relating to SDA in infectious disease diagnostics. During 2000, Becton Dickinson and we revised our relationship. We were granted rights to use SDA in the fields of IN VITRO human genetic testing and cancer diagnostics for use outside The Nanogen/Becton Dickinson Partnership. We believe that SDA may be an important element in the development of sample-to-answer applications for our technology platform.

THE NANOCHIP(TM) SYSTEM'S COMPONENTS

The NanoChip(TM) System consists of both a consumable cartridge containing a proprietary semiconductor microchip and a fully automated instrument that controls all aspects of microchip operations, processing, detection and reporting. The system has been designed so that after insertion of a consumable cartridge containing a test sample into the instrument, all subsequent steps are handled automatically under computer control.

CONSUMABLE CARTRIDGE

The consumable NanoChip(TM) Cartridge consists of a proprietary semiconductor microchip with electrical and fluidic connections to the instrument. We expect that over time the consumable cartridge and microchip may be manufactured in high volumes at a low cost relative to many current technologies.

SEMICONDUCTOR MICROCHIP

Our proprietary microchip utilizes advances in the semiconductor industry and is designed and constructed using microlithography and fabrication techniques. Our microchip is mounted within the consumable cartridge and is coated with a proprietary permeation layer to which either capture probes or target samples can be attached. We have developed arrays of various sizes utilizing both passive and active CMOS microchips, as well as flip chip assembly technologies. Our initial production of consumable cartridges employs 100 different test sites on the microchip.

PERMEATION LAYER

Our proprietary permeation layer, which is critical to the proper functioning of our system, is the interface between the surface of the microchip and the biological test environment. The permeation layer isolates the

biological materials from the harsh electrochemical environment near the electrode surface and provides the chemistry necessary for attachment of capture

probes or target samples.

CAPTURE PROBES OR TARGET SAMPLES

Capture probes or target samples are electronically addressed to the desired microlocations and attached to the permeation layer. Because independent control can be applied at any test site on our microchip, different capture probes or target samples can be addressed on the same microchip, allowing multiple tests to be processed simultaneously. Our cartridges can be customized by the end user in "build-your-own-chip" applications which will allow the customer to assemble specific probes onto a microchip to perform individualized analyses. In the future, we may also offer cartridges preloaded with sets of probes or samples.

OUR INSTRUMENTS

Our fully integrated NanoChip(TM) instrument system consists of four major subsystems: (1) a freestanding microchip Loader to perform electronic addressing of blank microchips, (2) a highly sensitive, laser-based fluorescence scanner that detects molecular binding, (3) a fluid handling subsystem that controls test sample application and washing steps, (2) and (3) are, collectively, the Reader, and (4) computer hardware and software that allow the operator to select assays from a graphical user menu which controls all microchip operations, tabulates test results and prints test reports.

MICROCHIP LOADER

For biomedical research applications, our system includes a cartridge/microchip Loader that will allow users to electronically address their own target samples or probes to test sites on up to four chips simultaneously. In addition, hybridization can be performed on the Loader or on the Reader. Multiple Loaders can operate concurrently under the control of one system.

FLUORESCENT ARRAY SCANNER

The fluorescent scanner component of the system uses pattern recognition techniques and optoelectronic technology to reduce instrument cost and size and eliminate the need for complicated array positioning mechanics. In its present configuration, the scanner is able to perform high sensitivity scans of arrays of 100 test sites in less than five minutes.

FLUIDICS STATION

Within the fluorescent array scanner component of the system, the fluidics station automates the movement of the reagents and test sample onto the consumable cartridge. The fluidic subassembly of the instrument includes a panel of precision syringe pumps, a cartridge-mounted sample assembly and fluidic connections between the instrument and the consumable cartridge.

COMPUTER HARDWARE AND SOFTWARE SYSTEM

A multi-tasking operating system and microprocessor control all aspects of the systems operations, including bar-coded assay selection, assay operation, fluorescent signal detection and signal processing, calculation of assay results and report generation. Each of the individual array locations is separately controlled by the microprocessor. Fluorescent signals emanating from positive test sites are scanned, monitored and quantitated.

NANOCHIP(TM) ANALYSIS PROCESS

CARTRIDGE
An active microelectronic chip is mounted within

a plastic molded cartridge. The bar-coded cartridge is delivered in a ready-to-address format with no genetic sequences pre-attached.

ELECTRONIC ADDRESSING
Users design and create their own genetic arrays on the microelectronic chip with Nanogen's automated system. A 96 well or 384 well microtiter plate containing different genetic sequences is placed in the Loader instrument. The system then automatically electronically addresses the microchip to the user-defined arrays.

ELECTRONIC HYBRIDIZATION AND STRINGENCY
Users add the test samples or probes to the cartridge and insert the cartridge into the Reader. The instrument then automatically performs electronic hybridization and the appropriate stringency control. The electronically enhanced process speeds and improves the genetic analysis, allowing single-base accuracy.

SIMPLE-TO-READ OUTPUT
Within minutes of inserting the bar-coded cartridge for analysis, easy-to-read and interpret output is available. Data can be automatically downloaded to network systems and to standard software spreadsheet packages. The entire electronic addressing and data output process can be completed rapidly, allowing users to accelerate their research process by creating new genetic arrays based on previous experimental results.

PRODUCTS AND APPLICATIONS UNDER DEVELOPMENT

GENOMICS AND BIOMEDICAL RESEARCH APPLICATIONS

We began commercialization of the NanoChip(TM) System during the second quarter of 2000. Unlike the high-density arrays and sequencing technologies now in the marketplace, our focus is on the targeted analysis of data from the genomics revolution and post genomics era--helping clinical researchers define the function of genes rather than discover new genes. We believe our technology is well suited for this research, given the speed, user programmability, multiplexing capability and sensitivity of our unique platform.

Given that researchers are just beginning to move beyond gene discovery into this targeted analysis area referred to as functional genomics, our product introduction may be well suited to meet this evolving market need. An independent market research study by Strategic Directions International published in December 1999 indicated that the market potential for microarrays is anticipated to grow rapidly from $200 million in 2000 to almost $800 million by 2003.

Our initial strategy for entering this market is to focus on sophisticated commercial and academic users such as the research laboratories of large hospitals, academic and government institutions and genomics and pharmaceutical companies. We provide technical support and applications specialists to assist these customers in applying the technology. Our initial product offering

includes features such as the ability to perform assays on SNPs, PMs and STRs in a multiplexed format using a variety of different methods. We plan to further define and develop additional capabilities, such as gene expression, on-chip amplification and sample processing. As these capabilities are added, we expect to start expanding our customer base to a wider group that may ultimately encompass a significant percentage of the biomedical research labs in the U.S. and other parts of the world.

DIAGNOSTICS APPLICATIONS

We anticipate the introduction of array-based diagnostic testing will grow as effective technologies are introduced and validated. This multi-step process may allow for the development of relevant genetic-based tests that may

evolve from biomedical research, and for the awareness and confidence in electronic-based technology to extend to medical practitioners. Finally, we anticipate the need for regulatory approval of certain diagnostic tests.

- Pharmacogenomics

We believe that the ability of our technology to screen simultaneously for various DNA sequences and the ability to differentiate between SNPs has potentially wide applicability to the field of genetic testing in general and pharmacogenomics in particular.

Our NanoChip(TM) System may provide pharmaceutical and biotechnology companies with the ability to identify important genetic variations early in the drug development process. We believe our system may help stratify patients during clinical trials and identify those receiving the maximum benefit from treatment. We intend ultimately to develop a small sample-to-answer, FDA-approved diagnostic test that can be used in a doctor's office potentially while a patient is waiting. We have a development program underway to develop a more compact version of our NanoChip(TM) System.

- Infectious diseases

We believe we have the potential to apply our technology in the field of infectious disease diagnostics to develop automated tests to replace the manual and time-intensive procedures used in hospitals and reference laboratories. The role of the clinical microbiology laboratory is to detect, identify and determine antibiotic sensitivity of disease causing microorganisms. To accomplish this task, colonies of microorganisms from patient specimens are grown, or cultured, in various growth media. Following colony growth, various direct and indirect techniques are utilized to determine the identity and, as required, the sensitivity of the microorganism to specific antibiotics. Using currently available technologies, the entire process may take days or weeks to complete while the patient, requiring immediate therapy, must be treated by the clinician based upon the best clinical facts available at that time. Upon receipt of the diagnostic analysis from the laboratory, the initial patient treatment protocol may need to be modified in order to treat the patient more effectively.

Current culture-based methods detect a single microorganism at one time. Because a particular infectious episode may be caused by one of many microorganisms or several microorganisms together, multiple tests may be required to determine the correct diagnosis. "Single tube" (one at a time) DNA probe diagnostics, which were first introduced to the marketplace in the mid-1980's, have been unsuccessful in displacing culture based diagnostic tests

in part due to their inability to identify several organisms simultaneously. Our technology addresses these shortcomings by allowing the simultaneous analysis of multiple microorganisms from a single patient sample. We believe our technology and integrated system may speed the time-to-result for diagnostic tests and patient treatment and offer our customers the opportunity to lower their costs and improve productivity by automating all or a significant portion of their labor-intensive testing.

