NANOGEN INC
Form 10-K
March 31, 2003

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

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

For the fiscal year ended December 31, 2002

OR

o **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 $0.001 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 ý NO o

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. o

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Act),

YES o NO ý

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 June 28, 2002 (the last day of the registrant s most recently completed second fiscal quarter), as reported on the Nasdaq National Market was approximately $20,142,311. Shares of common stock held by each executive officer and director and by each person (including shares beneficially owned by Citigroup, Inc.) who own 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 22,058,579 as of March 24, 2003.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive proxy statement for its annual meeting of stockholders to be held in 2003 are incorporated by reference in Items 10, 11, 12 and 13 of Part III of this Form 10-K.

NANOGEN, INC.

FORM 10-K

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SIGNATURES

PART I

Item 1. Business

Forward Looking Statement

This Form 10-K includes forward-looking statements about our business and results of operations that are subject to risks and uncertainties that could cause our actual results to vary materially from those reflected in the forward-looking statements. Words such as believes, anticipates, plans, estimates, future, could, may, should, would, expect, envision, potentially, variations of such words and similar expres to identify such forward-looking statements. The forward-looking statements contained in this Form 10-K include, but are not limited to, statements about matters including the following: (i) the development of the markets and demand for our products and services; (ii) our product development plans, including the introduction of new products, and anticipated activities designed to pursue these plans, including collaborations and other corporate partnering arrangements; (iii) our ability to generate substantial revenues from sales of products and consumable cartridges and reagents and continuing revenues from reagent rental agreements; (iv) the ability of our product platform to affect the market and become an industry standard; (v) our ability to generate license and other fee revenue in the future; (vi) the amounts we invest in research and development activities in the future; (vii) future levels of operating expenses associated with our business; (viii) future levels of interest income; (ix) any amounts we may be able to realize from the liquidation of our investments, including our investments in short-term securities; (x) operating results of joint ventures and other corporate partnering arrangements; (xi) the amounts and timing of our contractual obligations and capital commitments and (xii) our future capital needs and our ability to fund those needs. Factors that could cause or contribute to these differences include those discussed under the caption Factors that May Affect Results and elsewhere in this Form 10-K. Readers are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof. We disclaim any intent or obligation to update these forward-looking statements.

Our internet address (presented as a textual reference only) is www.nanogen.com. We make available through our website, free of charge, an annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to these reports filed with or furnished to the SEC under Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after we file them with, or furnish them to, the SEC.

Overview

Molecular Diagnostics Market

Increased awareness of the role of genes in regulating the functions of living organisms has generated a worldwide effort to identify and sequence genes and genomes of many organisms, including the estimated three billion nucleotide pairs of the human genome. In June 2000, the effort led by the Human Genome Project (sponsored by the Department of Energy and the National Institutes of Health) resulted in a first complete draft of the human genome sequence. While it is anticipated that many years of additional research will be required to understand the specific functions and roles in disease of each of these genes and their patterns of interaction, this research, commonly referred to as genomics, is leading to a new healthcare paradigm where disease is understood at the molecular level. It is believed that the use of genomics will lead to the introduction of new therapies, the development of targeted therapeutics and an abundance of new screening tests that will, in turn, shift the focus of medicine to proactive from reactive. Molecular diagnostic tools are integral to rendering genetic information accessible to researchers and

clinicians.

The market for molecular diagnostics tools, assays and other products has been estimated by an independent study conducted by industry experts Frost & Sullivan to be approximately $1.9 billion in 2002 and is predicted to grow to

$3.1 billion by 2005. Of the $1.9 billion spent in 2002, the Company believes that approximately seventy-five percent (75%) was spent on infectious disease testing products for such diseases as Human Immune Deficiency Virus (HIV) and Hepatitis C Virus (HCV) and the remaining twenty-five percent (25%) was spent for other products such as those used in genetic testing. As the molecular diagnostics market grows, we expect human genetic testing to represent an increasingly larger percentage of this annual amount.

The molecular diagnostics market currently primarily consists of customers in (1) research institutions such as universities, research hospitals, private companies and government institutions, (2) high complexity CLIA (Clinical Laboratory Improvements Act)-certified clinical diagnostics laboratories and (3) clinical diagnostics laboratories in hospitals, private companies and government clinics. Such customers are developing tests and assays to screen, predict, diagnose, treat or monitor individuals who have certain single nucleotide polymorphisms (SNP), short tandem repeats (STRs), insertions, deletions or other genetic mutations that are correlated with various disease states. Research customers normally develop and perform assays that are designed to correlate various SNPs or other mutations with certain disease states. High complexity CLIA-certified laboratories, which are regulated under the federal CLIA rules, normally develop and validate their own home brew tests or they may run assays purchased from platform manufacturers or others. In the development and validation of a home brew test, a laboratory may utilize Analyte Specific Reagents (ASRs). ASRs are reagents manufactured under the good manufacturing practices regulations and are subject to Food and Drug Administration (FDA) ASR regulations. As such, ASRs do not require the filing of a 510(k) or PreMarket Approval (PMA) application. Clinical diagnostic laboratories normally run clinical assays to help physicians diagnose and treat various diseases and typically such assays require a 510(k) or PMA application prior to being offered for sale or distribution.

Molecular diagnostics customers are seeking a versatile, accurate, simple and cost-effective platform technology on which to develop, validate and run simple and complex research and diagnostics tests and assays. While there are a number of platform technologies currently available to such molecular diagnostics customers, including those utilizing gel-based techniques such as Restriction Fragment Length Polymorphisms (RFLP), sequencing using capillary and gel-based techniques, dot-blot and glass slide based arrays, real-time PCR (polymerase chain reaction) methods and enzyme-based micro-well assays, it is our understanding that these technologies do not consistently meet their basic customer requirements. These platforms lack the versatility to perform both simple and complex assays customers are seeking a platform capable of developing, validating and running a broad menu of research, ASRs and clinical diagnostic tests. The molecular diagnostics customers also demand a technology platform that consistently provides results at a level approaching 100% accuracy. They also insist on operational simplicity, so that the laboratory technicians of any skill level may be used for its operation. Finally, they are seeking a cost-effective technology platform that will assist in optimizing its capital and labor costs.

We believe that the technology used to develop human genetic testing could also be applied in the future to other markets such as food, water and animal testing among other fields.

The Company

Nanogen develops and commercializes molecular diagnostics products and tests for the gene-based testing market for sale primarily in the United States, Europe and the Pacific Rim. By integrating microelectronics and molecular biology into a core proprietary technology platform, the Company seeks to establish the unique, open-architecture design of its primary products, the NanoChip® Molecular Biology Workstation and the NanoChip® Cartridge (collectively, the NanoChip® System) as the standard platform for molecular identification and analysis. Nanogen also seeks to become a leading supplier of molecular diagnostics testing products by developing ASRs and other commercial applications for the NanoChip® System. The Company continually conducts research and development by itself and with its subsidiary and third parties, to improve the NanoChip® System and to extend its technology to other applications such as biodefense, forensics and drug discovery (protein kinases).

