DISCOVERY PARTNERS INTERNATIONAL INC
Form 424A
April 15, 2004

QuickLinks -- Click here to rapidly navigate through this document

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Filed Pursuant to Rule 424(a)
File No. 333-113488

PROSPECTUS (Subject to Completion)

Dated April 14, 2004

7,222,000 Shares

Common Stock

We are selling no shares of common stock unless the underwriters exercise the over-allotment option referred to below. The selling stockholder, Axys Pharmaceuticals, Inc., is offering 7,222,000 shares of common stock. Our common shares are listed on the Nasdaq National Market under the symbol "DPII." On April 13, 2004, the last reported sale price of our common stock was $6.10 per share.

Our business and an investment in our common shares involve significant risks. These risks are described under the caption "Risk Factors" beginning on page 8 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price	**$**	**$**
Underwriting discounts and commissions	**$**	**$**
Proceeds, before expenses, to selling stockholder	**$**	**$**
Proceeds, before expenses, to us	**$**	**$**

The underwriters may also purchase up to 1,083,300 shares of our common stock from us at the public offering price, less underwriting discounts and commissions, to cover over-allotments. We will not receive any of the proceeds of the sale of shares by the selling stockholder, Axys Pharmaceuticals, Inc.

The underwriters expect to deliver the shares in New York, New York on , 2004.

SG Cowen

Merriman Curhan Ford & Co.

Roth Capital Partners

, 2004

TABLE OF CONTENTS

	Page
Prospectus Summary	1
Risk Factors	8
Forward-Looking Information	19
Use of Proceeds	20
Price Range of Common Stock	21
Selected Consolidated Financial Data	22
Management's Discussion and Analysis of Financial Condition and Results of Operations	23
Business	31
Management	46
Principal and Selling Stockholders	50
Certain United States Federal Income Tax Considerations	53
Underwriting	57
Legal Matters	59
Experts	59
Where You Can Find Additional Information	60

You should rely only on the information contained or incorporated by reference in this prospectus. Neither we nor Axys Pharmaceuticals, the selling stockholder, have authorized anyone to provide you with information that is different. We and Axys Pharmaceuticals are offering to sell and seeking offers to buy shares of our common stock only in jurisdictions where offers are permitted. The information contained or incorporated by reference in this prospectus is accurate only as of the date of this prospectus or the date of the applicable information that is incorporated by reference, regardless of the time of delivery of this prospectus or of any sale of our common stock.

We own a registered trademark and service mark in IRORI®. We also own the following trademarks among others: MicroKan®, Synthesis Manager®, Clevap®, NanoKan® and Xenometrix®. The following trademarks, among others, are currently pending registration: X-Kan , MiniKan , µARCS , ChemCard and Crystal Farm .

PROSPECTUS SUMMARY

The following summary is qualified in its entirety by, and should be read in conjunction with, the more detailed information and financial statements and notes thereto appearing elsewhere or incorporated by reference in this prospectus. Before you decide to invest in our common stock, you should carefully read the entire prospectus, and the documents incorporated by reference in the prospectus, including the risk factors and the other more detailed information and financial statements and related notes.

Offering Background

Under the terms of an investors' rights agreement entered into in April 2000 to which we and Axys Pharmaceuticals are parties, Axys Pharmaceuticals has the right to demand that we prepare and file with the Securities and Exchange Commission, or SEC, a registration statement covering the resale of any or all of the shares of our common stock issued to Axys Pharmaceuticals in April 2000 in connection with our acquisition of Axys Advanced Technologies, or AAT, along with shares issuable upon exercise of a warrant that we issued to Axys Pharmaceuticals at that time. Axys Pharmaceuticals has exercised its demand registration rights under the investors' rights agreement and requested that we register for resale in a firmly underwritten offering 7,222,000 of the shares of our common stock that we issued to Axys Pharmaceuticals in connection with the AAT acquisition. We have filed the registration statement of which this prospectus is a part to meet our obligations under the investors' rights agreement. The 7,222,000 shares being registered do not include the 200,000 shares of our common stock

issuable to Axys Pharmaceuticals upon exercise of the warrant referenced above, which has an exercise price of $8.00 per share and expires in May 2005. We have registered 1,083,300 shares of our common stock under the registration statement of which this prospectus is a part for sale by us only to cover over-allotments, if any, in connection with this offering. We will not receive any proceeds of the sale of shares by Axys Pharmaceuticals.

In November 2001, Axys Pharmaceuticals was acquired by the Celera Genomics Group of Applera Corporation and is now a wholly-owned subsidiary of Applera. Applera is a publicly-traded company with shares listed on the New York Stock Exchange. Axys Pharmaceuticals has informed us that, prior to its acquisition by Applera, it had granted options to purchase 337,500 of the shares of our common stock it held to seven of its employees, including two individuals who are now members of our board of directors, Mr. John P. Walker and Michael C. Venuti, Ph.D. In order to permit Axys Pharmaceuticals to deliver unencumbered shares to the underwriters in connection with this offering, Applera, on behalf of Axys Pharmaceuticals, has agreed to repurchase these options from the option holders, including Mr. Walker and Dr. Venuti, immediately prior to the closing of this offering, in exchange for cash equal to the number of shares covered by the applicable option multiplied by the difference between the per share proceeds to Axys Pharmaceuticals in this offering, net of underwriting discounts and commissions, and the per share exercise price of the option. Mr. Walker and Dr. Venuti are entering into these arrangements with Applera relating to these options solely to facilitate Axys Pharmaceuticals' sale of shares in this offering, and have not influenced or prompted Applera to offer these arrangements to them. Under these agreements, Mr. Walker's and Dr. Venuti's applicable options will only be bought out if the sale of shares by Axys Pharmaceuticals contemplated by this prospectus closes, and in that event, Mr. Walker and Dr. Venuti each will report a change in beneficial ownership of shares of our common stock in accordance with applicable SEC rules and regulations.

The Company

We collaborate with pharmaceutical and biopharmaceutical companies to advance their drug discovery process through our integrated and highly efficient collection of drug discovery technologies, products and services focused from the point immediately following identification of a drug target through when a drug candidate is ready for pre-clinical studies. Despite numerous technological advances in combinatorial chemistry, high-throughput screening, genomics and proteomics, the process of drug discovery remains slow, expensive and often unsuccessful. In order to make the drug discovery process faster, less expensive and more likely to generate a drug candidate, we offer products and services such as assays, chemical compound synthesis and automation tools, design and synthesis of proprietary libraries of compounds, high-throughput screening, lead optimization, drug discovery informatics and toxicology. These products and services can be provided individually or as an integrated solution, depending on our customers' requirements. We believe our depth of knowledge and experience, and our range of product offerings, across these areas of drug discovery differentiates us from our competitors. During 2003, we generated revenue from approximately 130 customers worldwide, including Pfizer, Merck, Novartis, Inspire Pharmaceuticals and GlaxoSmithKline.

Industry Background

The drug discovery process is undergoing fundamental changes as a result of advances in genomics and proteomics, which are the studies of genes and the proteins they encode. Prior to these advances, pharmaceutical and biopharmaceutical companies addressed fewer than 500 identified drug targets in the development of drugs. Industry experts predict that the application of genomics and proteomics will lead to the identification of thousands of new drug targets.

The abundant data generated as a result of the genomics and proteomics revolution has increased the demand for drug discovery products and services. Once a company has identified a potential drug target, it must still devote significant time and resources to validate the target's role in the disease process and screening libraries of chemical compounds against the target to identify potential drug candidates, which must be optimized further before commencement of human testing. The Pharmaceutical Research and Manufacturers of America reported that its members alone spent an estimated $32 billion worldwide in research and development in 2002, with approximately 25% of this total amount being spent on the stages of drug discovery in which we focus.

Our Products and Services

We provide products and services designed to make the drug discovery process faster, less expensive and more likely to generate a drug candidate. We bring together a significant combination of drug discovery expertise, technology and services to meet the needs of the pharmaceutical and biopharmaceutical industries. We do not discover or develop drugs for our own account and do not compete with our customers. We believe that an integrated approach to drug discovery is critical for the creation of higher quality drugs and we, therefore, offer products and services in many functional disciplines of the drug discovery process.

Assays

We design and conduct assays, or tests, that generate information about the effect of chemical compounds on a drug target. We believe that our assays help our customers better select drug candidates before moving to the more costly stages of pre-clinical and clinical testing. We develop our assays through our team of scientists who are experienced in working with major disease target classes in a number of significant therapeutic areas, such as cardiovascular, neurology, oncology and ophthalmology. We acquired the ability to provide assay development services through our acquisition of Discovery Technologies, Ltd. in 1999 and further internal development.

Automation Products and Services

We sell, and provide access to, our proprietary instruments and consumables that automate the process of making collections, or libraries, of chemical compounds. Our instruments are based on a patented core technology, which enables our customers to generate large collections of compounds with efficiency and speed.

Our current products that are based on proprietary technology were developed internally and include the NanoKan System, a high throughput chemistry system that can generate up to one million discrete compounds per year, the AutoSort System, an automated chemistry system and a manual chemistry system. All of these systems include hardware and software platforms and use consumables that our customers purchase for every compound that is synthesized using these automation systems. We also offer Crystal Farm, our proprietary self-contained crystallization and imaging system that provides automated high throughput incubation and imaging of thousands of protein crystallization experiments.

