## SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934

DATE OF REPORT: FEBRUARY 22, 2000 (Date of earliest event reported)

INCYTE PHARMACEUTICALS, INC. (Exact name of registrant as specified in its charter)

DELAWARE 0-27488 94-3136539 (State or other jurisdiction of incorporation) (Commission (IRS Employer File Number) Identification No.)

3174 PORTER DRIVE, PALO ALTO, CALIFORNIA 94304 (Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (650) 855-0555

# Item 5. Other Events.

Set forth below are updated descriptions of the business of and risk factors affecting an investment in Incyte Pharmaceuticals, Inc. (the "Company"). Also attached hereto as Exhibit 99.1 and incorporated by reference herein is the press release dated February 1, 2000 announcing the placement of \$150 million in convertible subordinated notes by the Company. In the descriptions of the business and risk factors below, all references to "Incyte," "we," "us," "our" or the "Company" mean Incyte Pharmaceuticals, Inc. and its subsidiaries, except where it is made clear that the term means only the parent company.

As used in this current report on Form 8-K, the words "expects," "anticipates," "estimates," "plans" and similar expressions are intended to identify forward-looking statements. These are statements that relate to future periods and include statements under the captions "Business" and "Risk Factors" as to our expected losses, the adequacy of capital resources, growth in operations, the ability to commercialize products developed under collaborations and alliances, our ability to complete the sequence of full-length genes in areas of therapeutic interest and file patents on these potential drug targets, our ability to integrate companies and operations that we have acquired or will acquire, our ability to implement online delivery of our database and software products, the scheduling and timing of current and future litigation, our strategy with regard to protecting our proprietary technology, our ability to compete and respond to rapid technological change and the performance and utility of our products and services. Forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from those projected. These risks and uncertainties include, but are not limited to, the extent to which the pharmaceuticals and biotechnology industries use genomic information in research and development, risks relating to development of new products and services and their use by our potential customers and collaborators, our ability to work with our collaborators to meet the goals of our collaborators and alliances, the effectiveness of our sequencing efforts, the impact of alternative technological advances and competition, changes in patent laws, and the risks set forth under "Risk Factors."

Incyte, LifeSeq and PathoSeq are our registered trademarks. ZooSeq, LifeTools,

LifeArray, LifeProt, LifeExpress, GeneAlbum and GEM are our trademarks. We also refer to trademarks of other corporations and organizations in this current report on Form 8-K.

#### **BUSINESS**

#### OVERVIEW

Incyte is a leading provider of genomic information-based products and services. These products and services include database products, genomic data management software tools, microarray-based gene expression services, genomic reagents and related services. We focus on providing an integrated platform of information technologies designed to assist pharmaceutical and biotechnology companies and academic researchers in the understanding of disease and the discovery and development of new drugs.

Our genomic databases integrate bioinformatics software with proprietary and, when appropriate, publicly available genomic information. In building the databases, we utilize high-throughput, computer-aided gene sequencing and analysis technologies to identify and characterize the expressed genes of the human genome, as well as certain animal, plant and microbial genomes. By searching our proprietary genomic databases, customers can integrate and analyze genomic information from multiple sources in order to discover genes that may represent the basis for new biological targets, therapeutic proteins, or gene therapy, antisense or diagnostic products. The pharmaceutical and biotechnology industries use our genomic products and services to accelerate the discovery and development of new diagnostic and therapeutic products. Our products and services can be applied to gene and target discovery, functional genomics studies, preclinical pharmacology and toxicology studies, and can aid in understanding and analyzing the results of clinical development studies.

We currently provide access to our genomic databases through collaborations with pharmaceutical and biotechnology companies worldwide. As of December 31, 1999, more than twenty companies had entered into multi-year agreements to obtain access to our databases on a non-exclusive basis. These companies include the following:

Abbott Laboratories
AstraZeneca PLC
Aventis S.A.
Bristol-Myers Squibb Company
Eli Lilly and Company
F. Hoffmann-La Roche Ltd.
Genentech, Inc.
Glaxo Wellcome plc

Johnson & Johnson
Millennium Pharmaceuticals, Inc.
Monsanto Company
Novartis AG
Pfizer Inc.
Pharmacia & Upjohn, Inc.
Schering AG
Schering-Plough, Ltd.

Revenues from these companies have primarily consisted of database access fees. Our LifeSeq Gold human gene sequence database agreements also provide for future milestone payments and royalties from the sale of products derived from proprietary information contained in one or more database modules.

Our portfolio of products and services includes:

- -- LifeSeq Gold human gene sequence and expression database;
- - PathoSeq microbial genomic database;
- - ZooSeq animal model gene sequence and expression database;
- -- LifeExpress gene expression and protein expression database;
- - SNP database that identifies common DNA sequence variants between individuals;
- -- LifeTools suite of bioinformatics software;
- - LifeArray gene expression data management and analysis software;
- - LifeProt protein expression data management and analysis software; and
- contract sequencing and other services.

The databases are available using the Oracle database architecture and operate on Sun Microsystems, Compaq and SGI workstations. As part of our strategy for expanding our customer base, we are developing the infrastructure to enable the online delivery of our database and software products.

## BACKGROUND

Genes, found in all living cells, are composed of DNA, which in turn is

composed of two strands of complementary nucleotides referred to as base pairs or bases. Nucleotides may be one of four different molecules-adenine, guanine, cytosine, or thymine-which are strung together in specific patterns to create genes. Genes provide the necessary information to create proteins, the molecules that carry out all functions within a cell. Many human diseases are associated with the inadequate or inappropriate presence, production or performance of proteins. As such, pharmaceutical and biotechnology companies often seek to develop drugs that will bind to a targeted protein involved in disease in order to regulate, inhibit or stimulate its biological activity. Other proteins, known as therapeutic proteins, have direct biological activity and may be capable of treating disease. Insulin and human growth hormone are examples of therapeutic proteins. Understanding the role genes play in disease, and the protein targets or therapeutic proteins that they encode, has thus become a significant area of interest and research within the pharmaceutical and biotechnology industries.

### Sequencing

One frequently employed method for determining gene function involves the grouping of genes into "related" families based on similarities, or homologies, in DNA sequence. DNA sequencing is a process that identifies the order of the bases in a segment of DNA. Once a gene's sequence is known, its function may be inferred by comparing its sequence with the sequences of other human genes of known function, because genes with homologous sequences may have related functions. Comparing gene sequences across species has also become a useful tool for understanding gene function, as frequently it is easier to first assess gene function in other organisms.

#### Gene Expression

Another method used to determine gene function focuses on the analysis of gene activity, referred to as expression, within a cell. When a gene is active, its DNA is copied into messenger RNA or "mRNA." The population of mRNA within a cell can be isolated and converted into complementary DNA or "cDNA," thereby creating a cDNA library that represents the population of mRNAs present in a cell type at a particular time. In a process called "gene expression profiling," high-throughput cDNA sequencing, computer analysis and microarray technologies can be used to identify which genes are active or inactive and, if active, at what levels. Expression profiles provide a more detailed picture of cellular genetics than conventional laboratory techniques by indicating which genes, both known and novel, are specifically correlated to discrete biological events in normal and disease-state cells.

## Microarray Technology

Microarray technology can be used to analyze the expression patterns or sequence variations in a large number of genes simultaneously. A microarray consists of fragments of a single strand DNA's double strand attached to a surface, usually a glass, plastic or silicon slide, in a grid-like formation. When cDNA that has been prepared from mRNA samples from normal and diseased cells is applied to the microarray, complementary strands attach to the DNA fragments on the microarray. Microarray technology allows the fabrication of very small grids containing probes for thousands of different genes. Microarrays can be used in drug discovery and development, to evaluate the behavior of a large number of related genes in a diseased tissue or in response to treatment with a new drug or in diagnostic testing to quickly detect the presence of a large number of disease markers.

#### Bioinformatics

Due to improvements in sequencing technology, genomic information from both public and private sources is increasing at a dramatic rate. As a result, bioinformatics, or the use of computers and sophisticated algorithms to store, analyze and interpret large volumes of biological data, is essential in order to capture value from this growing pool of data. To date, the main focus of bioinformatic and genomic tools has been drug discovery. The Company believes these tools, and those under development, will also assist researchers with the preclinical and clinical development process. For example, with the help of new technology and bioinformatic analyses scientists may be able to correlate genetic and physiologic response in preclinical animal models, examine gene expression profiles in drug-treated animals to assess the pharmacological activity and toxicity of new drugs, and stratify clinical trial patients according to their gene expression profiles.