- Other genetic testing applications

As the Human Genome Project opportunity and other public and private genetic sequencing efforts yield increasing amounts of genetic information, the demand for genetic predisposition testing will continue to grow. Because many important genetic diseases are ideally suited to diagnosis in multiplexed arrays, we believe that our technology platform could contribute significantly to the expansion of testing in this area. For example, in cancer diagnostics, certain mutations are indicative of a predisposition to certain types of cancer. Although many diseases involve multiple mutations, the ability to analyze all possible mutations has previously been expensive and impracticable. Our stringency control feature potentially permits rapid and accurate testing for these single point mutations. While our development efforts in this area with respect to specific genetic tests are still at an early stage, our core technology platform for other diagnostic applications may be well suited for these opportunities.

DRUG DISCOVERY APPLICATIONS

We believe we have a powerful tool which will help clarify appropriate pathways for therapeutic intervention, identify and evaluate lead compounds and simultaneously assess the efficacy and toxicology of these compounds in model systems. It is estimated that the preclinical drug discovery process takes an average of six and one-half years.

Consequently, we believe there is a significant demand for improved tools which accelerate the drug discovery process.

We believe the microelectronic array format and independent test site control of our system are well suited for applications in drug discovery. In addition, we believe the use of electronics beyond the microchip format may provide a valuable tool for the high throughput screening of compounds. One such application is the high throughput screening of drug candidates acting on protein kinases. Protein kinases are particularly important in signal transduction pathways and are thought to be key elements in many forms of cancer. Nanogen's electronic, fluorescent assays are free of antibodies and have the potential of improving the cost and quality of the screening process.

To advance our efforts in this area of drug discovery and optimization, we entered into a research and development collaboration with Aventis in 1998. This collaboration was focused on the development of novel electronic combinatorial approaches toward drug screening and discovery and was concluded at the end of 2000. We are negotiating a potential new relationship with Aventis relating to the research conducted and technology developed under this 1998 agreement. In 1999, we entered into an additional collaboration agreement with Aventis for two additional projects. Nanogen and Aventis have met all of the objectives to date for these two projects.

FORENSIC APPLICATIONS

STRs are the genetic sequences chosen by the U.S. government and various foreign governments to populate their national criminal identification databases. These databases are intended to provide nationwide tools for identifying repeat criminals by comparing a given piece of evidence or sample from a suspect with the sequences stored in the database. We believe our NanoChip(TM) System may be useful in human identity testing.

NON-BIOLOGICAL APPLICATIONS

We are applying our core microelectronics biochip technology to potential applications in non-biological areas which include nanotechnology, data storage and semiconductor manufacturing. Based on the intrinsic self-assembly and programmable qualities of DNA, our technology uses electrical current to direct the heterogeneous integration of a number of molecular and nonmolecular components onto a microelectronic chip. Our integrated "host substrate" or "motherboard" array capability could serve to provide researchers with useful new tools that permit them to take advantage of these valuable components.

Our electronic "pick and place" technology may have several advantages compared to the more difficult conventional processes. Our technology could facilitate the movement and assembly of microelectronic components ranging in size from molecular scale to micron scale, something traditional assembly methods cannot achieve. Also, using electric field specificity control, we may have the ability to form novel integrated devices in a more timely and cost-effective fashion. For example, we have evaluated the use of this platform technology to facilitate integration of different size components for the development of new photonic or electronic devices.

COLLABORATIVE ALLIANCES

We have established collaborative alliances in the areas of drug discovery and genomics as part of our strategy to expand the applications and accelerate the commercialization of products derived from our technology. During 1999, we expanded our relationship with Aventis by increasing the number of collaborative research and development projects from one to three. In January 2000 we entered into a manufacturing, development and distribution agreement with Hitachi, Ltd. In July 2000, we entered into an additional agreement with Hitachi, Ltd., Nissei Sangyo Co. Ltd. and Hitachi Instruments Service Co. Ltd. of Japan (collectively, "Hitachi") to develop, manufacture and distribute additional potential products based on the parties' proprietary technologies, potentially including, among other things, reduced-size instruments for genetic testing, integrated amplification and point-of-care detection. We anticipate being directly involved with marketing our first product line to the biomedical research and genomics market. Additionally, we may distribute products in Japan and selected Asian markets through the distribution arm of Hitachi, Nissei Sangyo Co., Ltd.

AVENTIS

In December 1997, we entered into a Letter Agreement with Aventis for an exclusive research and development collaboration relating to new drug discovery tools and immunodiagnostics research. In connection with the Letter Agreement, we entered into a definitive Collaborative Research and Development Agreement with an effective date of January 1, 1998. The arrangements for the commercialization of products, if any, developed as a result of the collaboration will be negotiated by the parties. The term of this collaboration agreement expired at the end of 2000. We are negotiating a potential new relationship with Aventis relating to the research conducted and technology developed under this 1998 agreement. In addition, in September 1999 we entered

into an additional collaboration agreement with Aventis that involves two new research and development programs focused on gene expression arrays and on an electronics-based high throughput screening system. We retain full commercialization rights for any products resulting from these new projects, while Aventis retains the right to use the technology for internal research and development.

As part of our 1998 collaboration, the Company issued to Aventis a warrant to purchase 120,238 shares of common stock exercisable through December 2003, which was exercised by Aventis in October 2000 at an agreed-upon exercise price of $6.17 per share. The Company has also agreed to issue to Aventis, upon the achievement of certain milestones, warrants to purchase up to approximately 360,000 additional shares of common stock at a 50 percent premium to the market price on the date the milestone is achieved. These warrants will have five-year maximum terms.

HITACHI

In January 2000, we executed an agreement with Hitachi, Ltd., effective as of December 15, 1999, for the full-scale commercial manufacturing and distribution of the NanoChip(TM) Molecular Biology Workstation in specified research markets. Hitachi, Ltd.'s Instrument Group provides technology and technical support to aid in the manufacturing scale-up of the NanoChip(TM) Molecular Biology Workstation's components.

Under this agreement, Hitachi, Ltd. has the right to be the sole distributor of Hitachi, Ltd. produced NanoChip(TM) Molecular Biology Workstations in Japan. Hitachi, Ltd. also has the non-exclusive right to distribute NanoChip(TM) Cartridges in Japan. We retained the right to distribute, directly or through others, Hitachi, Ltd. produced NanoChip(TM) Molecular Biology Workstations outside of Japan. In addition, we currently develop and manufacture the NanoChip(TM) Cartridges for distribution worldwide. Except for Hitachi, Ltd.'s exclusive distribution rights of Hitachi, Ltd. produced Workstations in Japan, the agreement is non-exclusive and excludes certain clinical markets. We also retain the right to form other manufacturing and distribution agreements.

In July 2000, we executed a ten-year agreement with Hitachi, Ltd., Nissei Sangyo Co. Ltd. and Hitachi Instruments Service Co. Ltd. of Japan (collectively, "Hitachi") to develop, manufacture and distribute products based on the parties' proprietary technologies, potentially including, among other things, reduced-size instruments for genetic testing, integrated amplification and point-of-care detection. The agreement provides that the parties will jointly determine which projects to prioritize over the term of the agreement. The agreement may be terminated before its expiration by either party, subject to certain restrictions. Pursuant to the terms of the agreement, Hitachi and Nanogen each may contribute up to $28.5 million in cash over the ten-year period. In addition, Hitachi made an equity investment in Nanogen by purchasing 74,590 shares of Nanogen's common stock worth approximately $2.0 million pursuant to a private sale by Nanogen based on a per share price of $26.813 (the fair market value as of the signing date of the Hitachi agreement). The agreement expands on the agreement executed by us and Hitachi in January 2000. Hitachi has the right to be the exclusive distributor of collaboration products in Japan and, based upon the attainment of minimum sales targets to be mutually agreed upon, in other Asian countries. We retain the exclusive right to distribute collaboration products outside of these countries. The agreement is non-exclusive and excludes some clinical markets.

BECTON DICKINSON

In connection with Nanogen's joint venture with Becton Dickinson in October 1997, The Nanogen/Becton Dickinson Partnership, or the Partnership, a Delaware

general partnership was established. The Partnership was formed to develop and commercialize products in the field of IN VITRO nucleic acid-based diagnostic and monitoring technologies in infectious diseases.

In September 2000, we and Becton Dickinson modified the joint venture to permit the partners the opportunity to commercialize certain of the Partnership's technology and allow them to collaborate with third parties to develop and commercialize certain products in the field of infectious diseases. Pursuant to amendments to the Master Agreement, the General Partnership Agreement and the Collaborative Research and Development and License Agreement, the Partnership exclusively licensed other Partnership technology developed up to that date to Becton Dickinson and Becton Dickinson exclusively sublicensed the Partnership technology to Nanogen to commercialize products in the field of infectious diseases. Becton Dickinson also agreed to non-exclusively license SDA technology to Nanogen for its use and for sublicensing purposes in the field of infectious diseases. Becton Dickinson also expanded the field of use for our SDA license outside of the Partnership to not only include IN VITRO human genetic testing and IN VITRO cancer diagnostics, but also IN VITRO testing of environmental, agricultural and veterinary samples. Pursuant to the amendments, Becton Dickinson paid us $300,000. We do not expect to receive any additional funding from Becton Dickinson.