Nanogen believes that its technology platform provides a key advantage over conventional manual and mechanical platforms in that it provides an accurate, simple, versatile and cost-effective integrated microelectronic system that is capable of improving the quality of molecular diagnostic testing while reducing the overall cost of such testing. At the heart of Nanogen s technology is a silicon chip called the NanoChip® Electronic Microarray. Each Electronic Microarray has 100 mircrolocations or test sites upon which genetic tests can be conducted. DNA or RNA is moved and concentrated by controlling the electric current at each test site, improving accuracy, speed

and flexibility. This electronic concentration of molecules greatly accelerates molecular binding at each test site. In addition, our technology allows the simultaneous analysis of multiple test results, or multiplexing, from a single sample. Current applications of the NanoChip® Electronic Microarray include SNPs, STRs, insertions, deletions and other mutation analyses.

Nanogen s mission is to deliver high quality, innovative molecular diagnostics products and services. The Company s current commercially available products include (1) the NanoChip® Molecular Biology Workstation, an automated, multi-purpose instrument primarily used for DNA-based analyses, (2) the NanoChip® Cartridge, which incorporates the NanoChip® Electronic Microarray and provides a flexible tool for the rapid identification and precise analysis of biological test samples containing charged molecules, (3) various ASRs for detection of gene mutations associated with diseases such as cystic fibrosis and hereditary hemochromotosis and (4) Nanogen s Assay Toolbox™, that is designed to help customers develop tests on the NanoChip® System. The Company also has several other ASRs and applications of its proprietary technology under development. The Company provides technical support and field applications assistance to service and support its customers.

Nanogen is a Delaware corporation and its stock is listed on the Nasdaq National Market under the symbol NGEN . Its corporate offices are located at 10398 Pacific Center Court, San Diego, California 92121. Our main telephone number is 858-410-4600.

Our Technology and Relevant Markets

Limitations of Current Molecular Diagnostic Assay Technologies

The initial technique for the analysis of genetic variations was hybridization, which was first developed in the 1970s. Hybridization relies on the principle that a unique piece of DNA will bind, or hybridize, most strongly to its exact complement. In hybridization, short, synthetic segments of DNA, also known as probes, are used to locate and bind to their counterparts within a mixture of sample DNA or RNA. Hybridization is often performed using instrumentation that incorporates a detection medium that provides a signal to indicate whether the probe has hybridized to the sample DNA or RNA. However, initial hybridization techniques had several limitations. Even minute changes in testing conditions, could dramatically affect the outcome of the hybridization reaction and, therefore, the reliability of test results.

Beginning in the 1980s, various techniques were invented with the objective of improving the reliability of hybridization. However, these methods did not generally provide a signal that was sufficient to be easily detectable. Therefore, in order to use these methods, it was necessary to first copy or amplify the segment of DNA or RNA to be analyzed using a technique known as polymerase chain reaction, or PCR. These initial techniques have significant limitations, including:

Highly Complex Product Development Process: Conventional methods frequently require trial and error testing to validate tests or product designs. Therefore, with conventional technologies, the process of developing a test, or product, for analyzing a specific genetic variation is highly complex and cannot be automated easily.

Inaccuracy: Accuracy is essential to adequately detect and quantify genetic variations, which may involve the analysis of thousands of genetic variations per individual. Conventional methods can result in one or more data points in 10 being incorrect. These inaccuracies are magnified in tests for multiple variations. For example, in a test panel involving six genetic variations, the overall panel accuracy for a technology having a 95% accuracy per result would be only 74%. Accuracy is critical in molecular diagnostics.

Difficulty of Use: Many of the conventional analysis methods involve multiple technical steps requiring human intervention, which make the analysis difficult to perform and challenging to automate.

Lack of Flexibility: Many of the conventional analysis methods use a passive array in which what is done to one site on the array, must be done to all sites. This results in a lack of flexibility for the customer in using these technologies as they cannot mix different assays on a single array or may not fully utilize every site on the array.

Limited Clinical Viability: Because of the low degree of accuracy and difficulties associated with product development and use, conventional research methods have not been broadly applicable to clinical settings.

Lack of Menu: Many of the existing methods of analysis require customers to purchase different instruments or technologies for each analysis performed.

Beyond the limitations indicated above, in order to capture and expand the market for genetic analysis, one must provide cost-effective and highly reliable tests.

Despite recent advances in technology, many bioassays are too specialized or inflexible to be used throughout the various departments of a diagnostics or research laboratory. Current bioassay tools were designed for large scale data generation and the automation of repetitious tasks such as very high throughput discovery. In addition, many of these systems are not useful in molecular, protein, enzyme, cell biology, and forensics laboratories. These technologies 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 and in particular in the molecular diagnostics market.

The Nanogen Microelectronic Solution

Today, clinical and research laboratories use a number of different platforms to perform a wide-range of different molecular tests. We are marketing the NanoChip® System based on our proprietary microelectronic technology. The Company believes that the NanoChip® System provides the following eight major advantages:

Accuracy: Accuracy is critical in laboratory analysis. To date, the NanoChip® System has been shown to be exceptionally accurate. Additionally, the NanoChip® System embodies the technology that allows multiplexing capability. This means that it allows two or more tests to be performed simultaneously, speeding results to the laboratory technician. This capability has been critical in developing the ASRs for use in detecting the 25 mutations associated with the diagnosis of cystic fibrosis.

Simplicity. The NanoChip® System is fully automated and once programmed and validated by the customer, has simple point and click software. It allows the laboratory technician to load samples and easily modify parameters to facilitate minimal hands on time.

Versatility: One of the key attributes that positions the NanoChip® System as the platform for molecular diagnostics is its unique, open architecture. The flexible, addressable nature of the NanoChip® Cartridge enables assay development from a variety of sources. We believe this is particularly important to customers in an emerging and

rapidly growing market like molecular diagnostics, where new markers are constantly being introduced. The ability of a molecular laboratory to respond quickly to customers who request a test for a new marker without having to procure a new platform is key to their success.

Profit Incentive: Nanogen s focus is to offer a compelling value proposition to end users by providing laboratories an alternative to sending out their tests to third party laboratories. With Nanogen products, these smaller laboratories should have the potential to earn additional profits by handling tests within their own facilities.

Fast Assay Design: Experimental design of tests and assays on the NanoChip® System is relatively straightforward. Our customers can develop, program and validate assays in their own laboratories, allowing for faster turnaround times (i.e., days versus weeks) for solutions to complex analyses.

Ease of use: Assays are easy to develop, validate and perform on our NanoChip® System. Our fully automated Loader allows the simultaneous programming and testing on up to four NanoChip® Cartridges. A loaded Cartridge is inserted and then analyzed on the Nanogen Reader. The NanoChip® System also includes proprietary software to automate testing operation. All test design and development must be validated by the end user prior to reporting any results. Data interpretation that is user defined is clear-cut and presented in a user-friendly format.

Throughput: The NanoChip® System s ability to program as many as 100 test sites per Cartridge (and up to four Cartridges per run) allows for higher throughput than is achievable with many competitive technologies. As testing volumes in molecular laboratories continue to grow, throughput is becoming increasingly important. This throughput capacity permits highly efficient workflow for many biomedical applications in a variety of laboratory settings. We believe that the NanoChip® System is scalable to eventually utilize a Cartridge with 400 test sites at a time.