## Single Nucleotide Polymorphism ("SNP") Discovery

Due to genetic variation, individuals may respond differently to treatment with the same drug. Few, if any, FDA-approved drugs are capable of successfully treating every individual diagnosed with a targeted disease. The differences in patients' responses to a drug are believed to result in part from differences in the sequence of nucleotides within genes. The most common form of sequence variation is known as a single nucleotide polymorphism or "SNP." A SNP is

defined as a single base difference within the same DNA region between two individuals. Some SNPs are "silent" and not associated with a disease or a patient's ability to respond to a particular therapy, and some SNPs occur at a frequency that is too low to justify large-scale patient screening. Thus, researchers need to do more than identify SNPs; they must identify the most frequently occurring SNPs and identify those that correlate with a patient's disease prognosis or ability to respond to a drug. Through our acquisition of Hexagen in September 1998, we are developing fluorescent single-strand confirmation polymorphism (fSSCP) technology, a high-throughput SNP discovery technology. fSSCP is particularly useful for identifying SNPs in genes not expressed or more rarely expressed. This gel-based system detects SNPs in multiple samples simultaneously by observing changes in the tertiary structure of single stranded DNA fragments due to base pair changes. Incyte is contributing technologies in the areas of electrophoresis, fluorescence chemistries, sequencing and bioinformatics in order to continue to develop and improve the accuracy and efficiency of this technology.

## Gene Mapping

Mapping refers to the determination of the physical location of a gene in the genome and the relative position of that gene to other genes along a chromosome. Physiological processes and associated diseases can be extremely complex and involve many genes. A gene can activate one or more different genes forming a cascade of genetically controlled events or a "pathway." When the genes involved in such a pathway are located within neighboring regions of DNA, mapping can allow the location of one member of the pathway to be used to identify the other members. In addition, genetically inherited diseases that have been passed from generation to generation may be associated with visible chromosome alterations, such as deletions of large segments of the chromosome or insertions within the chromosome. These physical chromosome abnormalities allow researchers to identify the DNA regions and genes that have a critical role in causing disease.

## **PROTEOMICS**

Proteomics is a relatively new field of study that involves the separation, identification, and characterization of proteins present in a biological sample. By comparing disease and control samples, it is possible to identify disease-specific proteins. These may have potential as targets for drug development or as molecular markers of disease. The power of proteomics lies in the ability to directly measure a gene product, determine subcellular localization and detect post-translational modifications.

## PRODUCTS AND SERVICES

Our current products and services include an integrated platform of genomic databases, data management software tools, microarray-based gene expression databases and services, and related reagents and services.

Genomic Databases. We provide our database collaborators with non-exclusive database access. Database collaborators receive periodic data updates as well as software upgrades and additional search and analysis tools when they become available. The fees and the period of access are negotiated independently with each company. Fees generally consist of database access fees, option fees, and non-exclusive or exclusive license fees corresponding to patent rights on proprietary sequences. We may also receive future milestone and royalty payments from database collaborators from the development and sale of their products derived from our technology and database information. Researchers can browse not only Incyte-generated data, but also public domain information. We currently offer the following database modules:

- - LifeSeq Gold Database. The LifeSeq Gold human sequence and expression database integrates the information from our LifeSeq public-domain and proprietary gene sequences and expression database; LifeSeq FL, full-length gene sequence database; and the sequence information from our GeneAlbum database and reagent set. LifeSeq Gold uses a novel method to assemble cDNA sequence fragments (ESTs) into genes, providing increased sensitivity for distinguishing between closely related sequences, including splice variants. Researchers can easily move from one module to another through the HTML-based graphical interface. The sequence database contains our computer-edited gene sequence files and is used by researchers to identify related or homologous genes. For example, a scientist may wish to identify new genes homologous to a gene identified through their own research and believed to be linked to a disease. The database contains biological information about each sequence in our sequence database, including tissue source, homologies, and annotations regarding characteristics of the gene sequence. Also, the database contains a gene expression profile for every tissue in the database combined with proprietary bioinformatics software to allow collaborators to browse data and compare differences in gene expression across cells, tissues, and different disease states. Thus, the database can be used to assist researchers in correlating the presence of specific genes to discrete biological events in normal and

disease-state cells. We continually add sequences and expression data from normal and diseased tissues to the LifeSeq Gold database.

- PathoSeq Database. The PathoSeq database currently contains proprietary and public domain genomic data for more than 40 medically relevant bacterial and fungal microorganisms. With drug-resistant strains of bacteria and other microorganisms posing an increasing threat to world health, pharmaceutical and biotechnology companies are searching for genes unique to these pathogens that will aid in the development of new drugs to treat infectious disease. Our proprietary bioinformatics process edits all sequence data to remove artifacts and contamination, assemble sequences, display the relative position of the DNA coding regions, and identify genes either common among multiple microorganisms or unique to one microbial genome. We believe PathoSeq can help researchers understand the biology of microorganisms, study the mechanisms of drug resistance, identify genes that may make effective drug targets, and, ultimately, develop new therapeutics to treat and prevent infectious disease.
- ZooSeq Database. The ZooSeq database was developed to aid pharmaceutical and biotechnology companies in designing and evaluating preclinical drug studies in animal models, a crucial step in the drug development process. The database currently contains gene sequence and expression data for the rat, mouse, and monkey-animals commonly used in preclinical drug toxicology and efficacy studies. By correlating a drug's effects on an animal with the animal's genetic makeup, and then cross-referencing these data with our human LifeSeq database, a researcher may better predict the drug's efficacy and side effects before moving to human clinical trials.
- LifeExpress Database. The LifeExpress database is a comprehensive, nonexclusive database of gene expression and protein expression on samples focusing on major therapeutic areas and pharmacology/toxicology. The protein expression modules of the LifeExpress database are developed in cooperation with collaborator Oxford GlycoSciences. The two subcategories of LifeExpress are TargetExpress and LeadExpress. Aimed at facilitating the discovery and validation of high value targets, TargetExpress provides further annotation and detailed expression information on known and unknown gene products. LeadExpress focuses on using genomic and proteomic technologies to further annotate chemical structures of common drug classes.
- -- IsSNPs. Our in silico SNP program identifies common SNPs by mining LifeSeq Gold and genomic sequence data. We have identified approximately 46,000 isSNPs and expect to identify a total of 100,000 isSNPs from LifeSeq Gold (over 60,000 from expressed regions) throughout the coming year.

Contract Sequencing. Contract sequencing services generally include generating sequence and bioinformatics data for customers using our core strengths in library construction, high-throughput cDNA sequencing and bioinformatics.

Software. We have developed an enterprise-wide genomic information management system capable of updating, reprocessing and integrating genetic data from multiple sources and from different organisms. This system allows the integration of our proprietary, subscriber-specific and public domain data, and is capable of comparing information from humans, animals, microbes, fungi and plants. The system incorporates the architecture necessary to integrate our software tools data visualization tools, data mining programs and project management capabilities, and is capable of being integrated with additional technologies developed to more efficiently manage and analyze genomic data.

- LifeTools, a suite of specialized bioinformatic software programs and project management tools, consists sequence analysis and data management tools for handling complex genomic information from multiple sources. LifeTools reads and edits raw sequence data, including data imported from public databases, and annotates and clusters sequence fragments based on sequence similarity. LifeTools includes a fast, scalable database search engine with intranet-based graphical tools for interactive queries and analyses. The LifeTools relational database management system stores and distributes sequence assembly, homology, tissue expression information and biological data. Our database management architecture is based on open system standards, providing interconnectivity between disparate systems and applications, and enterprise-wide access to data and functions.
- LifeArray software manages and analyzes data resulting from microarray hybridization experiments. It includes a searchable database that accommodates experiment results from a variety of microarray platforms. LifeArray provides an integrated data warehouse and analysis environment, which allows the customer to bring data from multiple microarray platforms into one integrated environment. LifeArray enables the user to visualize differential expression between biological samples and can track all details of microarrays, genes, biological samples, donor information, and experimental results in one integrated environment with a Java-based interface. It is an enterprise-wide system that can support as many simultaneous users as required, and grow to suit changing

- LifeProt software provides tools to query, display, and analyze the protein expression data resulting from two-dimensional gel experiments. Using the program's query capabilities, customers can quickly locate relevant sample data sets from among many stored in a central database. This database tracks experiment conditions, tissue, treatment, and donor information, as well as the sample data. The LifeProt software is an enterprise-wide system that uses a Java-based interface and is available across a company to scientists using a variety of different computers and operating systems.

Microarray-Based Services. We offer microarray-based gene expression services to the pharmaceutical, biotechnology, and agricultural industries and academic researchers. These services can be used to simultaneously evaluate the gene expression profile of a large number of genes. Our GEM microarray technology allows probes for up to 10,000 genes per microarray. Microarrays can be used to identify the genes involved in a complex disease pathway, examine a drug-treated tissue to understand how the drug affected the expression of important genes, and study several new drug candidates to determine if one has a more favorable effect on gene expression than the others. Experiments can use either prefabricated arrays or custom arrays. Prefabricated arrays contain either public domain genes or genes chosen from our databases. We currently offer 18 prefabricated microarrays, including an array containing the genes found in a microbial pathogen Staphlycoccus aureus, an array containing the genes found in the rat liver and kidney, and a series of arrays that contain Incyte proprietary genes. Custom arrays can contain genes provided by the customer or chosen by the customer from our proprietary databases.