Proprietary Libraries of Compounds

As a result of internal development and our acquisitions of AAT in 2000 and Systems Integration Drug Discovery Company, or SIDDCO, in 2001, we are able to offer a broad range of highly purified compound libraries that can be screened using assays. After compounds are screened, promising compounds, or hits, are then improved, or optimized, to generate drug candidates, or leads. Our approach to generating compound libraries provides the following advantages:

Purity: A high degree of purity is important to minimize false positives during screening. We can deliver compounds that are greater than the current industry standard of 90% pure, depending on customer specifications;

Diversity: Each discovery library of approximately 1,000 to 5,000 drug-like compounds is designed to contain a set of highly diverse compounds using our chemical mapping and differentiation software;

Ease of optimization: The individual chemistries for each library are highly validated and characterized. This allows rapid generation of focused libraries around hits and rapid follow-up and modification by medicinal chemistry programs; and

Re-supply and reproducibility: Our synthesis approaches produce large quantities of chemical compounds that allow rapid and cost effective restocking of customers' supplies. Our highly validated chemistries allow us or our customers to re-synthesize larger quantities on demand.

Screening

We offer high throughput screening services through an experienced staff of scientists located at our facility near Basel, Switzerland. We also offer our customers access to chemical compounds from many of the world's leading compound suppliers as well as a significant collection of internally developed compounds.

To improve the speed and cost effectiveness of the screening process, we have exclusively licensed from Abbott Laboratories and further developed µARCS, a next-generation high throughput screening technology. This platform provides rapid and cost effective, high performance, high throughput screening, while supporting a very broad range of biochemical and cellular assays. We initially acquired our ability to offer these screening services in our acquisition of Discovery Technologies, Ltd. in 1999 and have added to our capabilities through further internal development.

Hits-to-Optimized-Leads

Through a combination of internal development and our acquisitions of SIDDCO in 2001, Structural Proteomics in 2000, Xenometrix in 2001 and AAT in 2000, we have developed products and services to advance early stage screening hits to optimized drug leads. These products and services include the following:

Custom focused libraries. In addition to our collection of proprietary libraries, we design and produce custom, focused libraries based upon hits identified from screening. These hits may be from our compound libraries, our customer's internal compound collection or even from another compound library supplier.

Medicinal chemistry. We also provide a wide range of medicinal chemistry and other lead optimization services. This includes the synthesis of compounds that modify the original hit for improved potency, selectivity and other pharmaceutical characteristics. In some cases we provide medicinal chemistry services in conjunction with our computational drug discovery efforts to design and construct small libraries of compounds to act on specific targets that have known chemical structures.

Drug Discovery Informatics; ADME and Toxicology

In connection with our acquisitions in 2000 of AAT and Structural Proteomics, we acquired and we are further developing computational tools that we believe will allow us to substantially increase our knowledge of the characteristics of targets and leads, and their interaction with certain molecules. We believe these tools could potentially be applied throughout the drug discovery process to significantly reduce the time and cost of developing a drug. We currently have computer algorithms that allow us to design libraries of compounds with high diversity, thereby increasing the likelihood of finding hits during screening. We have developed novel algorithms to aid in the understanding and utilization of the data resulting from high throughput screening experiments. We have also developed a proprietary analysis tool which we believe will allow us to use screening data to identify the most likely type of drug target with which a compound may bind or interact. We use this tool to design highly effective compound libraries for our collaborators and customers.

We expect to further use our computational tools and screening data to help predict absorption, distribution, metabolism, and excretion, or ADME, and toxicological reactions to classes of compounds. This could allow our customers to avoid spending money and time on hits and leads that will ultimately fail due to their unfavorable ADME and toxicological characteristics.

Integrated Drug Discovery Programs

We offer an integrated collaborative drug discovery program that provides our customers with many of the tools and capabilities needed to find and advance leads to pre-clinical candidates. Through our collaborations we provide integrated access to our computational design and analysis, chemistry, and biology capabilities for the purpose of developing a pre-clinical lead for our customer's target. Each integrated drug discovery program is customized to increase the likelihood of success. We currently are conducting integrated drug discovery programs for Inspire Pharmaceuticals, Inc. and Theracos, Inc.

Our Strategy

Our strategy is to become the leading provider of a complete, integrated and highly efficient drug discovery platform designed to overcome many of the limitations associated with the slow and expensive traditional drug discovery process. Accordingly, we intend to implement our strategy by pursuing the following objectives:

Broaden and deepen our technology through internal invention and acquisition. We have assembled our current suite of advanced technologies, products and services both through internal invention and acquisition. We intend to continue to invest in internal research and development and to acquire and integrate innovative products and services in order to stay at the forefront of drug discovery technology.

Expand customer relationships through integration of products and services. We are using existing relationships with customers in individual areas of our business to sell products and services in multiple areas of drug discovery. We believe that our customers can best take advantage of the time and cost efficiencies of our products and services in integrated combinations.

Gain wider penetration of the biopharmaceutical industry. We will continue to focus on providing drug discovery products and services to the biopharmaceutical market. We have a skilled team of business development and marketing professionals targeting biopharmaceutical customers worldwide. We believe that as the biopharmaceutical industry continues to mature and generate additional drugs, the resources dedicated to drug discovery and development will increase and we believe that this may provide an opportunity to provide additional products and services to biopharmaceutical companies.

Continue to generate multiple revenue streams and diversify our revenue base. We sell a variety of products and services and we believe that our multiple revenue streams reduce the potential negative consequences to us if any one of our product or service areas ceases to be productive. We expect to continue to sell our products and services to our customers primarily for current revenue, but when appropriate, we may structure financial terms to include milestone payments or royalties based on the success of the ultimate commercialized product. It is also our intention to grow our business and expand our customer base, which would reduce our dependency on Pfizer, who accounted for 62% of total revenue in 2003.

Continue to expand our knowledge base and streamline the drug discovery process. Because of the large number and diversity of our customers, we generate and are exposed to large amounts of highly useful information about the drug discovery process and about the general interaction between types of chemistries and types of drug targets. We believe this knowledge will enable us to streamline the drug discovery process and to create new revenue opportunities.

Corporate Information

Our principal executive offices are located at 9640 Towne Centre Drive, San Diego, California 92121, and our telephone number is (858) 455-8600. Our website is located at www.discoverypartners.com. The contents of our website and any information that can be accessed through our website are not part of this prospectus.

The Offering

Selling stockholder	Axys Pharmaceuticals, Inc.
Common stock offered hereby by selling stockholder	7,222,000 shares
Common stock to be outstanding after the offering	24,641,607 shares
Use of proceeds	We will not receive any of the proceeds from the offering, unless the underwriters exercise their over-allotment option. In the event the underwriters exercise their over-allotment option, we will use the proceeds for general corporate purposes as further described in "Use of Proceeds."
Symbol	DPII

The share amounts in this table are based on shares outstanding as of March 4, 2004. The number of shares outstanding will not change as a result of this offering, unless the underwriters exercise their over-allotment option. This table excludes:

- 3,562,745 shares of common stock issuable upon the exercise of options outstanding at a weighted average exercise price of $5.45 per share;
- 200,000 shares of common stock issuable upon the exercise of a warrant held by the selling stockholder at an exercise price of $8.00 per share; and
- 1,812,211 additional shares of common stock available for future grant under our 2000 Stock Incentive Plan and Employee Stock Purchase Plan.

Except as otherwise noted, all information in this prospectus assumes the underwriters do not exercise their over-allotment option to purchase from us up to 1,083,300 shares.

Summary Consolidated Financial Data
(in thousands, except per share data)

	Years Ended December 31,				
	2003	**2002**	**2001**	**2000**	**1999**
Consolidated Statement of Operations Data:					
Revenues	$ 49,827	$ 41,315	$ 41,134	$ 36,264	$ 13,076
Cost of revenues and additional charges	31,669	35,487	24,857	18,343	8,235
Operating expenses	18,906	70,207	30,923	31,103	8,288
Total expenses	50,575	105,694	55,780	49,446	16,523
Loss from operations	(748)	(64,379)	(14,646)	(13,182)	(3,447)
Other income	1,807	2,267	3,498	1,485	77
Net income (loss)	$ 1,059	$ (62,112)	$ (11,148)	$ (11,697)	$ (3,370)
Net income (loss) per share, basic	$ 0.04	$ (2.55)	$ (0.46)	$ (0.89)	$ (3.00)
Net income (loss) per share, diluted	$ 0.04	$ (2.55)	$ (0.46)	$ (0.89)	$ (3.00)
Shares used in calculating net income (loss) per share, basic(1)	24,344	24,315	24,016	13,177	1,125
Shares used in calculating net income (loss) per share, diluted(1)	25,077	24,315	24,016	13,177	1,125

(1) Please see note 2 of the notes to our consolidated financial statements incorporated by reference in this prospectus for an explanation of the determination of the number of shares used in computing per share data.

	As of December 31, 2003
	(in thousands)
Selected Consolidated Balance Sheet Data:	
Cash, cash equivalents and short-term investments	$ 72,574

	As of December 31, 2003
Working capital	79,341
Total assets	109,184
Long-term obligations, less current portion	
Redeemable preferred stock	
Total stockholders' equity	98,247

RISK FACTORS

In addition to the other information contained herein, you should carefully consider the following risk factors in evaluating our company.

We derive a significant percentage of our revenues from a single customer. If this customer relationship terminated, we could have difficulty finding customers that would purchase our products and services in sufficient amounts to replace the capacity resulting from the loss of this significant customer.