Cost effectiveness: The NanoChip® System has been designed to be a cost-effective solution for most molecular testing. The NanoChip® System s custom features allow users to employ their own reagents or Nanogen s ASRs in designing and validating assays for their specific purposes. Moreover, much of 2002 was dedicated to developing a menu of ASRs that many laboratories perform routinely. Consumables such as ASRs represent a significant revenue stream for companies providing successful platforms. 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.

Nanogen s Core Technology

Nanogen s patented microelectronics-based technology uses the natural positive or negative charge of most biological molecules. Applying an electric current to individual test sites on the NanoChip® System enables rapid movement and concentration of the molecules. Nanogen s technology involves electronically addressing biotinylated DNA samples, hybridizing complementary DNA and applying stringency to remove nonspecifically bound DNA after hybridization. The NanoChip® System technology provides an open platform that allows customers to effectively develop, validate and run common assays as well as customize their own tests.

The NanoChip® System can integrate in a single platform the following electronic operational features:

Electronic addressing

Electronic addressing involves placing charged molecules at specific test sites on a NanoChip® microarray. When a biotinylated sample solution is introduced onto the array, the negatively charged sample rapidly moves to the selected positively charged sites, where it is concentrated and bound to the streptavidin in the permeation layer. The array is then washed and another sample can be added. Site by site, row by row, an array of samples are assembled on the array. Such user-definable microchip arrays allow the customer to respond quickly to the ever evolving list of genes to be tested.

Electronic concentration and hybridization

In a standard SNP assay, following electronic addressing, red and green fluorescently-labeled reporter probes are used to discriminate between wildtype, heterozygote and mutant DNA. The ability of the NanoChip® technology to very specifically control binding of samples to reporters is a key feature of the platform.

Stringency control

Stringency control enables removal of unbound and nonspecifically-bound DNA quickly and easily after hybridization, providing quality control and ensuring that any bound pairs of DNA are truly complimentary. Nanogen s technology allows the customer to select electronic, thermal or chemical techniques, depending on the application, for precise, accurate stringency control. This provides extremely high discrimination and confidence in results.

Electronic multiplexing

The multiplexing feature is an extension of the open platform of the NanoChip® System. The customer may analyze multiple genes from a single test site (representing one sample) or from multiple test sites (representing different samples). The customer also has the ability to electronically address multiplexed amplicons to a single test site.

The ability to control individual test sites permits biochemically unrelated molecules to be used simultaneously on the same microchip array. Conventional DNA arrays do not have this feature all process steps must be performed on an entire array. Nanogen s microelectronic array technology delivers increased versatility over 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, we revised our relationship with Becton Dickinson. Nanogen was 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. We also believe that SDA may potentially provide our customers with operational benefits such as being easier to use as well as cost advantages due to the high cost of the most common amplification method. Although the current NanoChip® System does not utilize SDA, we expect our next generation instrument to support SDA applications.

Commercialization Strategy: Platformation™

What is happening today in molecular diagnostics closely mirrors the activities that occurred in clinical chemistry laboratories thirty years ago. The first clinical chemistry tests were done by hand they were time intensive and required great skill not unlike some of today s molecular diagnostic assays. Then single assay systems were developed that reduced hands-on time and hastened the reporting of results to physicians. When multiple assay systems were introduced, a series of assays could be performed simultaneously. And finally clinical chemistry platforms were developed that enabled all chemistry assays to be performed on one system, further streamlining the laboratory. The bottom line: a transformation from manual assays to automated accurate systems that could perform multiple assays simultaneously, increasing the reporting efficiency and reducing the time to a reportable result.

Nanogen has focused on capturing the market right from the start by creating an open molecular diagnostics platform that we believe has the potential to become the gold standard of the industry. The process of consolidating a number of various molecular tests onto one platform is what we have termed Platformation . Nanogen s business strategy utilizes Platformation along with a razor/razorblade approach to sales and distribution of our products. The Company continually seeks to increase the installed base of the NanoChip® Systems and to establish our platform as a standard for the molecular diagnostics industry in order to reap the benefits of the higher margin profits on consumables such as the NanoChip® Cartridges, ASRs and other products. The NanoChip® System s open architecture facilitates development of molecular tests from multiple sources, driving the growth in assay development far beyond where Nanogen could take it on its own. From customers to development partners and licensing agreements, all act as an inspired research arm for NanoChip® assay development.

The NanoChip® System could transform molecular diagnostics, bringing to it the speed, efficiency and accuracy of a robust platform. As this market area grows and Nanogen s market share increases, the NanoChip® System could generate multiple revenue sources that will fuel next generation systems and the growth of the Company. Thus,

Platformation is not only the framework for tomorrow s molecular diagnostics laboratory; it is the foundation of Nanogen.

Nanogen s strategy to establish the NanoChip® System as the leading molecular diagnostics platform is five-fold. First, the Company seeks to increase the installed base for the NanoChip® System for use in high complexity CLIA certified and research laboratories through direct sales, reagent rental and cost per test agreements as well as development site agreements. Second, Nanogen seeks to continue to increase the breadth of its ASR menu on its NanoChip® System. We will determine on a case by case basis whether or not to file with the FDA for approval or clearance to market its first FDA-cleared product for sale to clinical diagnostics laboratories. Third, Nanogen intends to develop other products on its platform to facilitate customers development of their own home brew

tests on the System. Fourth, the Company plans to make improvements to the NanoChip® System and to increase the depth of other applications of the NanoChip® Electronic Microarray technology for other uses. And fifth, Nanogen intends to continually seek out strategic collaborations in order to strengthen our product menu, penetrate new markets, obtain new intellectual property and seek to enter the molecular diagnostics provider services market when appropriate.

Increase Installed Base of NanoChip® Systems

Nanogen seeks to increase the installed base of its NanoChip® Molecular Biology Workstation and to establish the NanoChip® System as the standard platform for the molecular diagnostics industry, in order to reap the benefits of the higher margin profits on consumables, such as the NanoChip® Cartridges, ASRs and other products. The Company has provided its customers with three main types of commercial transactions to obtain the NanoChip® System: outright sales, reagent rental agreements and/or cost per test agreements (collectively, reagent rentals) and development site agreements.

Nanogen typically sells its NanoChip® Systems directly to its customers through the Company s sales representatives in the U.S. or Europe or through distributors in other countries throughout the world. As of December 31, 2002, the Company had sold 45 NanoChip® Systems.