ELAN

In December 1997, we entered into an agreement with Elan Corporation, plc ("Elan") for a non-exclusive research and development agreement for the development of genomics and gene expression research tools. We and Elan have not agreed upon specific program objectives with respect to the nonexclusive research and development program. In 1999 and 1998, revenues earned by us pursuant to this agreement were approximately $568,000 and $929,000, respectively. No revenue was recognized under the agreement during 2000. We do not expect to receive any additional funding from Elan.

RESEARCH AND PRODUCT DEVELOPMENT

In the near term, Nanogen is working to develop its NanoChip(TM) System to provide gene expression analysis capabilities, a key component in realizing the potential of the post genomics era. Nanogen seeks to further develop the NanoChip(TM) System, integrating new features and broadening the applications of the currently marketed system, including enhancing chip design and capabilities to simplify instrument design. Nanogen's scientists will investigate new opportunities, while customers may create new assays by taking advantage of the flexible format of the system.

We also intend to pursue new opportunities utilizing electronics beyond the current microchip concept. Future technologies may include integration of sample processing and DNA amplification. The NanoChip(TM) System may be designed to provide analysis of other charged molecules and anitigen-antibody, enzyme substrate, cell-receptor, and cell-separation techniques. The NanoChip(TM) System eventually may also become a portable lab on a chip for use in the field, away from the laboratory bench.

Nanogen may also continue to develop leading edge technologies such as micro electro-mechanical systems ("MEMS"), micro-fluidics, miniaturized capillary electrophoresis and the application of electronics to high throughput screening.

One mechanism to fund and implement new technologies or applications is

through the government grant system. In 2000, Nanogen's scientists received grants from the Space and Naval Warfare Systems Center San Diego to develop an integrated electronics-based sample to answer technology and from the U.S. Army to develop technology to identify biological warfare compounds if used in combat against U.S. troops. The development of these new technologies represent important elements in Nanogen's long-term platform development strategy.

PROPRIETARY TECHNOLOGY AND PATENTS

As of December 31, 2000, we have twenty issued U.S. patents, thirteen foreign issued patents and a number of pending patent applications filed in the U.S. and abroad. In addition to pursuing patents and patent applications relating to our platform technology, we may enter into other license arrangements to obtain rights to third-party intellectual property where appropriate.

Our or our licensors' patent applications may not be issued. Issued patents may not be found valid if challenged. In addition, intellectual property rights licensed by us may not be successfully integrated into commercial products. Others may independently develop similar technologies or duplicate any technology developed by us. Because of the extensive time required for development, testing, and regulatory review of a potential product, it is possible that, before any of our products can be commercialized, any related patent may expire or remain in existence for only a short period following commercialization, thus reducing any advantage of the patent, which could adversely affect our ability to protect future product development and, consequently, our business, financial condition and results of operations.

We seek to protect our inventions through filing U.S. patents and foreign counterpart applications in selected other countries. Because patent applications in the U.S. are maintained in secrecy for at least eighteen months after the applications are filed and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain that we were the first to make the inventions covered by each of our issued or pending patent applications or that we were the first to file for protection of inventions set forth in such patent applications. Our planned or potential products may be covered by third-party patents or other intellectual property rights, in which case continued development and marketing of the products would require a license. Required licenses may not be available to us on acceptable terms, if at all. If we do not obtain these licenses, we could encounter delays in product introductions while we attempt to design around the patents, or could find that the development, manufacture or sale of products requiring these licenses is foreclosed.

We are aware of U.S. and corresponding foreign patents and applications which are assigned to Affymax Technologies, N.V., and Affymetrix which relate to certain devices having 1,000 or more groups of oligonucleotides occupying a total area of less than 1 cm(2) and 400 different oligonucleotides per cm(2) on a substrate. In the event that we proceed with the development of arrays with more than 400 groups of oligonucleotides, we expect to design our devices through, among other things, the selection of the physical dimensions, methods of binding and selection of support materials to avoid infringing these patents. We may not be able to design around these patents. We are aware of U.S. and European patents and patent applications owned by Isis Innovations Ltd. (E. M. Southern). We have opposed one allowed European patent which had broad claims to array technology for analyzing a predetermined polynucleotide sequence. Isis Innovations' position with respect to the opposed patent is that the claims relate to what it terms the "diagnostic mode." Those claims have now all been

narrowed to the point that if the claims are accepted by the European Patent Office, they would not be infringed by our technology. On May 5, 1998, The Opposition Division of the European Patent Office issued a provisional nonbinding opinion that the claims should be revoked. If the claims of the original European patent survive the opposition or if an application relating to arrays issues in another country with claims as broad as the original European patent, we would be subject to infringement claims that could delay or preclude sales of some or all of our anticipated diagnostic products.

In addition to the patent litigation with Motorola and MIT, and with CombiMatrix and Dr. Montgomery described in Item 3 herein, other litigation may be necessary to defend against or assert claims of infringement, to enforce patents issued to us, to protect trade secrets or know-how owned by us or to determine the scope and validity of the proprietary rights of others. In addition, interference proceedings declared by the U.S. Patent and Trademark Office may be necessary to determine the priority of inventions with respect to our patent applications. Litigation or interference proceedings could result in substantial costs to and diversion of our effort, and could have a material adverse effect on our business, financial condition, and results of operations. Any such efforts may not be successful.

We may rely on trade secrets to protect our technology. Trade secrets are difficult to protect. We seek to protect our proprietary technology and processes by confidentiality agreements with our employees and certain consultants and contractors. These agreements may be breached, we may not have adequate remedies for any breach and our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our employees or our consultants or contractors use intellectual property owned by others in their work for us, disputes may also arise as to the rights in related or resulting know-how and inventions. We are currently in litigation concerning trade secret issues against CombiMatrix and Dr. Montgomery as described in Item 3.

MANUFACTURING

In January 2000 we formed a collaboration with Hitachi for the manufacture of our NanoChip(TM) Molecular Biology Workstation instruments. In July 2000, we executed a ten-year agreement with Hitachi, Ltd., Nissei Sangyo Co. Ltd. and Hitachi Instruments Service Co. Ltd. of Japan to develop, manufacture and distribute products based on the parties' proprietary technologies. For the manufacture of the NanoChip(TM) Cartridge, we perform many of the proprietary assembly steps in-house. We believe our technology allows for large-scale microchip production at a relatively low cost. We believe that the implementation of this scalability and low cost will help promote the rapid acceptance of our proprietary semiconductor-based platform technology as an industry standard. However, achieving these efficiencies will require substantial commercial volumes and there can be no assurance we will be successful in generating sufficient demand to scale up manufacturing capacity to levels that will allow our products to be priced competitively.

SALES AND MARKETING

We began commercializing the NanoChip(TM) Molecular Biology Workstation during the second quarter of 2000. We have built a commercial structure which allows us to sell directly in certain markets, while selling through distributors and partners in other markets. Our commercial organization includes direct sales representatives and sales management, field support personnel and marketing. We began selling our product directly to customers in the United

States, Canada and selected European countries such as Germany and the United Kingdom. Hitachi's distribution company, Nissei Sangyo Co. Ltd. began distributing our product in Japan during the second half of 2000. We expect to augment our commercial selling process by adding distributor partners in other countries. To support the commercial efforts in Europe, in August 2000 we established Nanogen Europe B.V., a company with limited liability, in The Netherlands. This wholly-owned subsidiary operates as our primary European sales and marketing office. In San Diego, we are supporting world-wide field activities with a customer applications laboratory. This laboratory will be used to assist in early customer demonstrations, protocol development and training.

COMPETITION

As we develop applications of our technology, we expect to encounter intense competition from a number of companies that offer products competing in our targeted applications. We anticipate that our competitors in these areas will include health care companies that manufacture laboratory-based tests and analyzers, diagnostic and pharmaceutical companies, as well as companies developing drug discovery technologies. To the extent we are successful in developing products in these areas, we will face competition from established and development-stage companies.

In many instances, our competitors have substantially greater financial, technical, research, and other resources and larger, more established marketing, sales, distribution and service organizations than we. Moreover, competitors may offer broader product lines and have greater name recognition than we, and may offer discounts as a competitive tactic. In addition, several development stage companies are making or developing products that compete with our potential products. There can be no assurance that our competitors will not succeed in developing or marketing technologies or products that are more effective or commercially attractive than our potential products, or that would render our technologies and products obsolete. Also, we may not have the financial resources, technical expertise or marketing, distribution or support capabilities to compete successfully in the future. Our success will depend in large part on our ability to maintain a competitive position with respect to our technologies. Rapid technological development by others may also result in competing products or technologies.