We anticipate that a significant portion of our revenues for 2004 and 2005 will be derived from the chemistry collaboration we entered into with Pfizer originally in December 2001. In February 2004, the agreement with Pfizer was amended. Under this agreement, Pfizer has a contractual right to terminate the contract, with or without cause, upon six months notice beginning on January 5, 2005. Either party may also terminate the agreement upon the material, uncured breach of the other party, and Pfizer may terminate the agreement if we are acquired by a third party or in the event of a change in control of our Company. During 2003, revenue from Pfizer represented 62% of our total revenue. If our relationship with Pfizer or our contracts with other customers to whom we provide significant products or services are terminated, we will have substantial capacity available until we are able to find new customers for our products and services to utilize that capacity. We may be delayed in entering or not able to enter into contracts with new customers to utilize any available capacity. We will continue to bear the costs of that capacity until we are able to enter into contracts with customers for those products or services. Revenues with respect to those products and services may be delayed or we may not recognize revenues at all to the extent we are delayed in entering or not able to enter into contracts with new customers to utilize available capacity.

The drug discovery industry is highly competitive and subject to technological change, and we may not have the resources necessary to compete successfully.

We compete with companies in the United States and abroad that engage in the development and production of drug discovery products and services. These competitors include companies engaged in the following areas of drug discovery:

Assay development and screening;

Combinatorial chemistry instruments;

Compound libraries and lead optimization;

Informatics; and

Gene profiling.

Academic institutions, governmental agencies and other research organizations also conduct research in areas in which we provide services, either on their own or through collaborative efforts. Also, substantially all of our pharmaceutical and biopharmaceutical company customers have internal departments that provide some or all of the products and services we sell, so these customers may have limited needs for our products and services. Many of our competitors have more experience and have access to greater financial, technical, research, marketing, sales, distribution, service and other resources than we do. We may not yet be large enough to achieve satisfactory market recognition or operating

efficiencies, particularly in comparison to some competitors.

Moreover, the pharmaceutical and biopharmaceutical industries are characterized by continuous technological innovation. We anticipate that we will face increased competition in the future as new companies enter the market and our competitors make advanced technologies available. Technological advances or entirely different approaches that we or one or more of our competitors develop may

render our products, services and expertise obsolete or uneconomical. For example, advances in informatics and virtual screening may render some of our technologies, such as our large compound libraries, obsolete. Additionally, the existing approaches of our competitors or new approaches or technologies that our competitors develop may be more effective than those we develop. We may not be able to compete successfully with existing or future competitors.

In addition, due to improvements in global communications, combined with the supply of lower cost PhD level scientific talent, we face the growing threat of competition for our chemistry and computational chemistry services from low-cost offshore locations such as China, India and Eastern Europe.

If we do not generate adequate revenues from our µARCS investment in the near future, we may have to record significant impairment charges.

We have prepaid approximately $6.0 million to Abbott Laboratories for royalties related to the µARCS screening technology. This prepayment is carried on our balance sheet as prepaid royalty. If we are not successful in generating revenues in the future from this asset, we may be required to record impairment charges up to $6.0 million, which would materially hurt our profitability.

Our financial performance will depend on the prospects of the pharmaceutical and biopharmaceutical industries and the extent to which these industries engage outside parties to perform one or more aspects of their drug discovery process.

Our revenues depend to a large extent on research and development expenditures by the pharmaceutical and biopharmaceutical industries and companies in these industries outsourcing research and development projects. These expenditures are based on a wide variety of factors, including the resources available for purchasing research equipment, the spending priorities among various types of research and policies regarding expenditures during recessionary periods. In recent years, pharmaceutical companies have been attempting to contain spending on drug discovery and many biotechnology companies have found it difficult to raise capital to fund drug discovery activities. Geopolitical uncertainty or general economic downturns in our customers' industries or any decrease in research and development expenditures could harm our operations, as could increased acceptance of management theories that counsel against outsourcing of critical business functions. Any decrease in drug discovery spending by pharmaceutical and biopharmaceutical companies could cause our revenues to decline and hurt our profitability.

The concentration of the pharmaceutical industry and the current trend toward increasing consolidation could hurt our business prospects.

The pharmaceutical customer segment of the market for our products and services is highly concentrated, with approximately 50 large pharmaceutical companies conducting drug discovery research. We have lost customers due to consolidation of pharmaceutical companies and the continuation of this trend may reduce the number of our current and potential customers even further. As a result, a small number of customers could account for a substantial portion of our revenues. In addition, because of the heavy concentration of the pharmaceutical industry and the relatively high cost of our systems, such as NanoKan, µARCS and Crystal Farm, we expect there will be only a limited number of potential buyers for these systems.

Additional risks associated with a concentrated customer base include:

larger companies may develop and utilize in-house technology and expertise rather than using our products and services; and

larger customers may negotiate price discounts or other terms for our products and services that are unfavorable to us.

We may not achieve or maintain profitability in the future.

We have incurred significant operating and net losses since our inception. As of December 31, 2003, we had an accumulated deficit of $103.6 million. Although we generated net income of $1.1 million in 2003, we had net losses of $62.1 million and $11.1 million for the years ended December 31, 2002 and 2001, respectively. We may also in the future incur operating and net losses and negative cash flow from operations. We did not achieve operating profitability until the third quarter of 2003 and we may not be able to achieve or maintain profitability in any quarter in the future. Moreover, if we do achieve profitability, the level of any profitability cannot be predicted and may vary significantly from quarter to quarter.

Our discontinuation of the development of chemical compounds to be sold out of inventory places more emphasis on integrated drug discovery collaborations, an area of higher risk and complexity.

As a result of our decision to limit access to our proprietary chemistry compounds and capabilities solely to companies that enter into integrated drug discovery, chemistry or screening and optimization collaborations with us, we now rely on this relatively complex form of customer engagement to generate revenue. As a result of the inherent complexity of such collaborations, we have an increased risk of being unable to reach agreement with the prospective customer for such collaborations or of structuring sub-optimal arrangements that fail to adequately compensate us for the risks inherent in such collaborations.

We may fail to expand customer relationships through the integration of products and services.

We may not be able to use existing relationships with customers in individual areas of our business to sell products and services in multiple areas of drug discovery. We may not be successful in selling our offerings in combination across the range of drug discovery disciplines we serve because integrated combinations of our products and services may not achieve time and cost efficiencies for our customers, especially our large pharmaceutical company customers. Biotechnology companies may desire our integrated offerings but are often not sufficiently capitalized to pay for these services. In addition, we may not succeed in further integrating our offerings. If we do not achieve integration of our products and services, we may not be able to take advantage of potential revenue opportunities and differentiate ourselves from competitors.

Our products, services and technologies may never help discover drugs that receive Food and Drug Administration approval, which may make it difficult for us to gain new business.

To date, we are not aware of any of our customers having used any of our drug discovery products, services or technologies to develop a drug that ultimately has been approved by the Food and Drug Administration, and our customers may never do so. Whether our customers use our drug discovery products, services and technologies to develop any drugs that ultimately receive Food and Drug Administration approval will depend heavily on our scientific success and our customers' scientific success, as well as on our customers' ability to meet applicable Food and Drug Administration regulatory requirements. Our products, services and technologies may fail to assist our customers in achieving their drug discovery objectives, either on a timely basis or at all. For example, when our customers deliver proteins to us for assay development or chemistry library design ideas for chemical compound development and production, we may design assays or develop chemical compound libraries that fail to fully characterize the applicable protein's or compound's therapeutic potential, which could cause its further development to be delayed or abandoned. Additionally, our customers may not deliver to us proteins for assay development or chemistry library design ideas for chemical compound

development and production that yield promising lead compounds for further development. Our customers may also lack the resources or experience or be otherwise unable to comply with the Food and Drug Administration's clinical trial requirements. Certain of our competitors are able to claim that their drug discovery products or services have been used in developing drugs that received Food and Drug Administration approval. To the extent that potential customers consider demonstrated therapeutic success an important factor in selecting between us and our competitors, we may be competitively disadvantaged, which would negatively impact our ability to generate new business.

Our financial performance will depend on improved market conditions in the segments of the drug discovery and development process in which we participate.

The drug discovery and development process can be broadly separated into the following stages: Target identification; target validation; lead discovery; lead optimization; pre-clinical development; Investigational New Drug, or IND, filing; clinical trials, phases I-III; new drug application, or NDA; and post market surveillance. We currently participate in the areas of lead discovery and lead optimization. Based on

current industry averages, the cost of acquiring a validated target plus the costs of lead discovery and lead optimization are greater than the expected proceeds of out-licensing a potential drug candidate during the pre-clinical phase of drug development. This is primarily due to the negative imbalance between the relatively high cost of obtaining pre-clinical drug candidates, the high failure rate of such pre-clinical candidates, and the relatively low demand for such pre-clinical candidates that exists at present. It is estimated that a positive expected return on investment is not obtained until a drug candidate has passed through phase II clinical trials, which requires a significant commitment of resources to attain. Therefore, many drug companies may be deterred from engaging in drug discovery unless they have the substantial financial resources necessary to fund the drug discovery process all the way through phase II clinical trials. Unless advances are made to either reduce the cost or improve the success rate of pre-clinical drug candidates, or unless the market demand for such pre-clinical drug candidates improves, we might continue to face difficult market conditions for our products and services which might inhibit our growth.

We may not be able to achieve and maintain success in our offshore operations.

We recently entered into a research and development collaboration agreement under which we utilize scientists and equipment at a subcontractor's facility located in India to take advantage of a lower cost structure. However, we may not be able to achieve or maintain a successful relationship in this offshore location or realize lower costs. Additionally, such offshore business could suffer due to the geographical, time and distance challenges as well as cultural difficulties of managing such an operation, which could cause delays, customer dissatisfaction or other issues.

Many of our products and services have lengthy sales cycles, which could cause our operating results to fluctuate significantly from quarter to quarter.