The sale of NanoChip® Systems is only one piece of the revenue stream. As is common with clinical instruments, the consumables form a substantial revenue segment. NanoChip® Cartridges and those Cartridges and ASRs that are a part of each customer developed and validated assay will normally be ordered by customers to meet their testing demand. Nanogen anticipates demand to grow rapidly for certain ASRs, such as those for the detection of mutations in the CFTR gene that are associated with cystic fibrosis and the detection of mutations in the ApoE gene that are associated with Alzheimer s disease. While there may always be customers who wish to purchase the NanoChip® System outright, it is our belief that there will be many more within the high complexity CLIA-certified clinical laboratory market that will want to amortize the cost of the instrument over several years. These arrangements, called reagent rentals, have been the standard for the clinical instruments industry for the past 40 years, fueling the growth of industry leaders such as Beckman-Coulter, Abbott and Roche. Such agreements can span from three to five years and involve establishing a minimum monthly consumables ordering level. Based on that level and the term of the agreement, a premium is added to the cost of the consumables so that the total capital equipment cost of the NanoChip® System is recouped by the end of the agreement. The advantage of reagent rental agreements for Nanogen is that it locks in a minimum revenue flow over the term of each agreement after a normally brief validation period that normally varies from 30 to 90 days. Nanogen believes that many of its customers will increase their consumable ordering levels as new ASRs and ultimately FDA-cleared assays are made available. Because the customer s set premium level will be incorporated into each of these additional orders, Nanogen has the opportunity to obtain revenue over and above the cost of the original system during the life of the agreement. As of December 31, 2002, the Company had entered into 12 reagent rental agreements with customers, all of which were signed in 2002 and all of which were contingent upon the acceptance of the Company s ASR for the CFTR gene.

The increased use of reagent rental agreements is an indication of the Company s strategy to target more commercial transactions with high volume high complexity CLIA-certified laboratories. High complexity CLIA-certified clinical reference laboratories are traditionally the early adopters of new, innovative systems that bring efficiency to labor intensive assays. The Company s success in reaching beyond this core group into research hospitals and leading medical centers is a testament to the desire of these groups to enter into this testing segment.

The final type of agreement whereby a customer may use and eventually purchase a NanoChip® System, is a development site agreement. These development sites are normally with leading research organizations and laboratories or companies that will provide us with certain rights to commercialize the discoveries made using the our platform. These relationships have been focused on the discovery of the associations of specific genetic variations with major disease states, including cancer, hypertension, inflammation and cardiovascular disease. Our strategy is to offer our research collaborators early access in exchange for the rights to commercialize the discoveries they make using it. These rights may enable us to offer new genetic products for clinical research and clinical diagnostic applications if any are developed from the collaboration. Pursuant to development site

agreements, Nanogen installs a NanoChip® System at a customer site for a period ranging typically from six to nine months during which time the customer can test the System by developing, validating and running certain assays on the System. For the use of the System during this period, the Customer assigns to Nanogen rights to improvements to the System and Nanogen and the customer agree on certain Nanogen rights to any assays developed thereon. Once the development site period has terminated, the customer may then either return the System to the Company or purchase it through a sale or a reagent rental transaction. As of December 31, 2002, the Company had entered into 32 development site agreements with customers and converted 10 into commercial transactions that included 5 sales and 5 reagent rental transactions.

Increase the Breadth of the ASR Menu on the NanoChip® System to further Penetrate the Clinical Diagnostics Market

The second of Nanogen s five strategic goals is to increase the breadth of the NanoChip® System s ASR menu for commercial applications. Each Nanogen ASR includes specific reagents that enable the customer to develop, validate and perform a molecular test that determines the presence or absence of certain gene mutations associated with certain disease states. As part of Nanogen s Platformation strategy, the Company seeks to increase the number of commercially available ASRs that it provides its customers so as to both increase the attractiveness of the NanoChip® System to seek to gain some of the higher profit margins normally associated with the sale of such consumables.

During 2002, Nanogen introduced its first commercially available ASRs, that for Factor V Leiden, a gene mutation associated with the detection of thrombosis. The Company also undertook great efforts to develop a number of other ASRs. The Company internally developed and tested ASRs for mutations in the CFTR gene associated with the diagnosis of cystic fibrosis, for the mutations in the HFE gene associated with hereditary hemochromotosis and for a multiplexed Factor II/Factor V ASRs, all of which the Company introduced commercially in the first quarter of 2003.

Also, during 2002, Nanogen entered into license agreements and began development work on either ASRs or research reagents involving the following: ASPA gene mutations related to the diagnosis of Canavan disease (with the assistance of Nanogen Recognomics), the ApoE gene mutations associated with the diagnosis of Alzheimer s disease and for mutations in genes associated with the detection of beta thalasemia. Nanogen has also acquired rights from a third party to certain content potentially related to the diagnosis of epilepsy. The Company plans to introduce ASRs for detection of mutations in the ASPA gene associated with the diagnosis of Canavan disease, ASRs for ApoE and research reagents for the detection of mutations associated with beta thalasemia in the second quarter of 2003.

In addition, we expect to enter into more licensing and other collaborative agreements relating to securing rights to mutations to genes necessary to develop other ASRs.

In the future, we presently intend to file with the FDA for clearance to market both the NanoChip® System and certain of our products for clinical diagnostics. Nanogen is currently putting in place the internal procedures and groundwork necessary to submit such products for clearance in the near future. This may be a costly and time consuming process.

Development and Introduction of Research Products

Nanogen s third strategic goal is to develop products on its platform that facilitate customers development and validation of their own home brew tests on the NanoChip® System. In 2002, taking advantage of our open architecture system, we internally developed our Assay Toolbox™ product that provides research customers with the necessary tools and most of the reagents to develop and validate their own home brew tests on our System and take advantage of our open architecture system. We commercially launched the Assay Toolbox™ product in the first quarter of 2003 and believe that this product will help us further our Platformation goal. We also intend to develop and commercialize other valuable products for customers. 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 accurate and targeted technology. We seek to position the NanoChip® System as such a

technology. We intend to further pursue the genomics and biomedical research markets by taking advantage of the open architecture design of our technology that allows end users to develop and validate diagnostic tests to meet their individual research needs and help drive development of novel applications.

Improve the NanoChip® System and increase the depth of other applications of the NanoChip® Electronic Microarray technology.

Nanogen s fourth strategic goal is to develop improvements to the NanoChip® System over time through our engineering and advanced technology groups along with the manufacturer of the NanoChip® System, Hitachi High Technologies. Initially, improvements will be focused on cost reduction and throughput. In the long term, we would like to develop sample-to-answer systems which integrate otherwise time-consuming and labor-intensive sample preparation procedures on the disposable cartridge. The availability of this lab-on-a-chip technology would fulfill a substantial unmet need in both academic research and commercial sectors.

We also intend to continue the development of other technologies that may complement and improve the NanoChip® System, utilize the NanoChip® Electronic Microarray technology or are designed and developed by our employees, subsidiaries or collaborators. Such products include those currently developed by Nanogen in the forensics, biodefense, and protein kinase as well as those developed by Nanogen Recognomics in the fields of synthetic oligonucleotide chemistry and advanced molecular biology.

Continue to establish strategic collaborations in order to strengthen our product menu, penetrate new markets, obtain new intellectual property and enter the service market when appropriate.

Our fifth strategic goal is to continue to enter into collaborations to expand applications of our technology platform and to accelerate the commercialization of products in order to strengthen our product menu, penetrate new markets, obtain new intellectual property and enter the molecular diagnostics service provider market when appropriate. We will pursue additional collaborations in various forms, including research and development agreements, licensing agreements and joint ventures. These collaborations permit integration of the technology and resources of our partners with our technology, while allowing Nanogen to pursue diagnostics and genomics opportunities outside the scope of these collaborations.