GOVERNMENT REGULATION

For our initial commercial market, the biomedical research market, we do not anticipate the need for FDA or other regulatory approval. We have not applied for FDA or other regulatory approvals with respect to any of our products under development. We anticipate, however, that the manufacturing, labeling, distribution and marketing of some or all of the diagnostic products we may develop and commercialize in the future will be subject to regulation in the U.S. and in other countries. In addition to clinical diagnostic markets, we also may pursue forensic, agricultural, environmental, laboratory and industrial applications for our products which may be subject to different government regulation. Aspects of our manufacturing and marketing activities may also be subject to federal, state and local regulation by various governmental authorities.

In the U.S., the FDA regulates, as medical devices, most diagnostic tests and IN VITRO reagents that are marketed as finished test kits and equipment. Pursuant to the Federal Food, Drug, and Cosmetic Act, and the regulations promulgated thereunder, the FDA regulates the preclinical and clinical testing, design, manufacture, labeling, distribution and promotion of medical devices. We

will not be able to commence marketing or commercial sales in the U.S. of new medical devices that fall within the FDA's jurisdiction until we receive clearance or approval from the FDA, which can be a lengthy, expensive, and uncertain process. Noncompliance with applicable requirements can result in, among other things, administrative or judicially imposed sanctions such as injunctions, civil penalties, recall or seizure of products, total or partial suspension of production, failure of the government to grant premarket clearance or premarket approval for devices, withdrawal of marketing clearances or approvals, or criminal prosecution.

In the U.S., medical devices are generally classified into one of three classes (I.E., Class I, II or III) on the basis of the controls deemed necessary by the FDA to reasonably ensure their safety and effectiveness. Class I devices are subject to general controls (e.g., labeling, premarket notification, and adherence to Quality System Regulation, or QSR). Class II devices are subject to general and special controls (e.g., performance standards, postmarket surveillance, patient registries and FDA guidelines). Generally, Class III devices are those which must receive premarket approval by the FDA to ensure their safety and effectiveness (e.g., life-sustaining, life-supporting, and implantable devices or new devices which have been found not to be substantially equivalent to a legally marketed devices). Before a new device can be introduced in the market, the manufacturer must generally obtain FDA clearance of a 510(k) notification or approval of a PMA application. Our products will vary significantly in the degree of regulatory approvals required. We believe that certain of our products for research, genomics, drug discovery and industrial applications will not require regulatory approvals or clearance. Some diagnostic products will require 510(k) approvals while other diagnostic and genetic testing products will require PMA approvals.

A 510(k) clearance will generally only be granted if the information submitted to the FDA establishes that the device is "substantially equivalent" to a legally marketed predicate device. For any devices that are cleared through the 510(k) process, significant modifications or enhancements in the design or intended use that could significantly affect safety or effectiveness will require new 510(k) submissions. It generally takes at least nine to twelve months from submission to obtain 510(k) premarket clearance but the process may take longer.

The PMA approval process is more expensive, uncertain, and lengthy than the 510(k) clearance process. A PMA must prove the safety and effectiveness of the device to the FDA's satisfaction, which typically requires extensive data, including but not limited to, technical, preclinical, clinical trials, manufacturing and labeling to demonstrate the safety and effectiveness of the device. Although clinical investigations of most devices are subject to the investigational device exemption requirements, clinical investigations of IN VITRO diagnostic tests, such as our products and products under development, are exempt from the investigational device exemption requirements, including the need to obtain the FDA's prior approval, provided the testing is noninvasive, does not require an invasive sampling procedure that presents a significant risk, does not introduce energy into the subject, and is not used as a diagnostic procedure without confirmation by another medically established test or procedure. In addition, the IN VITRO diagnostic tests must be labeled for research use only or investigational use only, and distribution controls must be established to assure that IVDs distributed for research or clinical investigation are used only for those purposes.

The FDA may determine that we must adhere to the more costly, lengthy, and uncertain PMA approval process for our potential products. Significant modifications to the design, labeling or manufacturing process of an approved device may require approval by the FDA of a PMA supplement or a new PMA application.

After a PMA is accepted for filing, the FDA begins its review of the submitted information, which generally takes between one and two years, but may take significantly longer. During this review period, the FDA may request additional information or clarification of information already provided. Also during the review period, an advisory panel of experts from outside the FDA will be convened to review and evaluate the application and provide recommendations to the FDA as to the approvability of the device. We may not be able to obtain necessary approvals on a timely basis, if at all, and delays in obtaining or failure to obtain such approvals, the loss of previously obtained approvals, or failure to comply with existing or future regulatory requirements could have a material adverse effect on our business, financial condition and results of operations.

Manufacturers of medical devices for marketing in the U.S. are required to adhere to the QSR requirements (formerly Good Manufacturing Practices), which include testing, control and documentation requirements. Manufacturers must also comply with Medical Device Reporting requirements that a manufacturer report to the FDA any incident in which its product may have caused or contributed to a death or serious injury, or in which its product malfunctioned and would be likely to cause or contribute to a death or serious injury upon recurrence. Labeling and promotional activities are subject to scrutiny by the FDA and, in certain circumstances, by the Federal Trade Commission. FDA enforcement policy prohibits the marketing of approved medical devices for unapproved uses.

We may become subject to routine inspection by the FDA and certain state agencies for compliance with QSR requirements, medical device reporting requirements and other applicable regulations. The recently finalized QSR requirements include design controls that will likely increase the cost of compliance. We may incur significant costs to comply with laws and regulations in the future and these laws and regulations may have a material adverse effect upon our business, financial condition and results of operation.

Any of our customers using our potential future diagnostic devices for clinical use in the U.S. may be regulated under the Clinical Laboratory Improvement Amendments of 1988 or CLIA. CLIA is intended to ensure the quality and reliability of clinical laboratories in the U.S. by mandating specific standards in the areas of personnel qualification, administration, participation in proficiency testing, patient test management, quality control, quality assurance and inspections. The regulations promulgated under CLIA establish three levels of diagnostic tests ("waived," "moderately complex" and "highly complex"), and the standards applicable to a clinical laboratory depend on the level of the tests it performs. CLIA requirements may prevent some clinical laboratories from using our diagnostic products. Therefore, CLIA regulations and future administrative interpretations of CLIA may have a material adverse impact on us by limiting the potential market for our products.

The Food and Drug Administration Modernization Act of 1997 makes changes to the device provisions of the FD&C Act or the Act and other provisions in the Act affecting the regulation of devices. Among other things, the changes will affect the Investigational Device Exemption, 510(k) and PMA processes, and also will affect device standards and data requirements, procedures relating to humanitarian and breakthrough devices, tracking and postmarket surveillance, accredited third-party review, and the dissemination of off-label information. We cannot predict how or when these changes will be implemented or what effect the changes will have on the regulation of our products. There can be no assurance that the new legislation will not impose additional costs or lengthen review times for our products.

Additionally, should we develop food pathogen products, they will be subject to the regulations of various domestic and foreign government agencies which regulate food safety and food adulteration, including the U.S. Department of Agriculture.

EMPLOYEES

As of December 31, 2000, we had 175 full-time employees, of whom 39 hold Ph.D. degrees and 25 hold other advanced degrees. Approximately 89 are involved in research and development, 31 in operations, manufacturing and quality assurance, 30 in sales and marketing, and 25 in finance, legal and other administrative functions. Our success will depend in large part upon our ability to attract and retain employees. We face competition in this regard from other companies, research and academic institutions, government entities and other organizations. None of our employees is covered by a collective bargaining agreement, and we believe that we maintain good relations with our employees.

FACTORS THAT MAY AFFECT RESULTS

OUR PRODUCTS MAY NOT BE SUCCESSFULLY DEVELOPED, WHICH WOULD HARM US AND FORCE US TO CURTAIL OR CEASE OPERATIONS.

We are at an early stage of development. We currently have only two products for sale, our NanoChip(TM) Molecular Biology Workstation and our NanoChip(TM) Cartridge. All of our other products are under development.

Our NanoChip(TM) System or our other products may not be successfully developed or commercialized on a timely basis, or at all. If we are unable, for technological or other reasons, to complete the development, introduction or scale-up of manufacturing of our new products, or if our products do not achieve a significant level of market acceptance, we would be forced to curtail or cease operations.

Our success will depend upon our ability to overcome significant technological challenges and successfully introduce our products into the marketplace. A number of applications envisioned by us will require significant enhancements to our basic technology platform. There can be no assurance that we can successfully develop such enhancements.

LACK OF MARKET ACCEPTANCE OF OUR TECHNOLOGY WOULD HARM US.

We may not be able to develop commercially viable products. Neither the products we have developed nor those we develop in the future may be accepted in the marketplace. If we are unable to achieve market acceptance, we will not be able to generate sufficient product revenue to become profitable. Market acceptance will depend on many factors, including our ability to:

- convince prospective strategic partners and customers that our technology is an attractive alternative to other technologies;

- manufacture products in sufficient quantities with acceptable quality and at an acceptable cost; and

- sell, place and service sufficient quantities of our products.