Sales of many of our products and services typically involve significant technical evaluation and commitment of expense or capital by our customers. Accordingly, the sales cycles, or the time from finding a prospective customer through closing the sale, associated with these products or collaborations, typically range from six to eighteen months. Sales of these products and the formation of these collaborations are subject to a number of significant risks, including customers' budgetary constraints and internal acceptance reviews that are beyond our control. Due to these lengthy and unpredictable sales cycles, our operating results could fluctuate significantly from quarter to quarter. We expect to continue to experience significant fluctuations in quarterly operating results due to a variety of factors, such as general and industry specific economic conditions, that may affect the research and development expenditures of pharmaceutical and biopharmaceutical companies.

Our products and services involve significant scientific risk of fulfillment.

A large portion of our revenues relies upon our and our customers' scientific success. Our products, services and technologies may fail to assist our customers in achieving their drug discovery objectives, on a timely basis or at all. For example, when our customers deliver proteins to us for assay development or chemistry library design ideas for chemical compound development and production, we rely on our customers for timely delivery of those deliverables, and our customers rely on us for timely and effective assay design or compound library development and production that fulfills our scientific obligations to them. To the extent that either we experience delays or failures in receiving specific deliverables required for us to complete our objectives or we encounter delays in our ability to meet, or are unable to meet, our scientific obligations, we may be unable to receive and recognize revenues in accordance with our expectations.

If our revenues decline or do not grow as anticipated, we might not be able to correspondingly reduce our operating expenses.

A large portion of our expenses, including expenses for facilities, equipment and personnel, is relatively fixed. Accordingly, if revenues decline or do not grow as anticipated, we might not be able to correspondingly reduce our operating expenses. Failure to achieve anticipated levels of revenues could therefore significantly harm our operating results for a particular fiscal period.

Due to the possibility of fluctuations in our revenues (on an absolute basis and relative to our expenses), we believe that quarter-to-quarter comparisons of our operating results are not a reliable indication of our future performance.

If our products and services do not become widely used in the pharmaceutical and biopharmaceutical industries, it is unlikely that we will be profitable.

We have a limited history of offering our products and services, including informatics tools, biology services, µARCS, toxicology services, Crystal Farm and combinatorial chemistry instrumentation systems. It is uncertain whether our current customers will continue to use these products and services or whether new customers will use these products and services. In order to be successful, our products and services must meet the requirements of the pharmaceutical and biopharmaceutical industries, and we must convince potential customers to use our products

and services instead of competing technologies and offerings. Moreover, we cannot thrive unless we can achieve economies of scale on our various offerings. Market acceptance will depend on many factors, including our ability to:

- convince potential customers that our technologies are attractive alternatives to other technologies for drug discovery;
- manufacture products and conduct services in sufficient quantities with acceptable quality and at an acceptable cost;
- convince potential customers to purchase drug discovery products and services from us rather than developing them internally; and
- place and service sufficient quantities of our products.

Because of these and other factors, some of which are beyond our control, our products and services may not gain sufficient market acceptance.

The intellectual property rights on which we rely to protect the technology underlying our products and techniques may not be adequate, which could enable third parties to use our technology or very similar technology and could reduce our ability to compete in the market.

Our success will depend, in part, on our ability to obtain, protect and enforce patents on our technology and to protect our trade secrets. We also depend, in part, on patent rights that third parties license to us. Any patents we own or license may not afford meaningful protection for our technology and products. Others may challenge our patents or the patents of our licensors and, as a result, these patents could be narrowed, invalidated or rendered unenforceable. In addition, current and future patent applications on which we depend may not result in the issuance of patents in the United States or foreign countries. Competitors may develop products similar to ours that are not covered by our patents. Further, since there is a substantial backlog of patent applications at the U.S. Patent and Trademark Office, the approval or rejection of our or our competitors' patent applications may take several years.

Our European eukaryotic gene profiling patent was opposed by various companies. Oral proceedings were held before the Opposition Division of the European Patent Office in January 2003. At the conclusion of the hearing, the Opposition Division maintained our patent in amended form. The period during which an appeal of the Opposition Division decision could be made has expired. As amended, the patent claims kits and methods for identifying and characterizing the potential toxicity of a compound using expression profiles of four categories of stress.

In addition to patent protection, we also rely on copyright protection, trade secrets, know-how, continuing technological innovation and licensing opportunities. In an effort to maintain the confidentiality and ownership of our trade secrets and proprietary information, we require our employees, consultants and advisors to execute confidentiality and proprietary information agreements. However, these agreements may not provide us with adequate protection against improper use or disclosure of confidential information, and there may not be adequate remedies in the event of unauthorized use or disclosure. Furthermore, like many technology companies, we may from time to time hire scientific personnel formerly employed by other companies involved in one or more areas similar to the activities conducted by us. In some situations, our confidentiality and proprietary information agreements may conflict with, or be subject to, the rights of third parties with whom our employees, consultants or advisors have prior employment or consulting relationships.

We acquired an exclusive license to the µARCS technology from Abbott Laboratories. The µARCS technology provides high throughput screening of compounds against a very broad range of drug discovery targets. Under the license agreement, Abbott is required to seek patent coverage for the licensed technology. If any license disputes arise between us and Abbott relating to the µARCS technology and we are not able to resolve those disputes, or if Abbott is unsuccessful in obtaining adequate patent coverage for the µARCS technology, our ability to screen compounds may be compromised and we may not be able to prevent competitors, including Abbott, from using the µARCS technology, which could have a material adverse effect on our financial condition and results of operation.

Although we require our employees and consultants to maintain the confidentiality of all confidential information of previous employers, their prior affiliations may subject us or these individuals to allegations of trade secret misappropriation or other similar claims. Finally, others may independently develop substantially equivalent proprietary information and techniques, or otherwise gain access to our trade secrets. Our failure to protect our proprietary information and techniques may inhibit or limit our ability to exclude certain competitors from the market.

The drug discovery industry has a history of intellectual property litigation and we may be involved in intellectual property lawsuits, which may be lengthy and expensive.

In order to protect or enforce our patent rights, we may have to initiate legal or administrative proceedings against third parties. In addition, others may sue us or initiate interference proceedings against us for infringing their intellectual property rights, or we may find it necessary to initiate a lawsuit seeking a declaration from a court that we are not infringing the proprietary rights of others. The patent positions of pharmaceutical, biopharmaceutical and drug discovery companies are generally uncertain. A number of pharmaceutical companies, biopharmaceutical companies, independent researchers, universities and research institutions may have filed patent applications or may have been granted patents that cover technologies similar to the technologies owned by, or licensed to, us or our collaborators. A number of patents may have been issued or may be issued in the future that could cover certain aspects of our technology and that could prevent us from using technology that we use or expect to use. In addition, we are unable to determine all of the patents or patent applications that may materially affect our ability to make, use or sell any potential products. Legal or administrative proceedings relating to intellectual property would be expensive, take significant time and divert management's attention from other business concerns, no matter whether we win or lose. The cost of such litigation, interference or administrative proceedings could hurt our profitability.

Further, an unfavorable judgment in an administrative proceeding, interference or infringement lawsuit brought against us, in addition to any damages we might have to pay, could prevent us from obtaining intellectual property protection for our technology, require us to stop the infringing activity or obtain a license. Any required license may not be available to us on acceptable terms, or at all. In addition, some licenses may be nonexclusive, and therefore, our competitors may have access to the same technology that is licensed to us. If we fail to obtain a required license or are unable to design around a patent, we may be unable to sell some of our products or services.

Our stock price will likely be volatile.

The trading price of our common stock has been and will likely continue to be volatile and could be subject to fluctuations in price in response to various factors, many of which are beyond our control, including:

- actual or anticipated variations in quarterly operating results;
- announcements of technological innovations by us or our competitors;
- new products or services introduced or announced by us or our competitors;
- changes in financial estimates by (or the beginning or cessation of research coverage by) securities analysts;
- the announcement of financial results that do not meet or exceed the results anticipated by the public markets;
- conditions or trends in the pharmaceutical and biopharmaceutical industries or in the drug discovery services industry;
- announcements by us or our competitors of significant acquisitions, collaborations, joint ventures or capital commitments, or terminations of collaborations or joint ventures;
- the implementation or wind-down of stock buyback programs;

additions or departures of key personnel;

economic and political factors; and

sales of our common stock, including sales by any of our stockholders who beneficially own more than 5% of our common stock and who could potentially sell large amounts of our common stock at any one time.

In addition, price and volume fluctuations in the stock market in general, and the Nasdaq National Market and the market for technology companies in particular, have often been unrelated or disproportionate to the operating performance of those companies. Further, the market prices of securities of life sciences companies have been particularly volatile. Conditions or trends in the pharmaceutical and biopharmaceutical industries generally may cause further volatility in the trading price of our common stock, because the market may incorrectly perceive us as a pharmaceutical or biopharmaceutical company and our customers are pharmaceutical and biopharmaceutical companies. These broad market and industry factors may harm the market price of our common stock, regardless of our operating performance. In the past, plaintiffs have often instituted securities class action litigation following instances of volatility in the market price of a company's securities. A securities class action suit against us could result in potential liabilities, substantial costs and the diversion of management's attention and resources, regardless of whether we win or lose.

Our customers may restrict our use of scientific information, which could prevent us from using this information for additional revenue.

We plan to generate and use information that is not proprietary to our customers and which we derive from performing drug discovery services for our customers. However, our customers may not allow us to use information such as the general interaction between types of chemistries and types of drug targets that we generate when performing drug discovery services for them. Our current contracts typically restrict our use of certain scientific information we generate for our customers, such as the biological activity of chemical compounds with respect to drug targets, and future contracts also may restrict our use of additional scientific information. To the extent that our use of information is restricted, we may not be able to collect and aggregate scientific data and take advantage of potential revenue opportunities.