Nanogen s Current Products

NanoChip® System s Components

The Company is seeking to establish the NanoChip® System as the standard platform for the detection of genetic mutations and to develop applications for future clinical use. Nanogen markets its NanoChip® Molecular Biology Workstation to scientists and molecular diagnostics laboratories. The heart of Nanogen s offering is based on three different components: the Workstation, Cartridges and software.

The NanoChip® System consists of a consumable Cartridge containing a proprietary semiconductor microchip, the NanoChip® Electronic Microarray, a fully automated instrument and imbedded software that can be programmed by the end-user to control all aspects of microchip operations, processing, detection and reporting. The System has been designed so that once programmed, the end-user need only insert of a consumable Cartridge containing a test sample into the instrument and all subsequent steps may be handled automatically under computer control.

The NanoChip® Cartridge

The consumable NanoChip® 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 (the NanoChip® Electronic Microarray) utilizes advances in the semiconductor industry and is designed and constructed using microlithography and fabrication techniques. The NanoChip®

Electronic Microarray is mounted within the consumable cartridge and is coated with a proprietary permeation layer. We have developed arrays of various sizes utilizing both passive and active CMOS microchips, as well as flip chip assembly technologies. Our current production of consumable cartridges employs 100 different test sites on a single NanoChip® Electronic Microarray. We are additionally developing a cartridge that employees 400 different test sites on a single NanoChip® Electronic Microarray for our next generation instrument.

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 electrochemical environment near the electrode surface and provides the chemistry necessary for attachment of the samples.

Samples

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 samples can be addressed on the same microchip, allowing multiple tests to be processed on the same Cartridge. Our open architecture approach allows the customer to address their specific samples onto a microchip to perform individualized analyses.

The NanoChip® Molecular Biology Workstation

Our fully integrated NanoChip® 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 referred to as, the Reader), and (4) computer hardware and software that allow the operator to develop, validate and select protocols from a graphical user menu which controls all microchip operations, tabulates test results and prints test reports based upon user-defined inputs.

Microchip Loader

Our System includes a Cartridge/microchip Loader that will allow users to electronically address their own samples to selected 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 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

Within the fluorescent array scanner component of the System, the fluidics function 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 test selection, test operation, fluorescent signal detection and signal processing, calculation of assay results and report generation. The end-user must develop and validate the protocols used by the software as well as define the parameters used to calculate results and generate reports. Each of the individual array locations is separately controlled by the microprocessor. Fluorescent signals emanating from positive test sites are scanned, monitored and quantified.

NanoChip® Analysis Process

Cartridge

The electronic microchip 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, create and validate their own genetic tests on the microelectronic chip with our automated System. A 96 well or 384 well microtiter plate containing genetic sequences is placed in the Loader. The System then automatically electronically addresses the microchip with user-defined tests.

Hybridization and stringency

Users may add test samples to the Cartridge and insert the Cartridge into the Reader. The customer may then select to have the instrument automatically perform hybridization and the appropriate stringency control is selected by the user, chemical, thermal or electronic. 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 easy-to-interpret output is available based upon user-defined inputs. 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 tests based on previous experimental results.

Applications Manager Software (AMS)

Nanogen plans to offer by mid 2003 a separately priced software package designed to streamline routine or frequent testing for the same genetic markers. AMS enables users to run protocols they ve written and validated for the NanoChip® System in a simplified, menu driven, point-and-click fashion. This supplemental software offers the ease of use required of those laboratories that run the same set of tests on a regular basis. It was designed in response to high complexity CLIA certified clinical

laboratories that are frustrated by research orientation of the currently available software. We believe that this software will provide a significant competitive advantage for the NanoChip® System.

Analyte Specific Reagent (ASRs)

ASRs are the specific reagents that permit either research or high complexity CLIA certified laboratory customers to develop, validate and run certain SNP assays. Under the ASRs model, we sell not only NanoChip® Cartridges, but also the specific reagents that can be used to develop, validate and perform DNA-based tests. We expect to further increase the potential revenue from each analysis performed with the launch of the SDA method of amplification for use on our next generation instrument. We also believe that by providing ASRs for tests that are in high demand, such as those developed for the CFTR gene mutation associated with the diagnosis of cystic fibrosis, we are in a better position to begin data collection on a protocol-by-protocol basis for a potential FDA submission for certain kit-based assays. Such kit-based assays normally include a protocol, ASRs, other reagents and performance claims and can be used by a wider variety of customers to provide clinicians with results that they can provide to their patients.

We currently have four ASRs that are commercially available for (1) Factor V Leiden launched in 2002, (2) Factor II/Factor V multiplex launched in the first quarter 2003, (3) CFTR launched in the first quarter 2003 and (4) HFE launched in the first quarter 2003. Below is a more detailed description of the ASRs:

Factor V Leiden ASRs

Nanogen s Factor V (Leiden) ASRs determine if the G1691A mutation on Factor V (Leiden) gene is present in a sample by detecting the presence of a certain characteristic gene polymorphism. The Factor V (Leiden) ASRs consists of active reagents that CLIA-certified high complexity laboratories can use developing and validating their tests to detect this mutation. Factor V is a gene mutation associated with thrombosis. Thrombosis is defined as the formation, development or presence of a blood clot (thrombosis) in a blood vessel or the heart. Blood clots are associated with heart attack, stroke, and other severe health complications. Complete blockage of the vessel can lead to an embolism. Mutations in the Factor V (Leiden) gene have been linked to thrombotic events.

Factor II/Factor V Multiplex ASRs

Nanogen offers ASRs for the detection of two genetic mutations associated with thrombosis: the G1691A mutation on the Factor V (Leiden) gene and the G20210A mutation on the Factor II (Prothrombin) gene. CLIA certified high complexity laboratories may use the reagents to create and validate laboratory developed tests for detection of these two mutations. Currently, Nanogen is the only provider of the Factor V (Leiden) and Factor II (Prothrombin) mutations in a multiplexed format.

Nanogen s Factor II/Factor V ASRs are multiplexed ASRs meaning that the customer can develop and validate multiple Factor II and Factor V gene mutations from a single test site (representing one sample) or from multiple test sites (representing different samples). The customer also has the ability to electronically address multiplexed amplicons to a single test site. The ability to control individual test sites permits biochemically unrelated molecules to be used simultaneously on the same microchip array. Conventional DNA arrays do not have this feature; all process steps must be performed on an entire array. Nanogen s Factor II/Factor V ASRs are a prime example of how our unique microelectronic array technology delivers increased versatility over conventional methods.

CFTR ASRs

Nanogen s CFTR ASRs offer the customer the ability to develop and validate a test for the detection of the **25 CFTR mutations recommended by American College of Medical Genetics ACMG)/**American College of Obstetrics and Gynecology (ACOG) as part of a high complexity CLIA-certified laboratory homebrew assay.