In addition, our technology platform could be harmed by limited funding available for product and technology acquisitions by our customers, internal

obstacles to customer approvals of purchases of our products and market conditions in general.

COMMERCIALIZATION OF SOME OF OUR POTENTIAL PRODUCTS DEPENDS ON COLLABORATIONS WITH OTHERS. IF OUR COLLABORATORS ARE NOT SUCCESSFUL OR IF WE ARE UNABLE TO FIND COLLABORATORS IN THE FUTURE, WE MAY NOT BE ABLE TO DEVELOP THESE PRODUCTS.

Our strategy for the research, development and commercialization of some of our future products requires us to enter into contractual arrangements with corporate collaborators, licensors, licensees and others. Our success depends in part upon the performance by these collaborators of their responsibilities under these arrangements. Some collaborators may not perform their obligations as we expect or we may not derive any revenue from these arrangements.

We have collaborative agreements with a health care company, pharmaceutical companies and a developer and manufactuer of instrumentation products. We do not know whether these companies will successfully develop and market any products under our respective agreements. Moreover, some of our collaborators are also researching competing technologies targeted by our collaborative programs. We may be unsuccessful in entering into other collaborative arrangements to develop and commercialize our products. In addition, disputes may arise over ownership rights to intellectual property, know-how or technologies developed with our collaborators.

We currently have agreements with Aventis, Becton Dickinson, Elan and Hitachi, Ltd. that contemplate the commercialization of products resulting from research and development collaboration agreements between the parties. In addition, we have a manufacturing and distribution agreement with Hitachi. These collaborations may not be successful. During the year ended, December 31, 2000, Becton Dickinson agreed to pay $300,000 related to amendments of existing Partnership agreements. We do not expect to receive any additional funds from Becton Dickinson. We have not agreed upon specific program objectives with respect to our research and development agreement with Elan. We do not expect to receive any additional funds from Elan.

WE HAVE A HISTORY OF NET LOSSES. WE EXPECT TO CONTINUE TO INCUR NET LOSSES AND WE MAY NOT ACHIEVE OR MAINTAIN PROFITABILITY.

We began selling our first two products in the second quarter of 2000, but we did not sell significant quantities of our first products during fiscal 2000. From our inception to December 31, 2000, we have incurred cumulative net losses totaling approximately $90.9 million. Moreover, our negative cash flow and losses from operations will continue to increase for the foreseeable future. We may never generate sufficient product revenue to become profitable. We also expect to have quarter-to-quarter fluctuations in revenues, expenses and losses, some of which could be significant. The amount and timing of product revenue recognition may depend on whether potential customers for the NanoChip(TM) System choose to enter into title transfer or non-title transfer transactions.

To develop and sell our products successfully, we will need to increase our spending levels in research and development, as well as in selling, marketing and administration. We will have to incur these increased spending levels before knowing whether our products can be sold successfully.

WE MAY NEED ADDITIONAL CAPITAL IN THE FUTURE. IF ADDITIONAL CAPITAL IS NOT AVAILABLE, WE MAY HAVE TO CURTAIL OR CEASE OPERATIONS.

We may need to raise more money to continue the research and development

necessary to bring our products to market and to establish manufacturing and marketing capabilities. We may seek additional funds through public and private stock offerings, arrangements with corporate partners, borrowings under lease lines of credit or other sources. If we cannot raise more money we will have to reduce our capital expenditures, scale back our development of new products, reduce our workforce and license to others products or technologies that we otherwise would seek to commercialize ourselves. The amount of money we will need will depend on many factors, including among others:

- the progress of our research and development programs;

- the commercial arrangements we may establish;

- the time and costs involved in:

- scaling up our manufacturing capabilities;

- meeting regulatory requirements, including obtaining necessary regulatory clearances or approvals;

- filing, prosecuting, defending and enforcing patent claims and litigation; and

- the scope and results of our future preclinical studies and clinical trials, if any.

Additional capital may not be available on terms acceptable to us, or at all. Any additional equity financing may be dilutive to stockholders, and debt financing, if available, may include restrictive covenants.

COMPETING TECHNOLOGIES MAY ADVERSELY AFFECT US.

We expect to encounter intense competition from a number of companies that offer products in our targeted application areas. We anticipate that our competitors in these areas will include:

- health care and other companies that manufacture laboratory-based tests and analyzers;

- diagnostic and pharmaceutical companies; and

- companies developing drug discovery technologies.

If we are successful in developing products in these areas, we will face competition from established companies and numerous development-stage companies that continually enter these markets.

In many instances, our competitors have substantially greater financial, technical, research and other resources and larger, more established marketing, sales, distribution and service organizations than we. Moreover, these competitors may offer broader product lines and have greater name recognition than we and may offer discounts as a competitive tactic.

In addition, several development-stage companies are currently making or developing products that compete with or will compete with our potential products. Our competitors may succeed in developing, obtaining FDA approval for or marketing technologies or products that are more effective or commercially attractive than our potential products, or that render our technologies and

potential products obsolete. As these companies develop their technologies, they may develop proprietary positions which may prevent us from successfully commercializing products.

Also, we may not have the financial resources, technical expertise or marketing, distribution or support capabilities to compete successfully in the future.

THE UNCERTAINTY OF PATENT AND PROPRIETARY TECHNOLOGY PROTECTION MAY ADVERSELY AFFECT US.

Our success will depend in part on obtaining and maintaining meaningful patent protection on our inventions, technologies and discoveries. Our ability to compete effectively will depend on our ability to develop and maintain proprietary aspects of our technology, and to operate without infringing the proprietary rights of others, or to obtain rights to third-party proprietary rights, if necessary. Our pending patent applications may not result in the issuance of patents. Our patent applications may not have priority over others' applications, and even if issued, our patents may not offer protection against competitors with similar technologies. Any patents issued to us may be challenged, invalidated or circumvented and the rights created thereunder may not afford us a competitive advantage.

We also rely upon trade secrets, technical know-how and continuing inventions to develop and maintain our competitive position. Others may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology and we may not be able to meaningfully protect our trade secrets, or be capable of protecting our rights to our trade secrets. We seek to protect our technology and patents, in part, by confidentiality agreements with our employees and contractors. Our employees may breach their existing Proprietary Information, Inventions, and Dispute Resolution Agreements and these agreements may not protect our intellectual property. This could have a material adverse effect on us.

OUR PRODUCTS COULD INFRINGE ON THE INTELLECTUAL PROPERTY RIGHTS OF OTHERS, WHICH MAY SUBJECT US TO FUTURE LITIGATION AND CAUSE US TO BE UNABLE TO LICENSE TECHNOLOGY FROM THIRD PARTIES.

Our commercial success also depends in part on us neither infringing valid, enforceable patents or proprietary rights of third parties, nor breaching any licenses that may relate to our technologies and products. Besides the patent involved in litigation with Motorola, MIT and Genometrix described below, we are aware of other third-party patents that may relate to our technology. It is possible that we may unintentionally infringe these patents or other patents or proprietary rights of third parties. We may in the future receive notices claiming infringement from third parties as well as invitations to take licenses under third-party patents. Any legal action against us or our collaborative partners claiming damages and seeking to enjoin commercial activities relating to our products and processes affected by third-party rights may require us or our collaborative partners to obtain licenses in order to continue to manufacture or market the affected products and processes. In addition, these actions may subject us to potential liability for damages. We or our collaborative partners may not prevail in an action and any license required under a patent may not be made available on commercially acceptable terms, or at all.

There are many U.S. and foreign patents and patent applications held by third parties in our areas of interest, and we believe that, besides our litigation with Motorola, MIT and Genometrix described below, there may be significant other litigation in the industry regarding patent and other intellectual property rights. Additional litigation could result in substantial

costs and the diversion of management's efforts regardless of the result of the litigation. Additionally, the defense and prosecution of interference proceedings before the U.S. Patent and Trademark Office, or USPTO, and related administrative proceedings would result in substantial expense to us and significant diversion of effort by our technical and management personnel. We may in the future become subject to USPTO interference proceedings to determine the priority of inventions. In addition, laws of some foreign countries

do not protect intellectual property to the same extent as do laws in the U.S., which may subject us to additional difficulties in protecting our intellectual property in those countries.