DNA Reagents and Other Services. We offer a variety of DNA reagents and other services designed to assist its collaborators in using information from its databases in the customer's internal lab-based experiments. The cloned DNA fragments from which the information in our databases is derived represent valuable resources for researchers, enabling them to perform bench-style experiments to supplement the information obtained from searching our databases. We retain copies of all isolated clones corresponding to the sequences in the database. Our collaborators may request clones corresponding to a sequence of interest on a one-by-one basis or through the LifeSeq GeneAlbum component of LifeSeq Gold. GeneAlbum is a subscription-based service that provides database collaborators with large numbers of sequence verified DNA clones. In addition, we produce a broad line of genomic research products, such as DNA clones and insert libraries, and offers technical support services, including high-throughput DNA screening, custom robotic services, contract DNA preparation, contract mapping and fluorescent in situ hybridization, to assist researchers in the identification and isolation of novel genes.

## DATABASE PRODUCTION

We engage in the high-throughput automated sequencing of genes derived from tissue samples followed by the computer-aided analysis of each gene sequence to identify homologies to genes of known function in order to predict the biological function of newly identified sequences. The derivation of information in our databases involves the following steps:

- Tissue Access. We obtain tissue samples representing most major organs in the human body from various academic and commercial sources. Where possible, we obtain information as to the medical history and pathology of the tissue. The genetic material is isolated from the tissue and prepared for analysis. The results of this analysis, as well as the corresponding pathology and medical history information, are incorporated into the databases.
- High-Throughput cDNA Sequencing. We utilize specialized teams in an integrated approach to its high-throughput sequencing and analysis effort. Gene sequencing is performed using multiple work shifts to increase daily throughput. One team develops and prepares cDNA libraries from biological sources of interest, a second team prepares the cDNAs using robotic workstations to perform key steps that result in purified cDNAs for sequencing, and a third team operates the automated DNA sequencers.
- Bioinformatics. Sequence information generated from our high-throughput sequencing operations is uploaded to a network of servers. Our proprietary bioinformatic software then assembles and edits the sequence information. The sequence of each cDNA is compared via automated, computerized algorithms to the sequences of known genes in our databases and public domain databases to identify whether the cDNA codes for a known protein or is homologous to a known gene. Each sequence is annotated as to its cell or tissue source, its relative abundance and whether it is homologous to a known gene with known function. The bioinformatics staff monitors this computerized analysis and may perform additional analyses on sequence information. The finished data are then added to our proprietary sequence databases.

As of December 31, 1999, we had database collaboration agreements with more than 20 companies. Each collaborator has agreed to pay annual fees to receive non-exclusive access to one or more of our databases. One of these companies contributed 12% of total revenues in 1998. No customer contributed 10% or more of total revenues in 1999 or 1997. During 1999, our database collaborators included the following companies:

Abbott Laboratories
AstraZeneca PLC
Aventis S.A.
Bristol-Myers Squibb Company
Eli Lilly and Company
F. Hoffmann-La Roche Ltd.
Genentech, Inc.
Glaxo Wellcome plc

Johnson & Johnson
Millennium Pharmaceuticals, Inc.
Monsanto Company
Novartis AG
Pfizer Inc.
Pharmacia & Upjohn, Inc.
Schering AG
Schering-Plough, Ltd.

Some of our database agreements contain minimum annual update requirements, which if not met could result in our breach of the respective agreement. We cannot assure you that any of our database collaboration agreements will not be terminated earlier in accordance with their terms. In 1999 one LifeSeq Gold database collaborator did not renew their subscription. The impact of this did not have a significant impact on our results of operations or a material adverse impact on our business or financial condition. However, future loss of revenues from any individual database agreement, if terminated or not renewed, could have an adverse impact on our results of operations, although it is not anticipated to have a material adverse impact on our business or financial condition.

#### DEVELOPMENT PROGRAMS

Since our inception, we have made substantial investments in research and technology development. During the years ended December 31, 1999, 1998, and 1997 we spent approximately \$146.8 million, \$97.2 million, and \$72.5 million, respectively, on research and development activities. This investment in research and development includes an active program to enter into relationships with other technology-driven companies and, when appropriate, acquire licenses to technologies for evaluation or use in the production and analysis process. Not all of these technologies or relationships survive the evaluation process. We have entered into a number of research and development relationships with companies and research institutions.

In January 1998, we announced a relationship with Oxford GlycoSciences plc ("OGS") to investigate the use of proteomics, the large-scale, high-throughput analysis of protein expression, in the development of new information-based products. As part of the relationship, we made an equity investment in OGS. We and OGS entered into a collaborative agreement under which the two parties are developing data, software and related services, focusing on protein expression and sequence information from a variety of human tissues. As part of the collaborative agreement, we reimbursed OGS \$5.0 million in 1999 for services rendered and agreed to reimburse OGS for up to an additional \$5.0 million in 2000 if revenues are not sufficient to offset OGS' expenses for services to be rendered.

In August 1998, we initiated a series of programs in human genome sequencing, accelerated human genome mapping, bioinformatics and SNP discovery. The information resulting from these efforts will be used to supplement existing databases and to generate new databases and services. We are initiating SNP programs focused on specific candidate genes, gene families, disease pathways, therapeutic areas or drug targets that could be useful to individual pharmaceutical partners. These programs may include the identification of genes associated with a particular disease and an in depth study of the population frequency and disease correlation of SNPs within a selected DNA region. The SNP discovery efforts were assisted by our acquisition of Hexagen in September 1998.

We are developing various platforms that can be used for the high throughput screening of patient samples in order to correlate SNPs with patients' responses to drugs. These platforms may be used to offer genotyping and patient profiling services to pharmaceutical companies to help identify statistically significant and medically relevant associations between SNPs in specific genes and drug response or disease susceptibility. We expect that this service will be used to assist in the evaluation of new drugs in clinical trials and to assess clinical trial design.

## DIADEXUS JOINT VENTURE

In September 1997, we established a 50-50 joint venture company, diaDexus, LLC, with SmithKline Beecham Corporation. diaDexus is applying genomic and bioinformatic technologies to the discovery and commercialization of novel molecular diagnostic products. We provide diaDexus with non-exclusive access to our human and microbial databases (LifeSeq Gold and PathoSeq) for diagnostic

applications. diaDexus also has exclusive rights to develop diagnostic tests based on novel molecular targets and genetic alterations identified as part of SmithKline Beecham's drug discovery efforts. SmithKline Beecham and Incyte have also each assigned various additional technologies and intellectual property rights in the diagnostic field and initially contributed a combined total of \$25 million in funding to diaDexus. In July 1999, we and SmithKline Beecham each invested an additional \$2.5 million in the form of convertible notes that mature in April 2000. The notes will automatically convert into equity if certain funding requirements are met.

diaDexus is focusing initially on the generation of unique diagnostic markers for so-called "homebrew" tests-scientifically validated tests which are awaiting formal regulatory approval-for reference laboratory testing and for license to diagnostic kit manufacturers. Ultimately, diaDexus may develop its own capacity to manufacture kits for sale to clinical testing laboratories. The initial product range will focus on tests for disease detection. New tests for improved diagnosis, staging and patient stratification in infectious disease and oncology will be accorded particular emphasis.

#### PATENTS AND PROPRIETARY TECHNOLOGY

Our database business and competitive position are in part dependent upon our ability to protect our proprietary database information and software technology. We rely on patent, trade secret and copyright law, as well as nondisclosure and other contractual arrangements to protect our proprietary information.

Our ability to license proprietary genes and SNPs may be dependent upon our ability to obtain patents, protect trade secrets and operate without infringing upon the proprietary rights of others. Other pharmaceutical, biotechnology and biopharmaceutical companies, as well as academic and other institutions, have filed applications for, may have been issued patents or may obtain additional patents and proprietary rights, relating to products or processes competitive to our products or processes. Patent applications filed by competitors may claim some of the same gene sequences or partial gene sequences as those claimed in patent applications that we file. We are aware that some entities have made or have announced their intention to make gene sequences publicly available. Publication of sequence information may adversely affect our ability to obtain patent protection for sequences that have been made publicly available.

Our current policy is to file patent applications on what we believe to be novel full-length and partial gene sequences obtained through our high-throughput computer-aided gene sequencing efforts. We have filed U.S. patent applications in which we have claimed certain partial gene sequences and have filed patent applications in the U.S. and applications under the Patent Cooperation Treaty ("PCT"), designating countries in Europe as well as Canada and Japan, claiming full-length gene sequences associated with cells and tissues that are the subject of our high-throughput gene sequencing program. To date, we hold approximately 400 U.S. patents with respect to full-length gene sequences and one issued U.S. patent claiming multiple partial gene sequences. Currently, we have no registered copyrights for our database-related software.