These mutations are associated with the diagnosis of cystic fibrosis. Our ASRs are based upon the first molecular based test recommended for nationwide screening of healthy individuals. In early 2003, we completed beta-site testing of our set of ASRs for use in developing and validating tests for the mutations in the CFTR gene, which are associated with the diagnosis of cystic fibrosis, and commenced a controlled release of the product to market. Many people carry a single cystic fibrosis gene mutation, and they do not experience any significant health problems. In the general population, approximately 1 in 31 Americans carries the gene mutations. This is the reason ACOG announced that the Standard of Medical Care includes screening women contemplating pregnancy for cystic fibrosis. To meet the standard of medical care, a physician must at least offer screening to each woman contemplating pregnancy. However, the disease can only occur in babies with two carrier parents. If initial screening of the prospective mother is positive for the CFTR mutation, then further testing of the prospective father is warranted. When both parents are carriers, they have a 25% chance with every pregnancy of passing two copies of the defective gene to their child. The current recommendation from ACOG is for a 25-mutation screen. We believe that the ACOG recommendations may drive a significant increase in genetic testing for gene mutations associated with cystic fibrosis.

HFE ASRs

Nanogen offers ASRs for the development and validation of a test to detect the three mutations associated with hereditary hemochromatosis (HH). Reagents include oligonucleotides for the detection of nucleotides corresponding to the C282Y, H63D, and S65C mutations of the HFE gene. CLIA-certified high complexity laboratories may use the reagents to create and validate laboratory developed tests (LDT) for HFE. Currently, Nanogen s HFE ASRs are the only ASRs for use in developing and validating a test for the three mutations in the HFE gene.

Hereditary hemochromatosis is an autosomal recessive disorder characterized by unusually high levels of iron in the blood due to polymorphisms in the HFE gene. Excess iron accumulates over a period of years in the patients major organ systems. Clinical indications of HH include type II diabetes (also known as bronze diabetes), heart disease, arthritis, and liver disease.

Other Current Products

Assay ToolBox ™

The Nanogen Assay ToolBox is a collection of general purpose reagents and accessories used to facilitate assay and protocol development and validation on the NanoChip® platform. The Assay ToolBox components, together with oligos available from third party vendors, may be used to facilitate development and validation of laboratory developed tests by CLIA-certified high complexity laboratories or research laboratories. The unique, open-architecture of the NanoChip® Electronic Microarray and instrumentation enables researchers to define, select and build their own test panels. Customers may be required to obtain third party licenses to the specific gene mutations for the assays that they seek to develop or validate.

Products and Applications in Research and Development

We seek to further develop the NanoChip® System, integrating new features and broadening the applications of the currently marketed System, including enhancing chip design and capabilities to simplify instrument design. Our scientists will investigate new opportunities and develop and validate new protocols, ASRs and products for use on the NanoChip® System, while customers may create and validate new home brew 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. For example, future technologies may include integration of sample processing and DNA amplification. The NanoChip® System may be designed to provide analysis of other charged molecules and antigen-antibody, enzyme substrate, cell-receptor, and cell-separation techniques. The NanoChip® System eventually may also become a portable lab on a chip for use in the field, away from the laboratory bench.

Below is a brief description of some of future products and application currently in research and development at either the Company or with one of its collaborators.

Next Generation NanoChip® System

As part of the Nanogen Hitachi collaboration, we have been working on improvements to the current NanoChip® System and the development of a next generation NanoChip® System. We believe our next generation NanoChip® System must be more compact and less costly to access smaller hospital laboratories and other customers for molecular-based testing.

Additional Potential ASRs and other Products

ASRs for mutations in the ASPA Gene related to Canavan disease

During 2002, Nanogen entered into a non-exclusive license agreement with a third party that provided it with rights to develop ASRs for certain mutations in the ASPA gene associated with Canavan disease, a disease that has highest prevalence in the Ashkenazi Jewish community. This community has historically been very proactive in the United States in advocating that its members undergo genetic testing prior to having children. The ASPA mutation detection test is a key member of a panel of multiple tests frequently used in an Ashkenazi Jewish genetic disease screening panel. Cystic fibrosis also is a key part of this panel and Nanogen offers the ASRs to enable customers to develop and validate an assay to test for the specific mutations associated with the diagnosis of cystic fibrosis. Strategically, the ASPA ASRs are important as they provide patent licensure to the end user which has historically been a challenge for individual laboratories to obtain. This will allow many labs who are currently sending out this test to bring it in-house. Moreover, those labs that currently test internally typically run a home brew assay which most report as highly cumbersome. These ASRs will simplify and streamline their testing for this important gene.

During 2002, Nanogen and its subsidiary, Recognomics, jointly worked on developing and validating the ASRs and Nanogen currently has transferred the ASRs to an alpha test site. Nanogen currently expects to release the ASRs in the second quarter of 2003.

ApoE ASRs

In 2002, Nanogen non-exclusively licensed rights to develop and commercialize ASRs relating to ApoE gene mutations linked to the detection of Alzheimer s disease. The ASRs are currently in beta site testing and Nanogen expects to release the ASRs in the second quarter of 2003. Like the ASPA ASRs, strategically, the ApoE ASRs are important as they provide patent licensure to the end user which has historically been a challenge for individual laboratories to obtain. This will allow many labs who are currently sending out this test to bring it in-house. Since those labs that currently test internally typically run a home brew assay that most report as highly cumbersome, the ApoE ASRs will simplify and streamline their testing for this important gene.

ASRs for Genes related to epilepsy

In 2002, Nanogen entered into a development site agreement with Bionomics, an Australian company that provides for an option to the exclusive commercial rights for certain gene mutations believed to relate to epilepsy. Bionomics is currently in the initial stage of validating its hypothesis and developing a test for these mutations. Since this research is in the early stage of development, no definitive time table has been set for the release of any of such ASRs.

Beta thalassema research reagents

Nanogen has been working with a company in Europe to jointly develop a product for the detection of certain genes associated with the diagnosis of beta thalassimia, a disease that is most prevalent in the Mediterranean regions of Europe. These research reagents will be initially marketed through the European company as an alternative method for testing beta thalassemia in newborns. Nanogen expects to release these research reagents in the second quarter of 2003.

Advanced Technology and Research and Development

Besides the continued development of the NanoChip® System, ASRs and other similar products, we are currently conducting research and development into a number of other applications of our technology.

*Developing Advanced Technologies and Point-of-Care Applications***.**

In the long term, we plan to develop sample-to-answer systems which integrate otherwise time-consuming and labor-intensive sample preparation procedures on the disposable cartridge through the use of active microelectronics. The availability of this lab-on-a-chip technology would fulfill a substantial unmet need in both academic research and commercial sectors.

Nanogen Recognomics

Nanogen Recognomics, a joint venture of Nanogen and Aventis Research & Technologies, combines the NanoChip® technology and Aventis R&T´s intellectual property and expertise in synthetic oligonucleotide chemistry and advanced molecular biology to develop new products and applications for the NanoChip® System. Besides assisting us in the development of ASRs for the detection of genes associated with Canavan disease, their current research efforts include genetic-based in vitro human detection, diagnostics, screening and monitoring applications, including research into novel oligonucleotide chemistries.

Biodefense

Nanogen began work on biodefense-related technology for the United States Government in 1995. The work has expanded to include three current government grants to support biowarfare detection efforts (one ongoing DARPA grant and two DUST grants).

Specific development efforts include a prototype portable field-based detection device and an integrated micro-laboratory and assay protocol to analyze simulated biowarfare targets. Also under development are assays aimed at detection of specific biowarfare agents and infectious diseases and a self-contained portable system capable of performing on-chip non-PCR amplification and detection of potential biowarfare threats.