We are aware of U.S. and corresponding foreign patents and applications which are assigned to Affymax Technologies, N.V., and Affymetrix, Inc. which relate to certain devices having 1,000 or more groups of oligonucleotides occupying a total area of less than 1 cm(2), 400 different oligonucleotides per cm(2) on a substrate, and for gene expression, more than 100 different oligonucleotides at a density greater than about 60 different oligonucleotides per 1 cm(2). In the event that we proceed with the development of arrays with more than 400 groups of oligonucleotides, or for gene expression, with more than 100 different oligonucleotides, we expect to design our devices through, among other things, the selection of the physical dimensions, methods of binding, selection of support materials and intended uses of the device to avoid infringing these patents. We may not be able to design around these patents. We are aware of U.S. and European patents and patent applications owned by Isis Innovations Ltd. or Isis Innovations (E. M. Southern). We have opposed one allowed European patent which had broad claims to array technology for analyzing a predetermined polynucleotide sequence. Isis Innovations' position with respect to the opposed patent is that the claims relate to what it terms the "diagnostic mode." Those claims have now all been narrowed to the point that if the claims are accepted by the European Patent Office, they would not be infringed by our technology. On May 5, 1998, the Opposition Division of the European Patent Office issued a provisional nonbinding opinion that the claims should be revoked. If the claims of the original European patent survive the opposition or if an application relating to arrays issues in another country with claims as broad as the original European patent, we would be subject to infringement claims that could delay or preclude sales of some or all of our anticipated diagnostic products.

WE ARE INVOLVED IN INTELLECTUAL PROPERTY LITIGATION THAT IS AND MAY CONTINUE TO BE COSTLY, TIME-CONSUMING AND MAY IMPACT OUR COMPETITIVE POSITION.

In April 2000, we filed a complaint for declaratory judgment against Motorola, Inc. ("Motorola"), Beckman Coulter, Inc. ("Beckman") and Massachusetts Institute of Technology ("MIT") in the United States District Court for the Southern District of California. Prior to the filing of the complaint, the parties had been involved in licensing discussions concerning U.S. Patent No. 5,693,939 entitled "Optical and Electrical Methods and Apparatus For Molecule Detection" (the "'939 patent") which was licensed by MIT to Beckman in 1993 and to Genometrix, Inc. ("Genometrix") in 1994. Genometrix in turn granted its sublicensing rights to Motorola in 1999. The inventions claimed in the `939 patent were made with United States government funding through a grant from the Department of the Air Force. The complaint seeks, among other things, a declaration that we are entitled to a license to the government funded `939 patent and that we are not required to obtain a license from both Motorola and Beckman. Alternatively, the complaint seeks a declaratory judgment that the claims of the `939 patent are invalid and not infringed by us.

In May 2000, we reached a settlement with Beckman and dismissed Beckman from the lawsuit without prejudice. In connection with the settlement, we secured a license to the `939 patent from Beckman.

The action continues against Motorola and MIT. Motorola filed a counterclaim against us in May 2000, claiming infringement of the `939 patent and seeking monetary damages and injunctive relief. Motorola's counterclaim asserts that it has exclusive rights to certain claims in the `939 patent. In October 2000, our motion for leave to amend the complaint to add Genometrix as a defendant was granted. Fact discovery was substantially completed in early March 2001. The pretrial conference is currently scheduled for October 2001. No assurance can be given that a license to the `939 patent will be available from Motorola on commercially acceptable terms, or at all, or that we will prevail in the lawsuit. We have expended, and will continue to expend considerable financial resources and managerial efforts prosecuting the lawsuit and defending against Motorola's counterclaim, and against Motorola's, MIT's and Genometrix's affirmative defenses. We may not prevail in the action, which could have a material adverse effect on us.

In November 2000, we filed a complaint against CombiMatrix Corp. ("CombiMatrix") and Dr. Donald Montgomery in the United States District Court for the Southern District of California. Dr. Montgomery is a former Nanogen employee now affiliated with CombiMatrix.

The Nanogen complaint alleges that the naming of Dr. Montgomery as the sole inventor on U.S. Patent No. 6,093,302, entitled "Electrochemical Solid Phase Synthesis" (the "'302 patent"), and assignment of the `302 patent to CombiMatrix were incorrect and that the invention was made by Nanogen employees. The Complaint also alleges that inventions disclosed in the patent were Nanogen trade secrets and that CombiMatrix and Dr. Montgomery misappropriated these trade secrets by their actions, including publishing those trade secrets in patent applications. Nanogen's complaint, containing fourteen claims, seeks correction of inventorship, assignment of rights in the patent to Nanogen, an injunction preventing disclosure of trade secrets and damages for trade secret misappropriation.

On December 15, 2000, CombiMatrix and Dr. Montgomery filed a motion to dismiss Nanogen's complaint. On January 29, 2001, the motion was denied as to all claims except a claim for conversion, as to which the motion was granted without prejudice. We elected not to amend our complaint as to the conversion claim. On March 9, 2001, CombiMatrix and Dr. Montgomery answered Nanogen's complaint, asserted various affirmative defenses and filed a counterclaim for breach of contract against Nanogen for unspecified damages allegedly arising from the filing of the complaint at a time when CombiMatrix had announced its intent to make an initial public offering of its shares. The counterclaim asserts that Nanogen, by filing its complaint, breached a settlement agreement entered into between Nanogen and Dr. Montgomery in 1995. No assurances can be given that we will prevail in the lawsuit or that we can successfully defend ourselves against the counterclaim. We may have to expend considerable financial resources and managerial efforts prosecuting the lawsuit and defending against Dr. Montgomery's and CombiMatrix's counterclaim. We may not prevail in the action, which could have a material adverse effect on us.

THE REGULATORY APPROVAL PROCESS IS EXPENSIVE, TIME CONSUMING, UNCERTAIN AND MAY PREVENT US FROM OBTAINING REQUIRED APPROVALS FOR THE COMMERCIALIZATION OF OUR PRODUCTS.

We anticipate that the manufacturing, labeling, distribution and marketing of a number of any potential future diagnostic products will be subject to regulation in the U.S. and other countries. These regulations could subject us to several problems such as:

- failure to obtain necessary regulatory approvals or clearances for our products on a timely basis, or at all;

- delays in receipt of or failure to receive approvals or clearances;

- the loss of previously received approvals or clearances;

- limitations on intended uses imposed as a condition of approvals or clearances; or

- failure to comply with existing or future regulatory requirements.

In the U.S., the Food and Drug Administration, or FDA, regulates as medical devices most test systems, kits, and IN VITRO reagents that are marketed for human diagnostic use. Pursuant to the Federal Food, Drug, and Cosmetic Act, the FDA regulates the preclinical and clinical testing, design, safety, effectiveness, manufacture, labeling, distribution and promotion of medical devices. We will not be able to commence marketing or commercial sales in the U.S. of these products until we receive clearance or approval from the FDA, which can be a lengthy, expensive and uncertain process. We have not applied for FDA or other regulatory approvals with respect to any of our products under development. We may experience difficulties that could delay or prevent the successful development, introduction and marketing of proposed products. Regulatory clearance or approval of any proposed products may not be granted by the FDA or foreign regulatory authorities on a timely basis, if at all.

Noncompliance with applicable FDA requirements can result in:

- criminal prosecution, civil penalties, other administrative sanctions, or judicially imposed sanctions such as injunctions;

- recall or seizure of products;

- total or partial suspension of production;

- failure of the government to grant premarket clearance or premarket approval for devices or withdrawal of marketing clearances or approvals once granted.

The FDA also has the authority to request the recall, repair, replacement or refund of the cost of any regulated device manufactured or distributed by us. Any devices manufactured or distributed by us pursuant to FDA clearance or approvals are subject to thorough and continuing regulation by the FDA and certain state agencies, including the California Department of Health Services.

WE DEPEND ON SUPPLIERS FOR MATERIALS WHICH COULD IMPAIR OUR ABILITY TO MANUFACTURE OUR PRODUCTS.

Outside vendors provide key components and raw materials used by us and Hitachi in the manufacture of our products. Although we believe that alternative sources for these components and raw materials are available, any supply interruption in a limited or sole source component or raw material would harm our and Hitachi's ability to manufacture our products until a new source of

supply is identified and qualified. In addition, an uncorrected defect or supplier's variation in a component or raw material, either unknown to us or Hitachi or incompatible with our or Hitachi's manufacturing processes, could harm our or Hitachi's ability to manufacture products. We or Hitachi may not be able to find a sufficient alternative supplier in a reasonable time period, or on commercially reasonable terms, if at all. If we or Hitachi fail to obtain a supplier for the manufacture of components of our potential products, we may be forced to curtail or cease operations.

WE MAY NOT BE ABLE TO MANUFACTURE PRODUCTS ON A COMMERCIAL SCALE.

We and Hitachi rely on subcontractors to manufacture the limited quantities of microchips and other components we require for use by and sale to our customers, as well as for internal and collaborative purposes.

Manufacturing, supply and quality control problems may arise as we or Hitachi either alone, together or with subcontractors, attempt to scale up manufacturing procedures. We or Hitachi may not be able to scale-up in a timely manner or at a commercially reasonable cost. Problems could lead to delays or pose a threat to the ultimate commercialization of our products and cause us to fail.

We or Hitachi or any of our contract manufacturers could encounter manufacturing difficulties, including:

- the ability to scale up manufacturing capacity;

- production yields;

- quality control and assurance; or

- shortages of components or qualified personnel.