In 1996, the United States Patent and Trademark Office issued guidelines limiting the number of partial gene sequences that can be examined in a single patent application. Many of our patent applications containing multiple partial sequences contain more sequences than the maximum number allowed under the new guidelines. We are reviewing our options, and due to the resources needed to comply with the guidelines, we may decide to abandon patent applications for some of our partial gene sequences.

We have begun to file patent applications for patentable SNPs identified with our LifeSeq Gold database, through our human genome sequencing program, and through the use of our fSSCP discovery technology. These patents will claim rights to SNPs for diagnostic and genotyping purposes. As information relating to particular SNPs is developed, we plan to seek additional rights in those SNPs that are associated with specific diseases, functions or drug responses. The scope of patent protection for gene sequences, including SNPs, is highly uncertain, involves complex legal and factual questions and has recently been the subject of much controversy. No clear policy has emerged with respect to the breadth of claims allowable for SNPs. There is significant uncertainty as to what, if any, claims will be allowed on SNPs discovered through high throughput discovery programs.

As the biotechnology industry expands, more patents are issued and other companies engage in the business of discovering genes and other genomic-related businesses, the risk increases that our potential products, and the processes used to develop these products, may be subject to claims that they infringe the patents of others. Further, we are aware of several issued patents in the field of microarray or gridding technology, which can be utilized in the generation of gene expression information. Some of these patents are the subject of litigation. Therefore, our operations may require us to obtain licenses under

any of these patents or proprietary rights, and these licenses may not be made available on terms acceptable to us. 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. We believe that some of our patent applications cover genes that may also be claimed in patent applications filed by other parties. Interference proceedings may be necessary to establish which party was the first to invent a particular sequence for the purpose of patent protection. Several interferences involving our patent applications covering full length genes have been declared. Litigation or interference proceedings, regardless of the outcome, could result in substantial costs to us, and divert our efforts, and may have a material adverse effect on our business, operating results and financial condition. In addition, there can be no assurance that such proceedings or litigation would be resolved in our favor.

In January and September 1998, Affymetrix, Inc. filed lawsuits in the United States District Court for the District of Delaware alleging infringement of three U.S. patents by both Synteni and Incyte. Incyte believes that it and Synteni have meritorious defenses and intends to defend these suits vigorously. See "Risk Factors-We Are Involved in Patent Litigation, Which If We Do Not Resolve Favorably Could Negatively Impact Our Business."

## COMPETITION

There is a finite number of genes in the human genome, and competitors may seek to identify, sequence and determine in the shortest time possible the biological function of a large number of genes in order to obtain a proprietary position with respect to the largest number of new genes discovered. A number of companies, institutions, and government-financed entities are engaged in gene sequencing, gene discovery, gene expression analysis, positional cloning and other genomic service businesses. Many of these companies, institutions and entities have greater financial and human resources than we do. In addition, we are aware that other companies have developed databases containing gene sequence, gene expression, genetic variation or other genomic information and are marketing, or have announced their intention to market, their data to pharmaceutical companies. We expect that additional competitors may attempt to establish databases containing this information in the future.

In addition, competitors may discover and establish patent positions with respect to the gene sequences and polymorphisms in our databases. Further, some entities engaged in or with stated intentions to engage in gene sequencing have made or have stated their intention to make the results of their sequencing efforts publicly available. These patent positions, or the public availability of gene sequences comprising substantial portions of the human genome or on microbial or plant genes, could:

- - decrease the potential value of our databases to our subscribers; and
- - adversely affect our ability to realize royalties or other revenue from commercialization of products based upon such genetic information.

The gene sequencing machines that are utilized in our high-throughput computer-aided gene sequencing operations are commercially available and are currently being utilized by several competitors. Also, some of our competitors or potential competitors are in the process of developing, and may successfully develop, proprietary sequencing technologies that may be more advanced than the technology we use. In addition, we are aware that a number of companies are pursuing alternative methods for generating gene expression information, including some that have developed and are developing microarray technologies. At least one other company currently offers microarray-based services that might be competitive with those we offer. These advanced sequencing or gene expression technologies, if developed, may not be commercially available for our purchase or license on reasonable terms, if at all.

A number of companies have announced their intent to develop and market software to assist pharmaceutical companies and academic researchers in the management and analysis of their own genomic data, as well as the analysis of sequence data available in the public domain. Some of these entities have access to significantly greater resources than we do, and their products may achieve greater market acceptance than our products.

Our SNP discovery platform represents a modification of a process that is in the public domain. Other companies could make similar or superior improvements in this process.

- -- the features and ease of use of our database software;
- -- our experience in high-throughput gene sequencing;
- -- the cumulative size of our databases;
- - the quality of the data, including the annotations in our databases;

- - our computing infrastructure; and - - and our experience with bioinformatics and database software.

The genomics industry is characterized by extensive research efforts and rapid technological progress. New developments are expected to continue and there can be no assurance that discoveries by others will not render our services and potential products noncompetitive. In addition, significant levels of research in biotechnology and medicine occur in universities and other non-profit research institutions. These entities have become increasingly active in seeking patent protection and licensing revenues for their research results. These entities also compete with us in recruiting talented scientists. See "Risk Factors-We Experience Intense Competition and Rapid Technological Change and If We Do Not Compete Effectively Our Revenues May Decline."

#### GOVERNMENT REGULATION

Regulation by governmental authorities in the United States and other countries will be a significant factor in the production and marketing of any pharmaceutical products that may be developed by us or our licensees. At the present time, we do not intend to develop any pharmaceutical products ourselves. Our agreements with our LifeSeq Gold database subscribers provide for the payment to us of royalties on any pharmaceutical products developed by those subscribers derived from proprietary information obtained from our genomic databases. Thus, the receipt and timing of regulatory approvals for the marketing of such products may have a significant effect on our future revenues. Pharmaceutical products developed by licensees will require regulatory approval by governmental agencies prior to commercialization. In particular, human pharmaceutical therapeutic products are subject to rigorous preclinical and clinical testing and other approval procedures by the United States Food and Drug Administration in the United States and similar health authorities in foreign countries. Various federal and, in some cases, state statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of such pharmaceutical products, including the use, manufacture, storage, handling and disposal of hazardous materials and certain waste products. The process of obtaining these approvals and the subsequent compliance with appropriate federal and foreign statutes and regulations require the expenditure of substantial resources over a significant period of time, and there can be no assurance that any approvals will be granted on a timely basis, if at all. Any such delay in obtaining or failure to obtain such approvals could adversely affect our ability to earn milestone payments, royalties or other license-based fees. Additional governmental regulations that might arise from future legislation or administrative action cannot be predicted, and such regulations could delay or otherwise affect adversely regulatory approval of potential pharmaceutical products. See "Risk Factors-Our Revenues Are Derived Primarily from the Pharmaceutical and Biotechnology Industries and May Fluctuate Substantially Due to Reductions and Delays in Research and Development Expenditures."

## HUMAN RESOURCES

As of December 31, 1999, we had 1,108 full-time equivalent employees (195 of whom were contract or part-time employees), including 399 in sequencing, microarray, SNP and reagent production, 294 in bioinformatics, 239 in research and technology development, and 176 in marketing, sales and administrative positions. None of our employees is covered by collective bargaining agreements, and management considers relations with its employees to be good. Our future success will depend in part on the continued service of our key scientific, software, bioinformatics and management personnel and its ability to identify, hire and retain additional personnel, including personnel in the customer service, marketing and sales areas. There is intense competition for qualified personnel in the areas of our activities, especially with respect to experienced bioinformatics and software personnel, and there can be no assurance that we will be able to continue to attract and retain such personnel necessary for the development of our business. Failure to attract and retain key personnel could have a material adverse effect on our business, financial condition and operating results. See "Risk Factors-We May Have Difficulty Managing Our Growth, Which May Impact Our Ability to Optimize Our Resources" and "-We Depend on Key Employees in a Competitive Market for Skilled Personnel and the Loss of the Services of Any of Our Key Employees Would Materially Affect Our Business."

## RISK FACTORS

WE HAVE HAD ONLY LIMITED PERIODS OF PROFITABILITY AND WE EXPECT TO INCUR LOSSES IN THE FUTURE, WHICH MAY PREVENT US FROM RETURNING TO PROFITABILITY

We had net losses from inception in 1991 through 1996, reported net income in 1997 and 1998, and again incurred a net loss in 1999. Because of those losses, we had an accumulated deficit of \$55.2 million as of December 31, 1999. We intend to make significant investments in sequencing, bioinformatics, expression database development and single nucleotide polymorphism, or SNP,

discovery over the next six to nine months, so we expect to report net losses at least through the first three quarters of 2000 and for the year ending December 31, 2000. We may report net losses in future periods as well. We expect that our expenditures may continue to increase through the first three quarters of 2000 due in part to our continued investment in new product and technology development, including the continuation of our genomic sequencing, bioinformatics, expression database development, SNP-discovery programs, obligations under existing and future research and development alliances, and our increasing investment in marketing, sales and customer service. Our profitability depends on our ability to increase our revenues:

To generate significant revenues, we must obtain additional database collaborators and retain existing collaborators. While we had over 20 database agreements as of December 31, 1999, we may be unable to enter into any additional agreements. In 1999, one LifeSeq Gold database collaborator did not renew their subscription. Our other database collaborators may choose not to renew upon expiration of other existing agreements. Our database revenues are also affected by the extent to which existing collaborators expand their agreements with us to include our new database products and to the extent that existing collaborators reduce the number of products or services for which they subscribe. Some of our database agreements require us to meet performance obligations. A database collaborator can terminate its agreement before the end of its scheduled term if we breach the agreement and fail to cure the breach within a specified period.