Forensics

STRs are the genetic sequences chosen by the U.S. government and various foreign governments to populate their national criminal identification databases. Some foreign researchers and governments are also beginning to examine certain SNPs to develop such 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. Currently, we have four overseas development sites working on forensic applications. We believe our NanoChip® System may be useful in human identity testing.

Our research collaborations in the area of forensic applications include identity testing and have allowed us to further develop existing technology and explore new technology. Prior and current grants from the National Institute of Justice have involved sponsored research for forensic applications, such as the development of a portable system for human identification at the crime scene and the development of on-chip non-PCR amplification.

Kinase

Working with Aventis, Nanogen has developed an electronic, fluorescent kinase assay and instrument for use in drug discovery. The assay is configured for 384-well microtiter plates and uses no antibodies or radioactivity. While particularly attractive for serine/threonine kinases, the electronic assay can also be applied to phosphatases and proteases.

The assay principle involves kinase phosphorylation to invert the charge of a fluorophore-labeled peptide substrate, followed by electrophoresis to separate the phosphorylated and unphosphorylated peptides. The intensity of the fluorescence is quantitatively read on a conventional plate reader and directly related to the effectiveness of the inhibitor.

Nanogen has placed ElectroCapture HTS workstations in beta-site locations. Direct comparisons with fluorescence polarization, homogeneous time-resolved fluorescence and radioactive filter binding assays have been presented by Eli Lilly & Company and Aventis at several drug discovery conferences. The primary advantages our electronic technology identified by our collaborators are assay simplicity and low fluorescence compound interference. We have developed a proprietary method to quickly identify specific fluorophore labeled proprietary substrates for kinase and orphan kinases that are assay-ready. By combining the substrate identification method with our electronic assay, we believe that high-quality screening results can be generated for a large fraction of the kinases and phosphatases in the human genome. We will be identifying the on-going business strategy for the optimum commercial impact of this technology. Nanogen does not plan to commercialize the kinase technology on its own, but will identify third party collaborators to commercialize it.

Other Potential Applications

As the Human Genome Project opportunity and other public and private genetic sequencing efforts yield increasing amounts of genetic information, we believe that 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. 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.

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. In the meantime, a patient requiring immediate therapy, must often 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 offer our customers the opportunity to lower their costs and improve productivity by automating all or a significant portion of their labor-intensive testing.

Drug discovery applications

We believe we have a powerful tool, the ElectroCapture workstation, 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 pre-clinical drug discovery process takes an average of six and one-half years. Consequently, we believe there is a significant demand for improved tools that 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. Our electronic, fluorescent tests are free of antibodies and have the potential of improving the cost and quality of the screening process. We will be identifying the ongoing business strategy for the optimum commercialization of this technology.

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. Pharmacogenomics is the science of individualizing therapy based on genetic differences among patients.

Our NanoChip® 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.

Collaborative Alliances

We intend to continue to enter into collaborations to expand applications of our technology platform and to accelerate the commercialization of products. We will pursue additional collaborations in various forms, including research and development agreements, licensing agreements and joint ventures. These collaborations permit integration of the technology and resources of our partners with our technology, while allowing Nanogen to pursue diagnostics, drug discovery and genomics opportunities outside the scope of these collaborations.

We are currently involved in two material corporate collaborations. In July 2001, we formed a company with Aventis named Nanogen Recognomics GmbH. 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 are directly involved with marketing our first product line to the biomedical research and genomics market and clinical diagnostics labs. Additionally, we may distribute products in Japan and select Asian markets through the distribution arm of Hitachi High Technologies.

Aventis/Nanogen Recognomics

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 term of this original collaboration agreement expired at the end of 2000. In September 1999 we entered into an additional collaboration agreement with Aventis that involved 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. The September 1999 agreement expired at the end of 2001. We do not expect to receive additional funding for these projects.

In July 2001, we formed a company with Aventis named Nanogen Recognomics GmbH. This company may allow us to benefit from the development of new technological advances for our platform while still focusing on our near-term goal of entry into molecular diagnostics. Nanogen Recognomics adds intellectual property and expertise in synthetic oligonucleotide chemistry and advanced molecular biology to Nanogen.

As described earlier herein, Nanogen Recognomics combines the NanoChip® technology and Aventis R&T´s intellectual property and expertise in synthetic oligonucleotide chemistry and advanced molecular biology to develop new products and applications for the NanoChip® System. These current research efforts include genetic-based in vitro human detection, diagnostics, screening and monitoring applications, including research into novel oligonucleotide chemistries.

Hitachi

In January 2000, we executed an agreement with Hitachi, Ltd. for the full-scale commercial manufacturing and distribution of the NanoChip® Molecular Biology Workstation in specified research markets. Hitachi, Ltd. s Instrument Group provides technology and technical support to aid in the manufacturing of the NanoChip® Molecular Biology Workstation s components.

Under this agreement, Hitachi, Ltd. has the right to be the sole distributor of Hitachi, Ltd. produced NanoChip® Molecular Biology Workstations in Japan. Hitachi, Ltd. also has the non-exclusive right to distribute NanoChip® Cartridges in Japan. We retained the right to distribute, directly or through others, Hitachi, Ltd. produced NanoChip® Molecular Biology

Workstations outside of Japan. In addition, we currently develop and manufacture the NanoChip® Cartridges for distribution worldwide. 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 after July 26, 2003, subject to certain conditions. The agreement expands on the existing 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.

Government Grants

In 2002, we continued work under a number of biodefense-related technology grants for the United States Government. The work has expanded to include three current government grants to support biowarfare detection efforts (one ongoing DARPA grant and two DUST grants) In the latter part of 2002, we received an additional $1.7 million grant from the National Institute of Justice (NIJ) to continue an earlier NIJ grant for the development of a forensics detection system for the identification of certain relevant SNPs and STRs and we received a grant from the National Institute of Health for $162,000 for the development of a sample preparation system for the detection of certain biological agents.

Specific development efforts include a prototype portable field-based detection device and an integrated micro-laboratory and assay protocol to analyze simulated biowarfare targets. Also under development are assays aimed at detection of specific biowarfare agents and infectious diseases and a self-contained portable system capable of performing on-chip non-PCR amplification and detection of potential biowarfare threats.

We believe that the actions we are taking to develop our product platform for use in molecular diagnostics are directly portable and complementary to what we are doing in the biowarfare arena for the U.S. Army. As a result, we believe that our government and commercial programs complement one another.

Proprietary Technology and Patents

As of December 31, 2002, we have forty-seven issued U.S. patents and thirty-six foreign 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 have and 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 commercially 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 European patents and patent applications owned by Oxford Gene Technology (OGT). We have opposed one allowed European Patent that had broad claims to array technology for analyzing a predetermined polynucleotide sequence. OGT s position with respect to the opposed patent is that the claims relate to what it terms the diagnostic mode. Those claims have now been narrowed before the Opposition Division to the point that, if these claims remain final before the European Patent Office, we believe they would not be infringed by our technology. In the Oral Proceedings before the Opposition Division on November 13, 14, and 15, 2001, the Division determined that the claims language must be limited to arrays with smooth, impermeable surfaces. The case is currently on appeal. If the decision of the Opposition Division is successfully appealed by OGT and the original claims are reinstated, or if an application relating to arrays issued in another country with claims as broad as

the original European patent, we could be subject to infringement accusations that could delay or preclude sales of some or all of our anticipated diagnostic products.