Our manufacturing facilities and those of Hitachi and any other of our contract manufacturers are or will be subject to periodic regulatory inspections by the FDA and other federal, state and international regulatory agencies and these facilities are or may become subject to QSR requirements of the FDA. If we, Hitachi or our third-party manufacturers, fail to maintain facilities in accordance with QSR regulations, other international quality standards or other regulatory requirements then the manufacture process could be suspended or terminated which would harm us.

ENERGY SHORTAGES MAY ADVERSELY IMPACT OUR OPERATIONS.

California is currently experiencing shortages of electrical power and other energy sources. This condition has periodically resulted in rolling brownouts, or the temporary and generally unannounced loss of the primary electrical power source. Our laboratory facility in San Diego is powered by electricity. Currently, we do not have secondary electrical power sources to mitigate the impacts of temporary or longer-term electrical outages. It is not anticipated that the power shortages will abate soon, and therefore, our operating facilities may experience brown-outs, black-outs, or other consequences of the shortage, and may be subject to usage restrictions or other energy consumption regulations that could adversely impact or disrupt our research and development, manufacturing and other activities.

THE INCREASE IN THE NUMBER OF OUR SALES AND MARKETING EMPLOYEES MAY NOT RESULT IN INCREASES IN SALES OR PLACEMENTS OF THE NANOCHIP(TM) SYSTEM.

We increased the number of employees in our sales and marketing group from three at December 31, 1999 to twenty-six at December 31, 2000. In addition, in July 2000, we incorporated a subsidiary, Nanogen Europe B.V. in The Netherlands as our European sales office. At December 31, 2000, this office employed four European-based sales executives in the United Kingdom, Germany, The Netherlands and Denmark.

Developing, training and monitoring this sales and marketing force has required and will further require capital and time expenditures by Nanogen and certain of its employees. The size of our sales and marketing force may not result in increased sales or placements of the NanoChip(TM) System nor increased product revenues associated with such sales or placements. Nanogen may be required to increase or decrease the size of this sales and marketing force as deemed necessary and such increases or decreases in staff will require additional capital and time expenditures by Nanogen and its employees.

FAILURE TO EXPAND OUR INTERNATIONAL SALES AS WE INTEND WOULD REDUCE OUR ABILITY TO BECOME PROFITABLE.

We expect that a portion of our sales will be made outside the United States. A successful international effort will require us to develop relationships with international customers and partners. We may not be able to identify, attract or retain suitable international customers and partners. As a result, we may be unsuccessful in our international expansion efforts. Furthermore, expansion into international markets will require us to continue to establish and expand foreign sales and marketing efforts, hire additional sales and marketing personnel and maintain good relations with our foreign customers and partners.

International operations involve a number of risks not typically present in domestic operations, including:

- currency fluctuation risks;
- changes in regulatory requirements;
- costs and risks of deploying the NanoChip(TM)System in foreign countries;
- licenses, tariffs and other trade barriers;
- political and economic instability;
- difficulties in staffing and managing foreign offices;
- potentially adverse tax consequences; and
- the burden and significant expense of complying with a wide variety of complex foreign laws and treaties.

Our international sales and marketing efforts will also be subject to the risks associated with the imposition of legislation and regulations relating to the import or export of high technology products. We cannot predict whether tariffs or restrictions upon the importation or exportation of our products will be implemented by the United States or other countries.

We may lose money when we exchange foreign currency received from international sales into U.S. dollars. A portion of our business is expected to be conducted in currencies other than the U.S. dollar. We recognize foreign currency gains or losses arising from our operations in the period incurred. As a result, currency fluctuations between the U.S. dollar and the currencies in which we do business will cause foreign currency translation gains and losses.

We cannot predict the effects of exchange rate fluctuations upon our future operating results because of the number of currencies involved, the variability of currency exposure and the potential volatility of currency exchange rates. We do not currently engage in foreign exchange hedging transactions to manage our foreign currency exposure.

IF WE FAIL TO MANAGE OUR GROWTH, OUR BUSINESS COULD BE IMPAIRED.

We expect to continue to experience growth in the number of our employees and the scope of our operating and financial systems. This growth has resulted in an increase in responsibilities for both existing and new management personnel. Our ability to manage growth effectively will require us to continue to implement and improve our operational, financial and management information systems and to recruit, train, motivate and manage our employees. We may not be able to manage our growth and expansion, which would impair our business.

WE MAY HAVE SIGNIFICANT PRODUCT LIABILITY EXPOSURE.

We face an inherent business risk of exposure to product liability and other claims in the event that our technologies or products are alleged to have caused harm. These risks are inherent in the testing, manufacturing and marketing of our products. We may not be able to obtain insurance for such potential liability on acceptable terms with adequate coverage, or at reasonable costs. Any potential product liability claims could exceed the amount of our insurance coverage or may be excluded from coverage under the terms of the policy. Our insurance, once obtained, may not be renewed at a cost and level of coverage comparable to that then in effect.

IF WE LOSE OUR KEY PERSONNEL OR ARE UNABLE TO ATTRACT AND RETAIN ADDITIONAL PERSONNEL, WE MAY NOT BE ABLE TO PURSUE COLLABORATIONS OR DEVELOP OUR OWN PRODUCTS.

We are highly dependent on the principal members of our scientific, manufacturing, marketing and management personnel, the loss of whose services might significantly delay or prevent the achievement of our objectives. We face competition from other companies, academic institutions, government entities and other organizations in attracting and retaining personnel.

HEALTH CARE REFORM AND RESTRICTIONS ON REIMBURSEMENT MAY LIMIT OUR RETURNS ON POTENTIAL PRODUCTS.

Our ability to earn sufficient returns on our products will depend in part on the extent to which reimbursement for our products and related treatments will be available from:

- government health administration authorities;
- private health coverage insurers;
- managed care organizations; and
- other organizations.

If appropriate reimbursement cannot be obtained, we could be prevented from

successfully commercializing our potential products.

There are efforts by governmental and third party payors to contain or reduce the costs of health care through various means. We expect that there will continue to be a number of legislative proposals to implement government controls. The announcement of proposals or reforms could impair our ability to raise capital. The adoption of proposals or reforms could impair our business.

Additionally, third party payors are increasingly challenging the price of medical products and services. If purchasers or users of our products are not able to obtain adequate reimbursement for the cost of using our products, they may forego or reduce their use. Significant uncertainty exists as to the reimbursement status of newly approved health care products, and whether adequate third party coverage will be available.

IF ETHICAL AND OTHER CONCERNS SURROUNDING THE USE OF GENETIC INFORMATION BECOME WIDESPREAD, WE MAY HAVE LESS DEMAND FOR OUR PRODUCTS.

Genetic testing has raised ethical issues regarding confidentiality and the appropriate uses of the resulting information. For these reasons, governmental authorities may 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. Any of these scenarios could reduce the potential markets for our products, which could seriously harm our business, financial condition and results of operations.

WE USE HAZARDOUS 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 storage, use and disposal of hazardous materials including biological hazardous materials and radioactive compounds. We are subject to federal, state and local regulations governing the use, manufacture, storage, handling and disposal of materials and waste products. Although we believe that our safety procedures for handling and disposing of these hazardous materials comply with the standards prescribed by law and regulation, the risk of accidental contamination or injury from hazardous materials cannot be completely eliminated. In the event of an accident, we could be held liable for any damages that result, and any liability could exceed the limits or fall outside the coverage of our insurance. We may not be able to maintain insurance on acceptable terms, or at all. We could be required to incur significant costs to comply with current or future environmental laws and regulations.

OUR STOCK PRICE COULD CONTINUE TO BE HIGHLY VOLATILE AND OUR STOCKHOLDERS MAY NOT BE ABLE TO RESELL THEIR SHARES AT OR ABOVE THE PRICE THEY PAID FOR THEM.

The market price of our common stock, like that of many other life sciences companies, has been highly volatile and is likely to continue to be highly volatile. The following factors, among others, could have a significant impact on the market price of our common stock:

- the results of our premarket studies and clinical trials or those of our collaborators or competitors or for DNA testing in general;

- evidence of the safety or efficacy of our potential products or the products of our competitors;

- the announcement by us or our competitors of technological innovations or new products;

- the announcement by us of acquisitions by customers of our NanoChip(TM)System or our other products;

- announcements or developments relating to our litigation against Motorola, MIT and Genometrix and to our litigation against Combimatrix and Dr. Montgomery;

- developments concerning our patents or other proprietary rights or those of our competitors, including other litigation or patent office proceedings;

- loss of key personnel or the increase or decrease in size of our sales and marketing staff;

- governmental regulatory actions or the failure to gain necessary clearances or approvals;

- changes or announcements in reimbursement policies;

- developments with our collaborators;

- changes in or announcements relating to acquisition programs for our products, including the expiration or continuation of our development site agreements;

- period-to-period fluctuations in sales and our operating results;

- market conditions for life science stocks in general; and

- changes in estimates of our performance by securities analysts.

OUR ANTI-TAKEOVER PROVISIONS COULD DISCOURAGE POTENTIAL TAKEOVER ATTEMPTS AND MAKE ATTEMPTS BY STOCKHOLDERS TO CHANGE MANAGEMENT MORE DIFFICULT.