Our revenues and profitability will also depend on our ability to generate profits from microarray services and expression databases. We acquired Synteni, Inc. in January 1998 to provide microarray services and to generate information for expression databases. The contribution of our microarray operations to our operating results will depend on whether we can continue to obtain high-volume customers for microarray services and expression databases, whether we can continue to increase our microarray production capacity in a timely manner and with consistent volumes and quality, and the costs associated with increasing our microarray production capacity.

We do not expect milestone or royalty payments to contribute to revenues for a substantial period of time. Part of our strategy is to license to database collaborators our know how and patent rights associated with the gene sequences and related information in our proprietary databases, for use in the discovery and development of potential pharmaceutical, diagnostic or other products. Any potential product that is the subject of such a license will require several years of further development, clinical testing and regulatory approval before commercialization. In 1999, one customer paid future license fees, even though the customer has not developed a product using our database information. We are not assured of any additional milestone or royalty payments.

## OUR OPERATING RESULTS ARE UNPREDICTABLE AND MAY ADVERSELY IMPACT OUR STOCK PRICE

Our operating results are unpredictable and may fluctuate significantly from period to period due to a variety of factors, including:

- -- changes in the demand for our products and services;
- - the introduction of competitive databases or services, including public domain databases;
- -- the pricing of access to our databases;
- - the nature, pricing and timing of other products and services provided to our collaborators;
- ${\mbox{-}}$  changes in the research and development budgets of our collaborators and potential collaborators;
- -- depreciation expense from capital expenditures;
- - acquisition, licensing and other costs related to the expansion of our operations, including operating losses of acquired businesses such as Synteni and Hexagen;
- losses and expenses related to our investments in joint ventures and businesses, including our proportionate share of operating losses of our diaDexus. LLC. joint venture with SmithKline Beecham Corporation:
- diaDexus, LLC, joint venture with SmithKline Beecham Corporation;
   payments of milestones, license fees or research payments under the terms of our increasing number of external alliances; and
- -- expenses related to, and the results of, litigation and other proceedings relating to intellectual property rights (including the lawsuits filed by Affymetrix, Inc. described below).

In particular, revenues from our database business are unpredictable because:

- -- the timing of our database installations is determined by our collaborators;
- -- the sales cycle for our database products is lengthy; and
- -- the time required to complete custom orders can vary significantly.

We expect our expression databases to represent an increasing amount of our revenues. Also, revenues may be affected by developments in the Affymetrix litigation, which may cause potential customers to postpone or change their

decision to use our microarray services.

We are investing in a number of new areas to try to broaden our business. These areas include sequencing, bioinformatics, gene expression databases, SNP discovery, molecular diagnostics, proteomics, or the large scale, high-throughput analysis of protein expression, and the online delivery of our database and software products. Because many of these address new markets or involve untested technologies, they may not generate any revenues or provide an adequate return on our investment. In these cases, we may have to recognize expenses or losses.

We have significant fixed expenses, due in part to our need to continue to invest in product development and extensive support for our database collaborators. We may be unable to adjust our expenditures if revenues in a particular period fail to meet our expectations, which would adversely affect our operating results for that period. Forecasting operating and integration expenses for acquired businesses may be particularly difficult, especially where the acquired business focuses on technologies that do not have an established market.

We believe that period-to-period comparisons of our financial results will not necessarily be meaningful. You should not rely on these comparisons as an indication of our future performance. If our operating results in any future period fall below the expectations of securities analysts and investors, our stock price will likely fall, possibly by a significant amount.

WE EXPERIENCE INTENSE COMPETITION AND RAPID TECHNOLOGICAL CHANGE AND IF WE DO NOT COMPETE EFFECTIVELY OUR REVENUES MAY DECLINE

Genomic businesses are intensely competitive. The human genome contains a finite number of genes. Our competitors may seek to identify, sequence and determine the biological function of numerous genes in order to obtain a proprietary position with respect to new genes. A number of companies, other institutions and government-financed entities are engaged in gene sequencing, gene discovery, gene expression analysis, positional cloning, the study of genetic variation, and other genomic service businesses. Many of these companies, institutions and entities have greater financial and human resources than we do.

Some of our competitors have developed databases containing gene sequence, gene expression, genetic variation or other genomic information and are marketing or plan to market their data to pharmaceutical companies. Additional competitors may attempt to establish databases containing this information in the future. We expect that competition in our industry will continue to intensify. Several large pharmaceutical companies have formed a consortium to create a SNPs database and to make all of the information publicly available. The formation of this consortium could delay or reduce the potential revenues related to our SNP-related business.

Patent positions or public disclosures may reduce the value of our databases. Competitors may discover and establish patent positions with respect to gene sequences in our databases. Further, certain entities engaged in gene sequencing have made the results of their sequencing efforts publicly available. In January 2000, the Celera Genomics Group of PE Corporation announced that it has DNA sequence in its database that covers 90% of the human genome and plans to complete the sequencing of the human genome by the summer of 2000. Celera has announced that it has filed a provisional patent application on newly discovered partial genes and stated its intention to file full applications on medically important discoveries. The Human Genome Project, which is coordinated by the U.S. Department of Energy and the National Institutes of Health, has announced that a consortium of laboratories associated with the Project predicts that they will produce at least 90% of the human genome sequence in a "working draft form" by the spring of 2000 and that they intend to make the information publicly available. The public availability of gene sequences or resulting patent positions covering substantial portions of the human genome or microbial or plant genomes could reduce the potential value of our databases to our collaborators. It could also impair our ability to realize royalties or other revenue from any commercialized products based on this genetic information.

Competitors may develop superior technology. The gene sequencing machines used in our computer-aided sequencing operations are commercially available and are being used by at least one competitor. In addition, some of our competitors and potential competitors are developing proprietary sequencing technologies that may be more advanced than ours. PE Corporation began commercial shipments of a new gel-based sequencing machine, of which a large number have been provided to Celera Genomics Group. We may be unable to obtain access to sufficient quantities of these machines on acceptable terms.

In addition, a number of companies are pursuing alternative methods for generating gene expression information, including microarray technologies. These

advanced sequencing or gene expression technologies may not be commercially available for us to purchase or license on reasonable terms, if at all. At least one other company currently offers microarray-based services that might be competitive with ours.

Our SNP discovery platform represents a modification of a process that is in the public domain. We are seeking patent protection for these improvements, but have not yet received any patents. Other companies could make similar or superior improvements to this process without infringing our rights, and we may not have access to those improvements. The discovery of SNPs is a competitive area. Other companies may develop or obtain access to different SNP discovery platforms, to which we may not have access, that may make our technology obsolete.

We also face competition from providers of software. A number of companies have announced their intent to develop and market software to assist pharmaceutical companies and academic researchers in managing and analyzing their own genomic data and publicly available data.

We must continue to invest in new technologies. The genomics industry is characterized by extensive research efforts, resulting in rapid technological progress. To remain competitive, we must continue to expand our databases, improve our software, and invest in new technologies. New developments are expected to continue, and discoveries by others may render our services and potential products noncompetitive.

WE ARE INVOLVED IN PATENT LITIGATION, WHICH IF WE DO NOT RESOLVE FAVORABLY COULD NEGATIVELY IMPACT OUR BUSINESS

In January 1998, Affymetrix filed a lawsuit in federal court alleging infringement of U.S. patent number 5,445,934 by both Synteni and Incyte. The complaint alleges that the '934 patent has been infringed by Synteni's and Incyte's making, using, selling, importing, distributing or offering to sell high density arrays in the United States and that this infringement was willful. Affymetrix seeks a permanent injunction enjoining Synteni and Incyte from further infringement of the '934 patent and seeks damages, costs, attorneys' fees and interest. Affymetrix also requests triple damages based on allegedly willful infringement.