In addition to the patent litigation with Oxford Gene Technologies 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.

Manufacturing

In January 2000, we formed a collaboration with Hitachi for the manufacture of our NanoChip® 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® 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® Molecular Biology Workstation during the latter part of 2000. Since then, we have built a commercial structure that allows us to sell directly in certain markets, while selling through distributors and partners in other markets. We began selling our first ASRs for Factor V Leiden in Spring of 2002.

Our commercial organization includes direct sales representatives and sales management, customer support personnel, field support personnel and marketing. We began selling our product to customers in the United States, Canada, Mexico and several European countries. Hitachi s distribution company, Hitachi High Technologies, began distributing our product in Japan during the latter part of 2000 as well. We expect to augment our commercial selling process by adding additional 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 is used to assist in early customer demonstrations, protocol development and system and applications 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. The molecular diagnostic test market, in particular, is highly competitive, and we expect the intensity of competition to increase. We anticipate that our competitors 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 both in the United States and abroad.

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

Currently our NanoChip® System is registered for general purpose use in the U.S. and distributed for research use in Europe. The ASRs under development and commercially available are manufactured and distributed in the U.S. pursuant to 21CFR 864.4020. Future short term plans include distribution of these reagents for research use in Europe with eventual CE marking of test systems under the European IVDMDD regulations.

For our initial commercial markets, the biomedical research market and the high complexity CLIA certified laboratory market, we do not anticipate the need for FDA or other regulatory clearances for our NanoChip® System and certain ASRs prior to marketing. We have not applied for FDA or other regulatory clearances 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 our 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, Medical Device Reporting and adherence to Quality System Regulation, or QSR). Class II devices are subject to general and special controls (e.g., performance standards, premarket notification, postmarket surveillance, patient registries and FDA guidelines). Generally, Class III devices are new devices 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 legally marketed devices). Before a 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 labeled for research,

genomics, drug discovery and industrial applications will not require regulatory approvals or clearance. Some *in vitro* 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 three to six months or more from submission to obtain 510(k) premarket clearance, but the process may take longer if FDA requests more data or research.

The Premarket Approval (PMA) application 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 non significant risk *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. We believe our diagnostics are non significant risk devices because 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 and due diligence controls must be established by the company 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..

After a PMA is accepted for filing, the FDA begins its review of the submitted information, which generally takes between one and two years. During this review period, the FDA may request additional information or clarification of information already provided, as well as conduct a preapproval inspection of the manufacturing facility. If we are not in compliance with Quality System Regulations (QSRs) applicable to manufacturing, we will not receive PMA approval. 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 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 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.

There can be no assurance that 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, 2002, we had 195 full-time employees, of whom 37 hold Ph.D. degrees and 17 hold other advanced degrees. Approximately 81 are involved in research and development, 40 in operations, manufacturing and quality assurance, 40 in sales and marketing, and 34 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 are covered by a collective bargaining agreement.

Factors That May Affect Results

Our products may not be successfully developed or commercialized, which would harm us and force us to curtail or cease operations.

We are at an early stage of development. As of March 2003, we had only a limited product offering that includes our NanoChip® System, NanoChip® Cartridge, four ASRs and one other product. All of our other platforms and ASRs and other potential products are under development. Our NanoChip® System, ASRs 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.

As of December 31, 2002 we have sold a total of 45 NanoChip® Systems. We also placed instruments at various customer sites under development site agreements whereby title of the NanoChip® Molecular Biology Workstation did not pass to the customer and therefore no revenue was recognized.

We are also party to transactions known as reagent rentals and cost-per-test agreements. As of December 31, 2002, we entered into three reagent rental agreements and nine cost-per-test agreements for 2002. Under these types of transactions, we place a Workstation at a customer site with no upfront cost to the customer. The value of the instrument is typically recaptured through a contracted stream of future reagent sales, sold at a premium to cover the cost of the system. The nine cost-per-test transactions entered into in 2002 require customer acceptance of our CFTR

ASRs as a pre-condition to this commitment which we released in the first quarter of 2003. These reagent rentals and cost per test agreements might have an adverse impact on our short-term instrument sales revenue and cash flow as the revenues and cash received under these agreements are over the life of the contract, as reagents are shipped to the customer. Our success will depend upon our ability to continue to overcome significant technological challenges and successfully introduce our products into the marketplace. A number of applications envisioned by us may require significant enhancements to our basic technology platform. There can be no assurance that we can successfully develop such enhancements.

As of December 31, 2002, we have received approximately $388,000 in revenue from the sale of our NanoChip® Cartridges. Also, as of December 31, 2002, we have not yet recognized any revenue from the sale of our ASRs.

Lack of market acceptance of our technology would harm us.

Although we have developed a number of products as discussed above, we may not be able to further develop these products or to develop other commercially viable products. Even if we develop a product it may not 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. We may also be forced to carry greater inventories of our products for longer periods than we may have anticipated. If we are unable to sell the inventory of our products in a timely fashion and at anticipated price levels, we may not become profitable. In addition, we may have to take accounting charges and reduce the value of our product inventory to its net realizable value. 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 products requires us to enter into contractual arrangements with corporate collaborators, joint venture partners, licensors, licensees and others. Our success depends in part upon the performance by these collaboration partners and potential collaboration partners of their responsibilities under these arrangements. Some collaborators may not perform their obligations as we expect, and we may not derive any revenue or other benefits from these arrangements.

We have collaborative agreements with a developer and manufacturer of instrumentation products and we formed a new company with the research and development subsidiary of a pharmaceutical company. We do not know whether these collaborations 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 Hitachi that contemplate the commercialization of products resulting from the agreements between the parties. In addition, we have a manufacturing and distribution agreement with Hitachi. In June 2001, we formed a company, Nanogen Recognomics GmbH, with Aventis Research and Technologies & Co. KG, in which we own 60% of the stock of Nanogen Recognomics and Aventis R&T owns the remaining 40%. Nanogen Recognomics seeks to combine our NanoChip® technology and Aventis R & T s intellectual property and expertise in synthetic oligonucleotide chemistry and advanced molecular biology to develop new products and applications for the NanoChip® System. These collaborations may not be successful.

We have a history of net losses. We expect to continue to incur net losses and we may not achieve or maintain profitability.

From our inception to December 31, 2002, we have incurred cumulative net losses totaling approximately $145.7 million. Moreover, our negative cash flow and losses from operations will continue 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, which fluctuations could be significant. The amount and timing of product revenue recognition and cash flow may depend on whether potential customers for the NanoChip® System choose to enter into sales, reagent rentals, cost-per-test or development site transactions.

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

We will need additional capital in the future. If additional capital is not available, we may have to curtail or cease operations.

We will need to raise more money to continue the research and development necessary to further develop our current products to bring our products to market and to further our 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 seek to 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 meeting necessary Quality System Regulations or QSRs and obtaining necessary regulatory clearances or approvals;

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

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

Additional capital may no