Our ability to grow will depend on our attracting and retaining key executives, experienced scientists and sales personnel.

Our future success will depend to a significant extent on our ability to attract, retain and motivate highly skilled scientists and sales personnel. In addition, our business would be significantly harmed if we lost the services of Riccardo Pigliucci, our chief executive officer. We do not maintain life insurance on any of our officers. Our ability to maintain, expand or renew existing collaborations with our customers, enter into new collaborations and provide additional services to our existing customers depends, in large part, on our ability to hire and retain scientists with the skills necessary to keep pace with continuing changes in drug discovery technologies and sales personnel who are highly motivated. Additionally, it is difficult for us to find qualified sales personnel in light of the fact that our sales personnel generally hold PhD's in scientific fields. Our U.S. employees are "at will," which means that they may resign at any time, and we may dismiss them at any time (subject, in some cases, to severance payment obligations). We believe that there is a shortage of, and significant competition for, scientists with the skills and experience in the sciences necessary to perform the services we offer. We compete with pharmaceutical companies, biopharmaceutical companies, combinatorial chemistry companies, contract research companies and academic institutions for new personnel. If we do not attract new scientists or sales personnel or retain or motivate our existing personnel, we will not be able to grow.

We have acquired several businesses and face risks associated with integrating these businesses and potential future acquisitions.

We have acquired several businesses and plan to continue to review potential acquisition candidates in the ordinary course of our business, and our strategy includes building our business through acquisitions. Acquisitions involve numerous risks, including, among others, difficulties and expenses incurred in the consummation of acquisitions and assimilation of the operations, personnel and services or products of the acquired companies, difficulties of operating new businesses, the diversion of management's attention from other business concerns and the potential loss of key employees of the acquired company. In addition, acquired businesses may have management structures incompatible with our own and may experience difficulties in maintaining their existing levels of business after joining us. If we do not successfully integrate and grow the businesses we have acquired or any businesses we may acquire in the future, our business will suffer. Additionally, acquisition candidates may

not be available in the future or may not be available on terms and conditions acceptable to us. Acquisitions of foreign companies also may involve additional risks of assimilating different business practices, overcoming language and cultural barriers and foreign currency translation. We currently have no agreements or commitments with respect to any acquisition, and we may never successfully complete any additional acquisitions.

We may incur write-downs or write-offs in connection with potential future acquisitions, and exit costs, losses and liabilities in connection with potential future business divestitures or shut-downs.

We incurred a $50.9 million goodwill impairment charge during the fourth quarter of 2002, which represented the write-off of goodwill that we had accumulated in connection with several acquisitions. In the event that we make future acquisitions, we may take additional write-downs or write-offs associated with acquired assets, which could have a material adverse effect on our results of operations and financial condition. Any future acquisitions we make may also not improve our business as much as we expect, or be accretive to our earnings, which could cause the trading price of our common stock to decline. In addition, if any future acquisitions we make do not improve our business as much as we expect, we may choose to discontinue the businesses associated with those acquisitions by divestiture or by shutting those businesses down. We may also choose to divest or shut down existing businesses or product or service lines for strategic reasons. We may incur substantial exit costs, losses and liabilities in connection with any such divestiture or shut-down.

Our success will depend on our ability to manage growth and expansion.

Growth in our operations has placed and, if we grow in the future, will continue to place a significant strain on our operational, human and financial resources. We intend to continue to grow our business internally and by acquisition. As and if we expand our operations we will not necessarily have in place infrastructure and personnel sufficient to accommodate the increased size of our business. Our ability to effectively manage any growth through acquisitions or any internal growth will depend, in large part, on our ability to hire, train and assimilate additional management, professional, scientific and technical personnel and our ability to expand, improve and effectively use our operating, management, marketing and financial systems to accommodate our expanded operations. These tasks are made more difficult as we acquire businesses in geographically disparate locations.

Our operations could be interrupted by damage to our facilities.

Our results of operations are dependent upon the continued use of our highly specialized laboratories and equipment. Our operations are primarily concentrated in facilities in San Diego, California, South San Francisco, California and Allschwil, Switzerland. Natural disasters, such as earthquakes or fires, or terrorist acts could damage our laboratories or equipment and these events may materially interrupt our business. We maintain business interruption insurance to cover lost

revenues caused by certain of such occurrences. However, this insurance would not compensate us for the loss of opportunity and potential adverse impact on relations with existing customers created by an inability to meet our customers' needs in a timely manner, and may not compensate us for the physical damage to our facilities.

We have accrued significant net operating loss carryforwards that we believe we will not be able to fully use.

At December 31, 2003, we had federal and California income tax net operating loss carryforwards of approximately $21.8 million and $14.5 million, respectively. The federal and California tax loss carryforwards will begin to expire in 2010 and 2005, respectively, unless previously utilized. We believe that our ability to utilize our net operating loss carryforwards may be substantially restricted by the limitations of Section 382 of the Internal Revenue Code which apply when there are certain changes in ownership of a corporation. To the extent we begin to realize significant taxable income, these limitations may result in our incurring federal income tax liability notwithstanding the existence of otherwise available carryforwards. To date we have not quantified the potential impact of these limitations.

We are subject to foreign currency risk related to conducting business in multiple currencies.

Currency fluctuations between the U.S. dollar and the currencies in which we do business, including the British pound, the Japanese yen, the Swiss franc and the Euro, will cause foreign currency translation gains and losses. We cannot predict the effects of exchange rate fluctuations on our future operating results because of the number of currencies involved, changes in the percentage of our revenue that will be invoiced in foreign currencies, the variability of currency exposure and the potential volatility of currency exchange rates. Because we conduct business in multiple currencies we are subjected to economic and earnings risk. We do not currently engage in foreign exchange hedging transactions to manage our foreign currency exposure; however, we may begin to hedge certain transactions between the Swiss franc and other currencies that

are invoiced from our Swiss affiliate in order to minimize foreign exchange transaction gains and losses.

We may be subject to liability regarding hazardous materials.

Our products and services as well as our research and development processes involve the controlled use of hazardous materials. For example, we often use dangerous acids, bases, oxidants, radio isotopic and flammable materials. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of such materials and certain waste products. We cannot completely eliminate the risk of accidental contamination or injury from these materials. In the event of such an accident, we could be held liable for any damages that result, and any such liability could exceed our resources and disrupt our business. In addition, we may have to incur significant costs to comply with environmental laws and regulations related to the handling or disposal of such materials or waste products in the future, which would require us to spend substantial amounts of money.

Because it is unlikely that we will pay dividends, our stockholders will only be able to benefit from holding our stock if the stock price appreciates.

We have never paid cash dividends on our capital stock and do not anticipate paying any cash dividends in the foreseeable future.

Anti-takeover provisions in our stockholder rights plan and in our charter and bylaws could make a third-party acquisition of us difficult.

In 2003 we adopted a stockholder rights plan (a so-called "poison pill"). Also, our certificate of incorporation and bylaws contain provisions that could make it more difficult for a third party to acquire us, even if doing so would be beneficial to our stockholders. These provisions could limit the price that investors might be willing to pay in the future for shares of our common stock.

Sales of our common stock pursuant to this offering and otherwise may hurt our common stock's market price.

Axys Pharmaceuticals is selling approximately 29% of our outstanding shares of our common stock in this offering, which may cause the price of our stock to decline. Moreover, if our stockholders sell substantial amounts of our common stock in the public market following the offering, the market price of our common stock could decline. These sales might also make it more difficult for us to sell equity securities in the future at times and prices that we deem appropriate.

Subject to the exceptions described elsewhere in this prospectus under the heading "Underwriting," we and all of our executive officers and directors and Axys Pharmaceuticals have agreed not to offer, sell or otherwise dispose of any shares of capital stock or any securities which may be converted into or exchanged for any shares of our capital stock for a period of 90 days from the date of this prospectus, other than the shares being sold pursuant to this prospectus. However, the underwriters may waive this restriction and allow us or them to sell shares at any time. Shares of common stock subject to these lock-up agreements and held by executive officers and directors or issuable to Axys Pharmaceuticals upon exercise of a warrant it holds to purchase shares of our common stock will become eligible for sale in the public market upon expiration of these lock-up agreements, subject to limitations imposed by Rule 144 under the Securities Act of 1933, as amended.

FORWARD-LOOKING INFORMATION

Some of the statements contained in this prospectus or incorporated by reference into this prospectus are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, and are subject to the safe harbor created by the Securities Litigation Reform Act of 1995. These forward-looking statements relate to future events or our future financial and/or operating performance and can generally be identified as such because the context of the statement may include words such as "may," "will," "intends," "plans," "believes," "anticipates," "expects," "estimates," "predicts," "potential," "continue," or "opportunity," the negative of these words or words of similar import. Similarly, statements that describe our plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. These forward-looking statements are based largely on our

expectations and projections about future events and future trends affecting our business, and so are subject to risks and uncertainties that could cause actual results to differ materially from those anticipated as of the date of this prospectus or the date of documents incorporated by reference into this prospectus that include forward-looking statements. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus and in any documents incorporated by reference into this prospectus. The key factors that could cause actual results to differ materially from those expressed in the forward-looking statements include, but are not limited to, risks related to:

our dependence on Pfizer for a large part of our revenues;

competitive conditions in our industry in the United States and abroad;

technological change in the drug discovery industry;

our ability to realize returns and generate revenues from our investments in products, services and technologies for the drug discovery industry;

research and development expenditures by pharmaceutical and biopharmaceutical companies, and the extent to which pharmaceutical and biopharmaceutical companies outsource their research and development efforts;

the concentration of the pharmaceutical industry and the current trend toward increasing consolidation;

our success in securing and executing on integrated drug discovery collaborations;

our ability to expand customer relationships by selling products and services in multiple areas of drug discovery to existing customers;

our customers having therapeutic successes involving the use of our products and services;

our success with our offshore operations;

the lengthy sales cycles of our products and services;

our and our customers having scientific success in our collaborative efforts;

the fixed costs associated with our business;

the strength of our intellectual property rights and potential infringement of our intellectual property rights;

potential infringement by us of our competitors' intellectual property rights;

the volatility of our stock price;

our customers' restrictions on our use of scientific information;

our ability to attract and retain key executives, experienced scientists and sales personnel;

integrating businesses we have acquired and potential future acquisitions, and selecting appropriate candidates for potential future acquisitions;

write-downs or write-offs in connection with potential future acquisitions, and exit costs, losses and liabilities in connection with potential future business divestitures or shut-downs;

our ability to manage growth and expansion;

damage to our facilities from natural and other disasters;

our ability to use net operating loss carryforwards;

conducting transactions in foreign currencies;

our use of hazardous materials; and

anti-takeover provisions in our stockholder rights plan and in our charter and bylaws.