In September 1998, Affymetrix filed an additional lawsuit alleging infringement of U.S. patent numbers 5,744,305 and 5,800,992 by Synteni and Incyte. The complaint alleges that the '305 patent has been infringed by Synteni's and Incyte's making, using, selling, importing, distributing or offering to sell high density arrays in the United States. It also alleges that the '992 patent has been infringed by the use of Synteni's and Incyte's GEM microarray technology to conduct gene expression monitoring using two-color labeling and that this infringement was willful. Affymetrix had sought a preliminary injunction enjoining Synteni and Incyte from using GEM microarray technology to conduct this kind of gene expression monitoring, and a permanent injunction enjoining Synteni and Incyte from further infringing the '305 and '992 patents.

The lawsuits were initially filed in the United States District Court for the District of Delaware. In November 1998, the court granted Incyte's motion to transfer the suits to the United States District Court for the Northern District of California. Affymetrix's request for a preliminary injunction was denied in April 1999. As a result of the assignment of the case to a new judge, all scheduled trial and pretrial dates have been vacated. A new schedule is expected to be set by the court in late April 2000.

In April 1999, the Board of Patent Appeals and Interferences of United States Patent and Trademark Office declared interferences between pending patent applications licensed exclusively to us and the Affymetrix '305 and '992 patents. An interference proceeding is invoked by the Patent and Trademark Office when more than one patent applicant claims the same invention. The Board of Patent Appeals and Interferences evaluates all relevant facts, including those bearing on first to invent, validity, enablement and scope of claims, and then makes a determination as to who, if anyone, is entitled to the patent on the disputed invention. In September 1999, the Board of Patent Appeals and Interferences determined that Incyte had not met its prima facie case, and ruled that patents licensed by Incyte and Synteni from Stanford University were not entitled to priority over corresponding claims in the two Affymetrix patents. We have sought de novo review of the board decisions in the United States district court for the Northern District of California.

We believe we have meritorious defenses and intend to defend these suits vigorously. However, our defense may be unsuccessful. At this time, we cannot reasonably estimate the possible range of any loss resulting from these suits due to uncertainty about the ultimate outcome. We have spent and expect to continue to spend a significant amount of money and management time on this litigation. Also, if we are required to license any technology as a result of

these suits, we do not know whether we will be able to do so on commercially acceptable terms, if at all.

WE SPEND A SUBSTANTIAL AMOUNT OF MONEY ON NEW AND UNCERTAIN BUSINESSES AND DEMAND FOR OUR PRODUCTS AND SERVICES MAY BE INSUFFICIENT TO COVER OUR COSTS, WHICH COULD IMPACT OUR PROFITABILITY

There is no precedent for our microarray-based gene expression database or service businesses or the use of SNP-based genetic variation information. The usefulness of the information generated by these businesses is unproven. Our collaborators and potential collaborators may determine that our databases, software tools and microarray-related services are not useful or cost-effective. Due to the nature and price of some of the products and services we offer, only a limited number of companies are potential collaborators for those products and services. If we do not develop these new products and services in time to meet market demand or if there is insufficient demand for these products and services, we may not be able to cover our costs of developing these products and services or earn a sufficient return on our investment.

Additional factors that may affect demand for our products and services include:

- - the extent to which pharmaceutical and biotechnology companies conduct these activities in-house or through industry consortia;
- - the emergence of competitors offering similar services at competitive prices;
- - the extent to which the information in our databases is made public or is covered by others' patents;
- our ability to establish and enforce proprietary rights to our products;
- - regulatory developments or changes in public perceptions relating to the use of genetic information and the diagnosis and treatment of disease based on genetic information; and
- - technological innovations that are more advanced than the technologies that we have developed or that are available to us.

Many of these factors are beyond our control.

OUR NEW PROGRAMS RELATING TO THE ROLE OF GENETIC VARIATION IN DISEASE AND DRUG RESPONSE MAY NEVER GENERATE SIGNIFICANT REVENUES OR PROFITABLE OPERATIONS

We recently began to focus part of our business on developing databases and other products and services to assist pharmaceutical companies in a new and unproven area: the identification and correlation of genetic variation to disease and drug response. We will incur significant costs over the next several years in expanding our research and development in this area. These activities may never generate significant revenues or profitable operations.

This new aspect of our business will focus on SNPs, one type of genetic variation. The role of SNPs in disease and drug response is not fully understood, and relatively few, if any, therapeutic or diagnostic products based on SNPs have been developed and commercialized. Among other things, demand in this area may be adversely affected by ethical and social concerns about the confidentiality of patient-specific genetic information and about the use of genetic testing for diagnostic purposes.

Except for a few anecdotal examples, there is no proof that SNPs have any correlation to diseases or a patient's response to a particular drug or class of drug. Identifying statistically significant correlations is time-consuming and could involve the collection and screening of a large number of patient samples. We do not know if the SNPs we have discovered to date are suitable for these correlation studies. Nor do we currently have access to the patient samples needed or technology allowing us to rapidly and cost-effectively identify pre-determined SNPs in large numbers of patients.

Most SNPs may occur too infrequently to warrant their use in analyzing patients' genetic variation. We may have trouble identifying SNPs that both correlate with diseases or drug responses and occur frequently enough to justify their use by pharmaceutical companies.

Our success will also depend upon our ability to develop, use and enhance new and relatively unproven technologies. Our strategy of using high-throughput mutation detection processes and sequencing to identify SNPs and genes rapidly is unproven. Among other things, we will need to continue to improve the throughput of our SNP-discovery technology. We may not be able to achieve these necessary improvements, and other factors may impair our ability to develop our SNP-related products and services in time to be competitively available.

We make strategic investments in joint ventures or businesses that complement our business. These investments, such as our investment in diaDexus, may:

- - often be made in securities lacking a public trading market or subject to trading restrictions, either of which increases our risk and reduces the liquidity of our investment;
- - require us to record losses and expenses related to our ownership interest;
- require us to record charges related to the acquisition of in-process technologies or for the impairment in the value of the securities underlying our investment; and
- require us to invest greater amounts than anticipated or to devote substantial management time to the management of research and development relationships and joint ventures.

The market values of many of these investments fluctuate significantly. We evaluate our long-term equity investments for impairment of their values on a quarterly basis. Impairment could result in future charges to our earnings. These losses and expenses may exceed the amounts that we anticipated.

OUR SALES CYCLE IS LENGTHY AND THERE IS NO GUARANTEE THAT A SUBSCRIPTION OR SERVICES AGREEMENT WILL RESULT

Our ability to obtain new subscribers for our databases, software tools and microarray and other services depends upon prospective subscribers' perceptions that our products and services can help accelerate drug discovery efforts. Our database sales cycle is typically lengthy because we need to educate our potential subscribers and sell the benefits of our tools and services to a variety of constituencies within potential subscriber companies. In addition, each database subscription and microarray services agreement involves the negotiation of unique terms. We may expend substantial funds and management effort with no assurance that a subscription or services agreement will result. Actual and proposed consolidations of pharmaceutical companies have affected the timing and progress of our sales efforts. We expect that future proposed consolidations will have similar effects.

PATENTS AND OTHER PROPRIETARY RIGHTS PROVIDE UNCERTAIN PROTECTION OF OUR PROPRIETARY INFORMATION AND OUR INABILITY TO PROTECT A PATENT OR OTHER PROPRIETARY RIGHT MAY IMPACT OUR BUSINESS AND OPERATING RESULTS

We may be unable to protect our proprietary information, which may result in unauthorized use and a loss of revenue. Our business and competitive position depend upon our ability to protect our proprietary database information and software technology, but our strategy of obtaining proprietary rights in as many genes and SNPs as possible is unproven. Despite our efforts to protect this information and technology, unauthorized parties may attempt to obtain and use information that we regard as proprietary. Although our database subscription agreements require our subscribers to control access to our databases, policing unauthorized use of our databases and software may be difficult.

We pursue a policy of having our employees, consultants and advisors execute proprietary information and invention agreements when they begin working for us. However, these agreements may not provide meaningful protection for our trade secrets or other proprietary information in the event of unauthorized use or disclosure.

Our means of protecting our proprietary rights may not be adequate and our competitors may:

- - independently develop substantially equivalent proprietary information and techniques;
- -- otherwise gain access to our proprietary information; or
- - design around patents issued to us or our other intellectual property.

Our patent applications may conflict with others. Our current policy is to file patent applications on what we believe to be novel full-length and partial gene sequences obtained through our gene sequencing efforts. We have filed U.S. patent applications in which we have claimed certain partial gene sequences. We have also applied for patents in the U.S. and other countries claiming full-length gene sequences associated with cells and tissues involved in our gene sequencing program. We hold a number of issued U.S. patents on full-length genes and one issued U.S. patent claiming multiple partial gene

sequences. A number of entities make certain gene sequences publicly available, which may adversely affect our ability to obtain patents on those genes.

We believe that some of our patent applications claim genes that may also be claimed in patent applications filed by others. In some or all of these applications, a determination of priority of inventorship may need to be decided in an interference before the United States Patent and Trademark Office.