The approval of two-thirds of our voting stock is required to approve some transactions and to take some stockholder actions, including the calling of a special meeting of stockholders and the amendment of any of the anti-takeover provisions contained in our certificate of incorporation. Further, pursuant to the terms of our stockholder rights plan adopted in November 1998, as amended, we have distributed a dividend of one right for each outstanding share of common stock. These rights will cause substantial dilution to the ownership of a person or group that attempts to acquire us on terms not approved by our board of directors and may have the effect of deterring hostile takeover attempts.

IF WE MAKE ANY ACQUISITIONS, WE WILL INCUR A VARIETY OF COSTS AND MAY NEVER REALIZE THE ANTICIPATED BENEFITS.

If appropriate opportunities become available, we may attempt to acquire businesses, technologies, services or products that we believe are a strategic fit with our business. We currently have no commitments or agreements with respect to any material acquisitions. If we do undertake any transaction of this sort, the process of integrating an acquired business, technology, service or product may result in operating difficulties and expenditures and may absorb significant management attention that would otherwise be available for ongoing development of our business. Moreover, we may never realize the anticipated benefits of any acquisition. Future acquisitions could result in potentially

dilutive issuances of equity securities, the incurrence of debt, contingent liabilities and/or amortization expenses related to goodwill and other intangible assets, which could adversely affect our results of operations and financial condition.

ITEM 2. PROPERTIES

We currently lease an approximately 45,000 square foot facility in San Diego, California, under a lease expiring in 2005. We have an option to renew the lease on this facility for two additional five-year terms. The facility currently houses our administrative offices and research and development laboratories, and is expected to be sufficient to meet our currently anticipated facilities needs at least through 2002.

ITEM 3. LEGAL PROCEEDINGS

In April 2000, we filed a complaint for declaratory judgment against Motorola, Inc. ("Motorola"), Beckman Coulter, Inc. ("Beckman") and Massachusetts Institute of Technology ("MIT") in the United States District Court for the Southern District of California. Prior to the filing of the complaint, the parties had been involved in licensing discussions concerning U.S. Patent No. 5,693,939 entitled "Optical and Electrical Methods and Apparatus For Molecule Detection" (the "'939 patent") which was licensed by MIT to Beckman in 1993 and to Genometrix, Inc. ("Genometrix") in 1994. Genometrix in turn granted its sublicensing rights to Motorola in 1999. The inventions claimed in the `939 patent were made with United States government funding through a grant from the Department of the Air Force. The complaint seeks, among other things, a declaration that we are entitled to a license to the government funded `939 patent and that we are not required to obtain a license from both Motorola and Beckman. Alternatively, the complaint seeks a declaratory judgment that the claims of the `939 patent are invalid and not infringed by us.

In May 2000, we reached a settlement with Beckman and dismissed Beckman from the lawsuit without prejudice. In connection with the settlement, we secured a license to the `939 patent from Beckman.

The action continues against Motorola and MIT. Motorola filed a counterclaim against us in May 2000, claiming infringement of the `939 patent and seeking monetary damages and injunctive relief. Motorola's counterclaim asserts that it has exclusive rights to certain claims in the `939 patent. In October 2000, our motion for leave to amend the complaint to add Genometrix as a defendant was granted. Fact discovery was substantially completed in early March 2001. The pretrial conference is currently scheduled for October 2001. No assurance can be given that a license to the `939 patent will be available from Motorola on commercially acceptable terms, or at all, or that we will prevail in the lawsuit. We have expended, and will continue to expend considerable financial resources and

managerial efforts prosecuting the lawsuit and defending against Motorola's counterclaim, and against Motorola's, MIT's and Genometrix's affirmative defenses. We may not prevail in the action, which could have a material adverse effect on us.

In November 2000, we filed a complaint against CombiMatrix Corp. ("CombiMatrix") and Dr. Donald Montgomery in the United States District Court for the Southern District of California. Dr. Montgomery is a former Nanogen employee now affiliated with CombiMatrix.

The Nanogen complaint alleges that the naming of Dr. Montgomery as the sole inventor on U.S. Patent No. 6,093,302, entitled "Electrochemical Solid Phase Synthesis" (the "`302 patent"), and assignment of the `302 patent to CombiMatrix were incorrect and that the invention was made by Nanogen employees. The Complaint also alleges that inventions disclosed in the patent were Nanogen trade secrets and that CombiMatrix and Dr. Montgomery misappropriated these trade secrets by their actions, including publishing those trade secrets in patent applications. Nanogen's complaint, containing fourteen claims, seeks correction of inventorship, assignment of rights in the patent to Nanogen, an injunction preventing disclosure of trade secrets and damages for trade secret misappropriation.

On December 15, 2000, CombiMatrix and Dr. Montgomery filed a motion to dismiss Nanogen's complaint. On January 29, 2001, the motion was denied as to all claims except a claim for conversion, as to which the motion was granted without prejudice. We elected not to amend our complaint as to the conversion claim. On March 9, 2001, CombiMatrix and Dr. Montgomery answered Nanogen's complaint, asserted various affirmative defenses and filed a counterclaim for breach of contract against Nanogen for unspecified damages allegedly arising from the filing of the complaint at a time when CombiMatrix had announced its intent to make an initial public offering of its shares. The counterclaim asserts that Nanogen, by filing its complaint, breached a settlement agreement entered into between Nanogen and Dr. Montgomery in 1995. No assurances can be given that we will prevail in the lawsuit or that we can successfully defend ourselves against the counterclaim. We may have to expend considerable financial resources and managerial efforts prosecuting the lawsuit and defending against Dr. Montgomery's and CombiMatrix's counterclaim. We may not prevail in the action, which could have a material adverse effect on us.

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

There were no matters submitted to a vote of security holders during the quarter ended December 31, 2000.

PART II

ITEM 5. MARKET FOR THE REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

(a) Changes in Securities

In October 2000, we sold 120,238 shares of our common stock to Aventis Research and Technologies at a per share price of $6.17. We relied on the exemption from registration provided by Section 4(2) of the Securities Act of 1933 in making the sale, based in part on the institutional nature of the purchaser and representations and warranties of the purchaser.

In November 1998, our Board of Directors adopted a Stockholder Rights Plan which provides for a dividend of one Preferred Stock Purchase Right for each share of common stock to stockholders of record on November 30, 1998. Each Right will entitle stockholders to buy one one-thousandth of a share of Series A Participating Preferred Stock of the Company at an exercise price of $50.00, subject to antidilution adjustments. The Rights will become exercisable only if a person or group becomes the beneficial owner of 15% or more of the common stock, or commences a tender or exchange offer which would result in the offeror beneficially owning 15% or more of common stock, which is not approved by our

Board of Directors. The Board of Directors is entitled to redeem the Rights at $0.01 per Right at any time prior to the public announcement of the existence of a 15% holder. If not earlier terminated or redeemed, the Rights will expire on November 17, 2008.

On December 12, 2000, our Board of Directors amended the Rights Plan to allow Citigroup Inc. and its affiliates and associates to acquire the beneficial ownership of up to 25% of the outstanding common stock of the Company without triggering the ability of our stockholders to exercise the rights governed by the Rights Plan. The Board of Directors required Citigroup to maintain its status as a filer on Schedule 13G with respect to its beneficial ownership of our common stock to take advantage of this exception.

(c) Market Information

Our common stock began trading on the National Association of Securities Dealers Automated Quotation ("Nasdaq") National Market on April 14, 1998, under the symbol "NGEN." Prior to that date, there was no established trading market for our common stock. The following table sets forth the range of high and low sales prices as reported for our common stock by Nasdaq for the periods indicated:

Fiscal 1999:	High	Low
1st Quarter	$ 9.64	$ 3.89
2nd Quarter	$ 9.75	$ 6.25
3rd Quarter	$ 8.64	$ 5.75
4th Quarter	$ 24.50	$ 6.50
Fiscal 2000:		
1st Quarter	$ 101.94	$ 18.00
2nd Quarter	$ 43.00	$ 14.50
3rd Quarter	$ 43.00	$ 17.25
4th Quarter	$ 20.44	$ 7.69

As of March 23, 2001, there were approximately 200 shareholders of record of our common stock. We have not paid any cash dividends to date and do not anticipate any being paid in the foreseeable future.

ITEM 6. SELECTED FINANCIAL DATA

The selected financial data set forth below with respect to our consolidated financial statements has been derived from the audited financial statements. The data set forth below should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and notes thereto appearing elsewhere

herein:

	YEARS ENDED DECEMBER 31			
	2000	1999	1998	
	(IN THOUSANDS, EXCEPT PER SHARE			
CONSOLIDATED STATEMENT OF OPERATIONS DATA:				
Revenues:				
Product	$ 919	$ --	$ --	
Sponsored research	8,457	5,688	5,461	
Contract and grant	1,856	2,431	2,172	
Total revenues	11,232	8,119	7,633	
Operating expenses:				
Cost of sales	599	--	--	
Research and development	18,905	25,284	23,002	
General				