Because the risk factors identified above, as well as the risk factors beginning on page 8 of this prospectus and factors discussed elsewhere in this prospectus and in the documents incorporated by reference into this prospectus, may cause actual results to differ materially from those expressed in any forward-looking statements made by us or on our behalf, you should not place undue reliance on any forward-looking statements. You should read these factors and the other cautionary statements we make as being applicable to all related forward-looking statements that we make. In addition, past financial and/or operating performance is not necessarily a reliable indicator of future performance and you should not use our historical performance to anticipate results or future period trends. We undertake no obligation to publicly release any revisions to the forward-looking statements or reflect events or circumstances after the date of this prospectus or the date of documents incorporated by reference into this prospectus that include forward-looking statements.

USE OF PROCEEDS

We will not receive any proceeds from the sale of the shares of common stock offered by Axys Pharmaceuticals under this prospectus. We will only receive proceeds from this offering in the event that the underwriters exercise their over-allotment option. In the event that the underwriters exercise their over-allotment option in full, we will sell 1,083,300 shares of common stock and our estimated net proceeds from the sale, after deducting underwriting discounts and commissions, would be approximately $6.2 million, assuming an offering price to the public of $6.10 per share. Pursuant to the terms of an investors' rights agreement entered into in April 2000 to which we and Axys Pharmaceuticals are parties, all expenses incurred in connection with this offering are payable by Axys Pharmaceuticals, other than underwriting discounts and commissions payable by us on any shares the underwriters purchase from us in exercising their over-allotment option.

We intend to use the net proceeds to us, if any, from this offering for general corporate purposes, including working capital and research and development. We may also use the net proceeds to us, if any, from this offering to acquire or invest in complementary businesses, joint ventures, strategic alliances, products, or technologies. We currently have no commitments with respect to any acquisition or investment.

If we receive any net proceeds in this offering, the amounts and timing of our actual expenditures using those net proceeds will depend on numerous factors, including the status of our product and technology development efforts, our sales and marketing activities, technological advances in the drug discovery industry, the amount of cash generated or used by our operations and competitive conditions in the drug discovery industry. We will retain broad discretion in the allocation and use of any net proceeds we receive in this offering. Pending the uses described above, we intend to invest any net proceeds with the objectives of preserving principal while maintaining adequate liquidity to meet

projected cash requirements and to achieve a yield on investments.

PRICE RANGE OF COMMON STOCK

Our common stock is traded on the Nasdaq National Market, under the symbol DPII. The following table sets forth the range of high and low sales prices on the Nasdaq National Market of our common stock for the quarterly periods indicated, as reported by Nasdaq.

	High	Low
Year Ending December 31, 2004:		
First Quarter	$ 6.50	$ 5.48
Second Quarter (through April 13, 2004)	6.35	5.75
Year Ended December 31, 2003:		
First Quarter	$ 3.04	$ 2.30
Second Quarter	4.94	2.63
Third Quarter	6.45	4.22
Fourth Quarter	6.74	5.25
Year Ended December 31, 2002:		
First Quarter	$ 9.73	$ 4.95
Second Quarter	8.15	4.66
Third Quarter	6.56	2.80
Fourth Quarter	3.41	2.13

On April 13, 2004, the last reported sale price for our common stock on the Nasdaq National Market was $6.10 per share. As of March 4, 2004, there were 24,641,607 shares of our common stock outstanding held by approximately 123 holders of record.

SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated financial data has been derived from our audited financial statements and related notes incorporated by reference in this prospectus and should be read in conjunction with our financial statements and related notes thereto incorporated by reference into this prospectus and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this prospectus.

Our statement of operations data for the years ended December 31, 2001, 2002 and 2003 and balance sheet data as of December 31, 2002 and 2003 are derived from our audited financial statements incorporated by reference in this prospectus. Statement of operations data for the years ended December 31, 1999 and 2000 and balance sheet data as of December 31, 1999, 2000 and 2001 are derived from our audited financial statements not included or incorporated by reference in this prospectus.

	Years Ended December 31,				
	2003	2002	2001	2000	1999
	(In thousands, except per share data)				
Consolidated Statement of Operations Data:					
Revenues	$ 49,827	$ 41,315	$ 41,134	$ 36,264	$ 13,076
Cost of revenues:					
Cost of revenues before additional charges	31,669	28,221	20,460	18,343	8,235

	Years Ended December 31,				
Additional charges:					
Provision for discontinued products and obsolete inventory		5,781	4,397		
Anticipated contract loss		1,485			
Total cost of revenues	31,669	35,487	24,857	18,343	8,235
Gross margin	18,158	5,828	16,277	17,921	4,841
Operating expenses:					
Research and development	2,554	6,222	12,982	8,934	3,538
Selling, general and administrative	13,964	12,271	11,019	8,414	4,439
Restructuring	1,873				
Impairment of goodwill and other intangible assets		51,091			
Amortization of stock-based compensation and other non-cash compensation charges	515	623	1,074	1,376	311
Amortization of goodwill			5,848	3,379	
Write-off of in-process research and development				9,000	
Total operating expenses	18,906	70,207	30,923	31,103	8,288
Loss from operations	(748)	(64,379)	(14,646)	(13,182)	(3,447)
Interest income, net	1,757	2,037	3,252	1,247	211
Foreign currency transaction gains (losses) and other income (expense), net	50	230	246	238	(134)
Net income (loss)	$ 1,059	$ (62,112)	$ (11,148)	$ (11,697)	$ (3,370)
Net income (loss) per share, basic	$ 0.04	$ (2.55)	$ (0.46)	$ (0.89)	$ (3.00)
Net income (loss) per share, diluted	$ 0.04	$ (2.55)	$ (0.46)	$ (0.89)	$ (3.00)
Shares used in calculating net income (loss) per share, basic	24,344	24,315	24,016	13,177	1,125
Shares used in calculating net income (loss) per share, diluted	25,077	24,315	24,016	13,177	1,125
Other Data:					
Net cash provided by (used in) operating activities	$ 8,127	$ (2,135)	$ (1,529)	$ 3,360	$ (5,735)
Net cash used in investing activities	(8,098)	(39,646)	(45,450)	(9,204)	(5,894)
Net cash (used in) provided by financing activities	(634)	(610)	477	100,453	3,799

	As of December 31,				
	2003	2002	2001	2000	1999
	(In thousands)				
Selected Consolidated Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 72,574	$ 69,636	$ 77,265	$ 97,690	$ 2,885
Working capital (deficit)	79,341	77,892	88,550	106,987	(3,663)
Total assets	109,184	104,443	167,022	178,293	21,652
Long-term obligations, less current portion		306	1,082	944	1,910
Redeemable preferred stock					27,907
Total stockholders' equity (deficit)	98,247	96,532	157,042	166,562	(19,269)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

We were founded in 1995 as IRORI. In October 1998, we changed our name to Discovery Partners International and in July 2000 we completed our initial public offering and simultaneously reincorporated in the state of Delaware.

We sell a broad range of products and services to pharmaceutical and biopharmaceutical companies to make the drug discovery process for our customers faster, less expensive and more effective at generating drug candidates. We focus on the portion of the drug discovery process that begins after identification of a drug target through when a drug candidate is ready for pre-clinical studies. Our major products and services are as follows:

We develop, produce and sell collections of chemical compounds that pharmaceutical and biopharmaceutical companies test for their potential use as new drugs or for use as the chemical starting point for new drugs.

We develop, manufacture and sell proprietary instruments and the associated line of consumable supplies that are used by the pharmaceutical and biopharmaceutical industries in their own in-house drug discovery chemistry operations.

We provide testing services to our customers in which chemical compounds are tested for their biological activity as potential drugs.

We provide computational software tools that guide the entire process of chemical compound design, development and testing.

We license our proprietary gene profiling system that characterizes a cell's response upon exposure to compounds and other agents by the pattern of gene expression in the cell.

We have made a number of acquisitions in recent years that have significantly expanded our overall size and have allowed us to offer customers this broad range of integrated drug discovery products and services from a single provider:

In December 1999, we acquired Discovery Technologies, Ltd. (now known as Discovery Partners International AG) to provide assay development and high throughput screening services. This addition enabled us to offer screening services together with compounds.

In April 2000, we acquired Axys Advanced Technologies, for a total consideration of 7,429,641 shares of our common stock and $600,000. This acquisition enabled us to offer the development and production of large compound libraries.

In May 2000, we acquired 75% of the outstanding shares of Structural Proteomics. This acquisition provided us with computational software and services. At the end of 2002 we acquired all of the remaining shares of Structural Proteomics.