Enforcement of gene patents is uncertain and gene patents may be found unenforceable, resulting in a loss of competitive benefit. One of our strategies is to obtain proprietary rights in as many genes (including partial gene sequences) and SNPs as possible. While the USPTO has issued patents covering full-length genes, partial gene sequences and SNPs, we do not know whether or how courts may enforce those patents, if that becomes necessary. If a court finds these types of inventions to be unpatentable, or interprets them narrowly, the benefits of our strategy may not materialize.

We may decide to abandon patent applications, which could diminish the value of our patent portfolio and possibly our future revenues. The USPTO has had a substantial backlog of biotechnology patent applications, particularly those claiming gene sequences. In 1996, the USPTO issued guidelines limiting the number of partial gene sequences that can be examined within a single patent application. Many of our patent applications contain more partial sequences than the maximum number allowed under these guidelines. Due to the resources needed to comply with the guidelines, we may decide to abandon patent applications for some of our partial gene sequences.

Because filing large numbers of patent applications and maintaining issued patents can be very costly, we may choose not to pursue every application. If we do not pursue patent protection for all of our full-length and partial gene sequences, the value of our intellectual property portfolio could be diminished. Because of the possible delay in obtaining allowance of some of our patent applications, and the secrecy of patent applications, we do not know if other applications having priority over ours have been filed.

We may need to refile some of our patent applications and the period of patent protection has been shortened, which may affect our potential revenues and profits. The value of our patents depends in part on their duration. The U.S. patent laws were amended in 1995 to change the term of patent protection from 17 years from patent issuance to 20 years from the earliest effective filing date of the application. Because the average time from filing to issuance of biotechnology applications is at least one year and may be more than three years depending on the subject matter, a 20-year patent term from the filing date may result in substantially shorter patent protection, which may adversely affect our rights under any patents that we obtain. We may need to refile applications claiming large numbers of gene sequences and, in these situations, the patent term will be measured from the date of the earliest priority application. This would shorten our period of patent exclusivity.

International patent protection is particularly uncertain, and opposition proceedings in foreign countries may be costly and divert management resources. Biotechnology patent law outside the United States is even more uncertain than in the United States and is currently undergoing review and revision in many countries. Further, the laws of some foreign countries may not protect our intellectual property rights to the same extent as U.S. laws. We may participate in opposition proceedings to determine the validity of our or our competitors' foreign patents, which could result in substantial costs and diversion of our efforts.

WE MAY BE SUBJECT TO ADDITIONAL LITIGATION AND INFRINGEMENT CLAIMS THAT COULD BE COSTLY AND DISRUPT OUR BUSINESS

The technology that we use to develop our products, and those that we incorporate in our products, may be subject to claims that they infringe the patents or proprietary rights of others. The risk of this occurring will tend to increase as the genomics, biotechnology and software industries expand, more patents are issued and other companies attempt to discover genes and SNPs and engage in other genomic-related businesses.

As is typical in the genomics, biotechnology and software industries, we have received, and we will probably receive in the future, notices from third parties alleging patent infringement. We believe that we are not infringing the patent rights of any such third party. Except for Affymetrix, no third party has filed a patent lawsuit against us.

We may, however, be involved in future lawsuits alleging patent infringement or other intellectual property rights violations. In addition, litigation may be necessary to:

- enforce our patents;
- -- protect our trade secrets or know-how; or
- - determine the enforceability, scope and validity of the proprietary rights of others.

We may be unsuccessful in defending or pursuing these lawsuits. Regardless of the outcome, litigation can be very costly and can divert management's efforts. An adverse determination may subject us to significant liabilities or require us to seek licenses to other parties' patents or proprietary rights. We may also be restricted or prevented from manufacturing or selling our products. Further, we may not be able to obtain the necessary licenses on acceptable terms, if at all.

WE MAY ENCOUNTER PROBLEMS IN MEETING CUSTOMERS' SOFTWARE NEEDS, WHICH COULD ADVERSELY IMPACT OUR REVENUES AND THE GOODWILL OF OUR CUSTOMERS

Our databases also require software support and will need to incorporate features determined by database collaborators. If we experience delays or difficulties in implementing our database software or collaborator-requested features, we may be unable to service our collaborators.

PAST ACQUISITIONS HAVE AND ANY FUTURE ACQUISITIONS THAT WE MAY MAKE COULD ADVERSELY AFFECT OUR OPERATIONS OR FINANCIAL RESULTS

As part of our business strategy, we may acquire other assets, technologies and businesses. We acquired Synteni in January 1998 and Hexagen in September 1998.

These and any future acquisitions involve risks such as the following:

- -- we may be exposed to unknown liabilities of acquired companies;
- - our acquisition and integration costs may be higher than we anticipated and may cause our quarterly and annual operating results to fluctuate;
- - we may experience difficulty and expense in assimilating the operations and personnel of the acquired businesses, disrupting our business and diverting management's time and attention;
- - we may be unable to integrate or complete the development and application of acquired technology;
- -- we may experience difficulties in establishing and maintaining uniform standards, controls, procedures and policies;
- - our relationships with key customers of acquired businesses may be impaired, due to changes in management and ownership of the acquired businesses;
- - we may be unable to retain key employees of the acquired businesses;
- -- we may incur amortization expenses if an acquisition results in significant goodwill or other intangible assets; and
- - our stockholders may be diluted if we pay for the acquisition with equity securities.

In addition, if we acquire additional businesses that are not located near our Palo Alto, California headquarters, we may experience more difficulty integrating and managing the acquired businesses' operations.

WE MAY HAVE DIFFICULTY MANAGING OUR GROWTH, WHICH MAY IMPACT OUR ABILITY TO OPTIMIZE OUR RESOURCES

We expect to continue to experience significant growth in the number of our employees and the scope of our operations. This growth has placed, and may continue to place, a significant strain on our management and operations. Our ability to manage this growth will depend upon our ability to attract, hire and retain skilled employees. Our success will also depend on the ability of our officers and key employees to continue to implement and improve our operational and other systems and to hire, train and manage our employees.

In addition, we must continue to invest in customer support resources as the number of database collaborators and their requests for support increase. Our database collaborators typically have worldwide operations and may require support at multiple U.S. and foreign sites. To provide this support, we may need to open offices in addition to our Palo Alto, California headquarters and our offices in Fremont, California, St. Louis, Missouri and Cambridge, England, which could result in additional burdens on our systems and resources.

WE DEPEND ON KEY EMPLOYEES IN A COMPETITIVE MARKET FOR SKILLED PERSONNEL AND THE LOSS OF THE SERVICES OF ANY OF OUR KEY EMPLOYEES WOULD MATERIALLY AFFECT OUR BUSINESS

We are highly dependent on the principal members of our management, operations and scientific staff, including Roy A. Whitfield, our Chief Executive Officer, and Randal W. Scott, our President and Chief Scientific Officer. The loss of either of these persons' services may have a material adverse effect on our business. We have not entered into any employment agreement with either of these persons and do not maintain a key person life insurance policy on the life of any employee.

Our future success also will depend in part on the continued service of our key scientific, software, bioinformatics and management personnel and our ability to identify, hire and retain additional personnel, including customer service, marketing and sales staff. We experience intense competition for qualified personnel. We may not be able to continue to attract and retain personnel necessary for the development of our business.

OUR INABILITY TO OBTAIN NECESSARY EQUIPMENT, SUPPLIES AND DATA FROM THIRD PARTIES MAY ADVERSELY IMPACT OUR RESULTS

We rely on a small number of suppliers of gene sequencing machines and reagents required for gene sequencing. Although we are evaluating alternative gene sequencing machines, they may not be available in sufficient quantities or at acceptable costs. In addition, if a third party claims that our use of these machines infringes their patent rights, our use of these machines could become more costly or could be prevented. If we are unable to obtain additional machines or an adequate supply of reagents or other materials at commercially reasonable rates, our ability to identify genes and SNPs would be adversely affected.

We rely on outside sources for tissue samples from which we isolate genetic material used in our operations. Our business could be adversely affected if we lose access to some of these sources, or if they charged us higher access fees or imposed tighter restrictions on our use of the information generated from the samples.

We cannot control the performance of collaborators. We may enter into research and development relationships with corporate and academic collaborators and others. The success of these relationships depends upon third parties' performance of their responsibilities. Our ability to develop these relationships is uncertain, and any established relationships may prove unsuccessful. Our collaborators may also be pursuing alternative technologies or developing alternative products on their own or in collaboration with others, including our competitors.

We rely on third-party data sources. We rely on scientific and other data supplied by others, including our academic collaborators and sources of tissue samples. This data could contain errors or other defects, which could corrupt our databases. In addition, we cannot guarantee that our data sources acquired this information in compliance with legal requirements. If either of these happen and become known, our business prospects could be adversely affected.

OUR ACTIVITIES INVOLVE HAZARDOUS MATERIALS AND MAY SUBJECT US TO COSTLY ENVIRONMENTAL LIABILITY

Our research and development involves the controlled use of hazardous and radioactive materials and biological waste. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these materials and certain waste products. Although we believe that our safety procedures for handling and disposing of these materials comply with legally prescribed standards, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of an accident, we could be held liable for damages, and this liability could exceed our resources.