In January 2001, we acquired Systems Integration Drug Discovery Company, or SIDDCO, enhancing our capabilities in combinatorial chemistry research and development.

In May 2001, we acquired Xenometrix, Inc. This acquisition provided us with rights to a proprietary gene profiling system that we offer and license and enabled us to offer toxicology research products and services.

Some of these acquisitions have resulted in write-offs, as described below.

The pharmaceutical and biopharmaceutical industries provide substantially all of our revenues.

Critical Accounting Policies

This discussion and analysis of our financial condition and results of operations is based upon our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses. On an ongoing basis, we evaluate our estimates. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates, and the estimates themselves might be different if we used different assumptions.

We believe the following critical accounting policies involve significant judgments and estimates that are used in the preparation of our financial statements.

Revenue recognition. Revenue from product sales, which include the sale of instruments, related consumables, and chemical compounds, is recorded as products are shipped if the costs of such shipments can be reasonably estimated and if all the customer's acceptance criteria have been met. Certain of our contracts for product sales include customer acceptance provisions that give our customers the right of replacement if the delivered product does not meet specified criteria; however, we have historically demonstrated that the products meet the specified criteria and the number of customers exercising their right of replacement has been insignificant and therefore, once we have completed our internal testing, we recognize revenue without providing for such contingency upon shipment. Development contract revenues and high-throughput screening service revenues are recognized on a percentage-of-completion basis. Advances received under these development contracts and high-throughput screening service agreements are initially recorded as deferred revenue, which is then recognized as costs are incurred over the term of the contract. Certain of these contracts may allow the customer the right to reject the work performed; however, we have no material history of such rejections and historically we have been able to recognize revenue without providing for such contingency. Revenue from drug discovery and chemistry service agreements that are compensated on a full-time equivalent, or FTE, basis is recognized on a monthly basis and is based upon the number of FTE employees that actually worked on each project and the agreed-upon rate per FTE per month. Royalty revenue due to us under the Xenometrix patent licensing agreements is recognized upon receipt of monies, provided we have no future obligation with respect to such payments. From time to time we receive requests from customers to bill and hold goods for them. In these cases, as long as the specific revenue recognition criteria under accounting principles generally accepted in the United States at the time of the bill and hold are met, including the customer accepting the risk of loss and the transfer of ownership of such goods occurring prior to shipment, the revenue is recognized.

In February 2003, we entered into an agreement with GlaxoSmithKline, or GSK. In accordance with the agreement, we agreed to develop and supply to GSK two complete X-Kan Chemistry Synthesis Systems. X-Kans are chemical microreactors that combine the two-dimensional tagging features of the previously introduced NanoKan technology with an increased size and scale that are similar to the currently available MicroKan and MiniKan products. Revenue under this agreement is recognized on a percentage-of-completion basis, up to contractual limits.

In July 2003, we entered into an agreement with Bruker AXS Inc. Under the terms of the agreement, we appointed Bruker AXS the worldwide distributor for our Crystal Farm line of protein crystallography products. In accordance with SFAS No. 48, *Revenue Recognition When Right of Return Exists*, and due to the limited sales history we have with this product line, we defer the recognition of revenue until either Bruker AXS receives final acceptance or payment from the ultimate customer, or we receive final acceptance or payment from Bruker AXS.

Inventory. Inventories are recorded at the lower of cost or market. We write-down our inventory for estimated obsolescence or non-marketability if there is an excess of cost of inventory over the

estimated market value based upon assumptions about future demand and market conditions. If actual market conditions are less favorable than we have projected, additional inventory write-downs may be required. During the second quarter of 2002, we identified changes in the market for chemical compound libraries including a shift in demand from diverse purified compounds to purified targeted compounds and an increased demand to bring proprietary assets into drug discovery collaborations. As a result, we made a decision to cease developing, producing and selling our non-exclusive chemical compounds on a stand-alone basis to third parties and, instead, will make these compounds available only as part of collaborations with our future customers; however, there are no assurances that this strategy will be successful. As of December 31, 2003, 92% of our inventory reserve is associated with our chemical compound finished goods inventory. A significant portion of our net inventory balance represents work-in-process related to two multi-year chemistry collaborations. Estimated losses on any deliverables are recorded when they become apparent. As of December 31, 2003, we have reserved approximately $939,000 against the work-in-process representing the anticipated losses on the sale of chemical compound libraries.

Long-lived assets. In accounting for long-lived assets, we make estimates about the expected useful lives and the potential for impairment. Changes in the marketplace, technology or our operations could result in changes to these estimates. Our long-lived assets are evaluated for impairment when events and circumstances indicate that the assets may be impaired. If impairment is indicated, we reduce the carrying value of the asset to fair value. As of December 31, 2003, we have prepaid $6.0 million to Abbott Laboratories for royalties related to the μARCS screening technology. This prepayment is carried on our balance sheet as long-term prepaid royalty. To date, we have not amortized this asset because it has not achieved commercial feasibility. This technology, however, is currently being evaluated by a major pharmaceutical company and based on this ongoing evaluation and potential revenues from this and other potential customers, we believe that the carrying value of the asset is not impaired. Because we expect this asset to achieve commercial feasibility, we plan to begin amortization of this asset no later than the second half of 2004 whether or not we generate revenues from this asset. If we are not successful in generating sufficient revenues in the future from this asset, we may be required to record impairment charges up to $6.0 million.

During the year ended December 31, 2003, we determined that various fixed assets were impaired as these assets were no longer going to be held for sale or used internally. Accordingly, these assets were reduced by $373,000 to the estimated fair value of zero.

Results of Operations

Revenue. Total revenue in 2003 increased 21% to $49.8 million from $41.3 million in 2002 and $41.1 million in 2001. The increase from 2002 to 2003 resulted primarily from increases in exclusive compound supply and screening revenues offset by a decrease in nonexclusive compound supply revenues. The increase from 2001 to 2002 resulted primarily from an increase in exclusive compound supply revenue as well as revenues generated by the Xenometrix subsidiary, which we acquired in May 2001. These increases were offset by decreases in nonexclusive compound supply sales, instrumentation system sales, consumable sales and screening revenues. In 2003 and 2002, 62% and 41%, respectively, of our revenue came from our combinatorial chemistry contract with Pfizer, and we anticipate that this contract will also provide for a high percentage of 2004 and 2005 revenue. However, Pfizer has the right to terminate the contract without cause beginning January 1, 2005 by giving six months' notice.

Cost of revenues. Cost of revenues for 2002 includes a charge of $5.8 million related to provisions for discontinued products. During the three months ended June 30, 2002, we identified changes in the market for chemical compound libraries including a shift in demand from diverse nonexclusive purified compounds to exclusive purified targeted compounds and an increased demand to bring proprietary assets into drug discovery collaborations. As a result, we made a decision to cease selling our nonexclusive chemical compounds on a stand-alone basis to third parties and, instead, will make these

compounds available only as part of collaborations with our future partners; however, there are no assurances that this strategy will be successful. Accordingly, we increased our inventory reserve by approximately $5.8 million to fully reserve for the chemical compound libraries as of June 30, 2002 and recorded this charge as cost of revenue.

At the time, we had contract obligations to deliver compounds each quarter through the second quarter of 2003. The pricing of the compounds included in this contract assumed that we would sell these compounds, under certain conditions, to multiple other customers. As a result of our decision to cease selling these compounds on a stand-alone basis, we anticipated that these additional sales would not be realized and, thus, a loss was anticipated for this contract. Accordingly, an anticipated loss accrual was recorded as of June 30, 2002 totaling $1.5 million. During 2002, we incurred a loss totaling $647,000 related to the sale of compounds under this contract reducing the contract loss accrual to $837,000 as of December 31, 2002. On March 31, 2003, this contract was terminated at the customer's request. During the first quarter of 2003, we incurred an additional loss on the contract totaling $400,000 reducing the contract loss accrual to $437,000. In accordance with the termination agreement, we were paid $600,000 as an early termination fee, which is included in revenue. Additionally, the remaining $437,000 contract loss accrual was no longer required and was thus eliminated with a corresponding decrease to cost of sales for the first quarter 2003.

Cost of revenues for 2001 includes a charge of $4.4 million for obsolete inventory reserves. During the third quarter of 2001, we experienced a shift in our mix of sales orders indicating a decrease in demand for certain of our inventoried chemical compound libraries, specifically large diversity libraries containing non-purified compounds. As a result of the changes in the marketplace, we assessed our ending inventory and increased our reserves for specifically identified obsolete inventory.

Gross margins. Gross margin increased to $18.2 million in 2003 from $5.8 million in 2002 and $16.3 million in 2001. Gross margin as a percentage of revenues was 36% in 2003 compared to 14% in 2002 and 40% in 2001. Gross margin in 2002 included provisions related to the discontinuation of our non-exclusive compound supply business equaling 18% of revenue. Gross margin in 2001 included a reserve for specifically identified obsolete inventory equaling 11% of revenue. The improvement in gross margin for 2003 was primarily due to the absence of provisions related to the discontinued product line. Additionally, higher screening volumes, higher exclusive chemistry compound production volumes with increased yields due to improvements in our production processes and lower material costs associated with inventory cost management initiatives undertaken in 2003 more than offset decreases in instrumentation gross margins in 2003 over 2002. We expect gross margins in 2004 to improve over 2003.

Gross margin as a percent of revenue decreased in 2002 compared to 2001 primarily due to the impact of the Pfizer contract described below, lower screening and system volumes, and a loss on a separate fixed-price exclusive chemistry contract. In December of 2001 we entered into a multi-million dollar, multi-year contract with Pfizer. This collaboration required significant exclusive development effort. As a result, a significant amount of cost that historically had been classified as research and development shifted to cost of revenues, thereby reducing our gross margin percentage but correspondingly reducing our research and development expenses.