We believe that we are in compliance in all material respects with applicable environmental laws and regulations and currently do not expect to make material additional capital expenditures for environmental control facilities in the near term. However, we may have to incur significant costs to comply with current or future environmental laws and regulations.

OUR REVENUES ARE DERIVED PRIMARILY FROM THE PHARMACEUTICAL AND BIOTECHNOLOGY INDUSTRIES AND MAY FLUCTUATE SUBSTANTIALLY DUE TO REDUCTIONS AND DELAYS IN RESEARCH AND DEVELOPMENT EXPENDITURES

We expect that our revenues in the foreseeable future will be derived primarily from products and services provided to the pharmaceutical and biotechnology industries. Accordingly, our success will depend directly upon the success of the companies within these industries and their demand for our

products and services. Our operating results may fluctuate substantially due to reductions and delays in research and development expenditures by companies in these industries. These reductions and delays may result from factors such as:

- -- changes in economic conditions;
- -- consolidation in the pharmaceutical industry;
- - changes in the regulatory environment affecting health care and health care providers;
- - pricing pressures;
- - market-driven pressures on companies to consolidate and reduce costs; and
- other factors affecting research and development spending.

These factors are not within our control.

#### WE MAY NEED TO RAISE ADDITIONAL CAPITAL THAT MAY NOT BE AVAILABLE WHEN NEEDED

Based upon our current plans, we believe that our existing resources and our anticipated cash flow from operations will satisfy our capital needs for at least the next twelve months. Our cash requirements depend on numerous factors, including:

- - our ability to attract and retain collaborators for our databases and other products and services;
- - expenditures in connection with alliances, license agreements and acquisitions of and investments in complementary technologies and businesses;
- - the need to increase research and development spending as a result of competing technological and market developments;
- - the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;
- - the purchase of additional capital equipment, including equipment necessary to process data for our databases and to ensure that our sequencing and microarray operations remain competitive;
- capital expenditures required to expand our facilities; and
- -- costs associated with the integration of acquired operations.

Changes in our research and development plans or other changes affecting our operating expenses may alter the timing and amount of expenditures of our capital resources. If we need additional funding, we may be unable to obtain it on favorable terms, or at all. If adequate funds are not available, we may have to curtail operations significantly or obtain funds by entering into arrangements requiring us to relinquish rights to certain technologies, products or markets. In addition, if we raise funds by selling stock or convertible securities, our existing stockholders could suffer dilution.

## OUR BUSINESS COULD BE AFFECTED BY THE YEAR 2000 ISSUE

As a result of computer programs being written using two digits, rather than four, to represent year dates, the performance of our computer systems and those of our suppliers and customers in the Year 2000 and beyond is uncertain. Any computer programs that have time-sensitive software may recognize a date using "00" as the Year 1900 rather than the Year 2000. In addition, some computer programs that were date sensitive to the Year 2000 may not have been programmed to process the Year 2000 as a leap year. These Year 2000 issues could result in a system failure or miscalculations which disrupt our operations, such as a temporary inability to process transactions, send invoices or engage in other normal business activities.

We rely, both domestically and internationally, upon various vendors, government agencies, utility companies, telecommunications service companies, delivery service companies and other service providers. We have no control over these third parties and, although to date they have not experienced a significant adverse impact from the transition to the Year 2000, they may suffer a Year 2000 business disruption at any time in the Year 2000 and beyond.

Year 2000 problems could disrupt our business and require us to incur significant, unanticipated expenses to remedy them. They could also result in claims and litigation against us, which could subject us to significant costs and could require substantial attention from our management. Similarly, the demand for our products could be affected by Year 2000 issues affecting our customers, which would harm our operating results. To date, we are not aware of

any major Year 2000 problems, but there can be no assurance that there will be no Year 2000 disruptions in the coming months.

#### OUR BUSINESS COULD BE INTERRUPTED BY NATURAL DISASTERS

We conduct our sequencing and a significant portion of our other activities at our facilities in Palo Alto, California, and conduct our microarray-related activities at our facilities in Fremont, California. Both locations are in a seismically active area. Although we maintain business interruption insurance, we do not have or plan to obtain earthquake insurance. A major catastrophe (such as an earthquake or other natural disaster) could result in a prolonged interruption of our business.

SUBSTANTIAL LEVERAGE AND DEBT SERVICE OBLIGATIONS MAY ADVERSELY AFFECT OUR CASH FLOW

As a result of our February 2000 sale of \$200 million of our convertible subordinated notes due 2007, we will have substantial amounts of outstanding indebtedness. As a result of this indebtedness, our principal and interest payment obligations have increased substantially. There is the possibility that we may be unable to generate cash sufficient to pay the principal of, interest on and other amounts due in respect of our indebtedness when due. We also expect to add additional equipment loans and lease lines to finance capital expenditures and may obtain additional long term debt, working capital lines of credit and lease lines. There can be no assurance that any financing arrangements will be available.

Our substantial leverage could have significant negative consequences, including:

- - increasing our vulnerability to general adverse economic and industry conditions;
- -- limiting our ability to obtain additional financing;
- requiring the dedication of a substantial portion of our expected cash flow from operations to service our indebtedness, thereby reducing the amount of our expected cash flow available for other purposes, including working capital and capital expenditures;
- - limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; or
- - placing us at a possible competitive disadvantage compared to less leveraged competitors and competitors that have better access to capital resources.

## OUR STOCK PRICE HAS BEEN AND WILL LIKELY CONTINUE TO BE VOLATILE

Our stock price has been and is likely to be highly volatile, particularly due to our relatively limited trading volume. Our stock price could fluctuate significantly due to a number of factors, including:

- variations in our anticipated or actual operating results;
- sales of substantial amounts of our stock;
- - announcements about us or about our competitors, including technological innovations or new products or services;
- -- litigation and other developments relating to our patents or other proprietary rights or those of our competitors;
- conditions in the life sciences, pharmaceuticals or genomics industries;
- -- governmental regulation and legislation; and
- -- changes in securities analysts' estimates of our performance, or our failure to meet analysts' expectations.

Many of these factors are beyond our control.

In addition, the stock markets in general, and the Nasdaq National Market and the market for life sciences and technology companies in particular, have experienced extreme price and volume fluctuations recently. These fluctuations often have been unrelated or disproportionate to the operating performance of these companies. These broad market and industry factors may adversely affect the market price of our common stock, regardless of our actual operating performance.

In the past, companies that have experienced volatility in the market prices of their stock have been the object of securities class action litigation. If we were the object of securities class action litigation, it could result in substantial costs and a diversion of management's attention and resources.

- Item 7. Financial Statements and Exhibits.
  - (c) Exhibits

99.1 Press release dated February 1, 2000 announcing the placement of \$150 million in convertible subordinated notes by the Company.

## SIGNATURE

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

Dated: February 22, 2000

INCYTE PHARMACEUTICALS, INC.

By: /s/ John M. Vuko

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Name:

John M. Vuko Executive Vice President and Title:

Chief Financial Officer

EXHIBIT 99.1

FOR IMMEDIATE RELEASE

INCYTE John Vuko Chief Financial Officer (650) 845-4106

INCYTE ANNOUNCES PLACEMENT OF \$150 MILLION IN CONVERTIBLE SUBORDINATED NOTES

PALO ALTO, CA, FEBRUARY 1, 2000 -- Incyte Pharmaceuticals, Inc. (Nasdaq: INCY) announced today the private placement of \$150 million of its 5.5% Convertible Subordinated Notes due 2007. The offering is expected to close on February 4, 2000. The Company has also granted to the initial purchasers an option to purchase up to an additional \$50 million in principal amounts of Notes. The Notes are convertible into Incyte common stock at an initial conversion price of approximately \$134.84 per share.

The Company stated that it expects to use the net proceeds of the offering for working capital and general corporate purposes. Proceeds may also be used to make strategic investments, acquire or license technology or products, or acquire businesses that may complement its business.

This press release does not constitute an offer to sell or the solicitation of an offer to buy any security. The Notes have not been registered under the Securities Act of 1933 or applicable state securities laws and may not be offered or sold in the United States absent registration under the Securities Act and applicable state securities laws or an applicable exemption from registration requirements.

Except for the historical information contained herein, the matters set forth in this press release, such as statements as to the expected use of net proceeds, are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially, including market and other conditions that may affect Incyte's ability to complete the offering, the expected closing date of the offering, the satisfaction of customary closing conditions, the impact of alternative technological advances and competition, changes in the focus of Incyte's research and development activities, developments in litigation, and other risks detailed from time to time in Incyte's SEC reports, including its Quarterly Report on Form 10-Q for the quarter ended September 30, 1999. Incyte disclaims any intent or obligation to update these forward-looking statements.