Research and development expenses. Research and development expenses consist primarily of salaries and benefits, supplies and expensed development materials, and facilities costs including equipment depreciation. Research and development expenses decreased 59% in 2003 to $2.6 million compared to 2002. Research and development expenses decreased 52% in 2002 to $6.2 million compared to $13.0 million in 2001. Research and development decreased from 2002 to 2003 due to the redeployment of development scientists and engineers to the direct revenue generating activities of customer funded research and development programs and collaborations. Such costs are included in cost of revenues rather than in research and development expenses. Research and development expenses decreased from 2001 to 2002 primarily as a result of the shift of development expenses to cost

of revenues associated with the Pfizer contract, as well as the decision to discontinue the development of chemical compounds to be sold out of inventory. Research and development expenses as a percentage of revenues were 5% in 2003, 15% in 2002 and 32% in 2001. We expect to increase our research and development spending in total dollars and as a percentage of revenues in 2004 compared to 2003.

Selling, general and administrative expenses. Selling, general and administrative expenses consist primarily of salaries and benefits for sales, marketing and administrative personnel, advertising and promotional expenses, professional services, and facilities costs. Selling, general and administrative expenses increased 14% to $14.0 million in 2003 compared to 2002. Selling, general and administrative expenses increased 11% to $12.3 million in 2002 compared to $11.0 million in 2001. The increase from 2002 to 2003 was due primarily to increased personnel and related costs, including higher levels of incentive compensation accruals and due to additional business development personnel and their related travel and other expenses, offset by decreases related to the closure of our Tucson facility in April 2003. The increase from 2001 to 2002 was due primarily to additional personnel hired and relocation costs associated with the appointments of the Chief Operating and Chief Financial Officers, and payments to a strategic consulting firm. Selling, general and administrative expenses as a percentage of revenues were 28% in 2003, 30% in 2002 and 27% in 2001. We do not expect selling, general and administrative expenses as a percentage of revenue to change significantly in 2004 compared to 2003.

Restructuring expenses. Restructuring expenses related to the closure of our Tucson facility were $1.9 million in 2003 consisting of moving, relocation and other costs. We do not expect to incur any additional restructuring charges related to the Tucson closure.

Impairment of goodwill and other intangible assets. In accordance with SFAS 142, we performed our annual impairment test as of October 1, 2002. This impairment test involved a two-step approach. The first step involved estimating our fair value and comparing it to the carrying value of recorded assets. Under SFAS No. 142, if the fair value of our identifiable reporting units is greater than the recorded assets for such reporting units, on a case by case basis, then the first test is passed and no further impairment testing is required. Due to a significant decline in our market capitalization and those of our peers between January 1, 2002 and October 1, 2002, the carrying value of the recorded assets exceeded the estimated fair value for each of our identifiable reporting units as of October 1, 2002. As a result of this potential indication of impairment, we performed the second step of impairment testing, which involved allocating the fair value to all of our assets and liabilities, including unrecorded intangible assets, in order to determine the deemed fair value, if any, of goodwill. Both impairment test steps required us to make significant assumptions and estimates, including the determination of the fair value of identifiable reporting units as well as the fair value of specific assets and liabilities. This process, which utilized a combination of discounted cash flow and market multiple approaches to

determining fair market value, required us to estimate future cash flows and applicable discount rates. The analysis resulted in a $50.9 million goodwill impairment charge in the fourth quarter of 2002, which represented the write-off of all goodwill existing on the books. In the event we make future acquisitions that result in goodwill being recorded, we will be required to perform this test, at a minimum, on an annual basis.

Similarly, as of December 31, 2002 we determined that the carrying value of an intangible asset related to customer contracts recorded in connection with the SIDDCO acquisition was impaired. Accordingly, the asset was reduced by $173,000 to its fair value of zero.

Stock-based compensation. During 1999 and 2000, we granted stock options with exercise prices that were less than the estimated fair value of the underlying shares of common stock on the date of grant. Additionally, we awarded 52,500 shares of restricted stock and rights to acquire 190,000 shares of restricted stock in August 2003. As a result, we have recorded deferred stock-based compensation to be amortized on an accelerated basis over the period that these options, restricted stock grants and rights

to acquire restricted stock vest. The deferred stock-based compensation expense for 2003 was approximately $515,000 compared to approximately $623,000 for 2002 and $1.1 million for 2001. Based on 2004 anticipated grant levels, we expect deferred stock-based compensation for 2004 to be approximately $750,000.

Amortization of goodwill. We recognized no goodwill amortization expense during 2003 and 2002 compared to approximately $5.8 million in goodwill amortization expense recognized during 2001. This decrease is due to the adoption of SFAS No. 142, *Goodwill and Other Intangible Assets,* effective January 1, 2002. SFAS No. 142 required that we cease the periodic amortization of goodwill and certain other intangibles resulting from acquisitions made before July 1, 2001.

Interest income, net of interest expense. We realized $1.8 million in net interest income in 2003, compared to net interest income of approximately $2.0 million in 2002 and $3.3 million in 2001. The decrease in net interest income in 2003 and 2002 is primarily due to a decline in U.S. interest rates and a decrease in the average cash balance.

Income taxes. At December 31, 2003, we had federal and California income tax net operating loss carryforwards of approximately $21.8 million and $14.5 million, respectively. We believe Section 382 of the Internal Revenue Code will significantly limit utilization of the net operating loss carryforwards but have not yet quantified the extent of the limitation. The difference between the federal and California net tax operating loss carryforwards is primarily attributable to the capitalization of research and development expenses and the percentage limitation on the carryover of net operating losses for California income tax purposes. The federal and California tax loss carryforwards will begin to expire in 2010 and 2005, respectively, unless previously utilized. We also have federal and California research tax credit carryforwards of approximately $2.7 million and $1.4 million, respectively. The federal research tax credit carryforwards will begin to expire in 2011 unless previously utilized. The California research tax credits will carry forward indefinitely. As of December 31, 2003, we had approximately $36.8 million in tax-deductible goodwill and other intangibles related to the purchase of Axys Advanced Technologies in April 2000. The majority of this amount is amortized over a 15-year period for tax purposes. We have provided a 100% valuation allowance against the related deferred tax assets as realization of such tax benefits is uncertain.

Although we have continued to experience revenue growth, this trend may not continue. We derive a significant percentage (62% in 2003 and 41% in 2002) of our revenues from a single customer under a chemistry collaboration agreement. This contract may be terminated with six months notice after January 5, 2005 or the terms of this contract or others may not be favorable to us in the future. Additionally, a large portion of our expenses is relatively fixed in nature. Accordingly, if revenues decline or do not grow as anticipated, we may not be able to correspondingly reduce our operating expenses, which would harm our operating results for a particular fiscal period.

In addition, we believe our operating results may fluctuate significantly from quarter to quarter due to the possibility of fluctuations in revenues as well as other factors, many of which are outside of our control, such as, customers' budgetary constraints. Consequently, we believe that quarter-to-quarter comparisons of our operating results are not a good indication of our future performance.

Liquidity and Capital Resources

Since our inception, we have funded our operations with $39.0 million of private equity financings and $94.7 million of net proceeds from our initial public offering in July 2000.

At December 31, 2003, cash and cash equivalents and short-term investments totaled approximately $72.6 million, compared to $69.6 million at December 31, 2002 and $77.3 million at December 31, 2001.

Operating Activities. We rely on cash flows from operations to provide working capital for current and future operations. We believe we have sufficient cash resources to fund existing operations through

2005. Cash flows from operating activities totaled $8.1 million in 2003, an improvement over 2002 and 2001 in which we used $2.1 million and $1.5 million in operating activities, respectively. The increase in operating cash flows in 2003 was primarily due to improved operating results, an increase in prepayments received from our customers and a decrease in inventory. Inventory levels have decreased over the past year due to savings in materials costs and operating efficiencies. We expect decreases in prepayments and, to the extent we are able to achieve our revenue goals for 2004, increases in accounts receivable and inventory in 2004, which could negatively impact our cash flows from operations in the future.

Investing Activities. Cash used in investing activities totaled $8.1 million in 2003 compared to $39.6 million and $45.5 million in 2002 and 2001, respectively. The decrease in cash used in investing activities is due primarily to the adoption of our new investment policy in the second half of 2001 whereby our surplus cash was invested in highly liquid investments. The primary objective for our investment portfolio is to preserve principal while maintaining adequate liquidity to meet projected cash requirements. A secondary objective is to achieve a yield on investments commensurate with the risk levels associated with the primary objective. In each of the years ended December 31, 2003, 2002 and 2001 we paid $2.0 million in prepaid royalties as required under our exclusive µARCS license agreement with Abbott Laboratories, which we carry on the balance sheet as prepaid royalty. No additional prepayments are required under this agreement.

We currently anticipate investing between approximately $2.5 million to $3.5 million in 2004 for leasehold improvements and capital equipment necessary to support future revenue growth. Our actual future capital requirements will depend on a number of factors, including our success in increasing sales of both existing and new products and services, expenses associated with unforeseen litigation, regulatory changes, competition and technological developments, and potential future merger and acquisition activity as well as research and development spending.

Financing Activities. Cash used in financing activities totaled $0.6 million in 2003 and 2002 compared to cash provided by financing activities in 2001 of $0.5 million. Historically, we have had debt obligations under lease and line of credit agreements. Net payments made under these agreements totaled $1.1 million, $1.3 million and $0.8 million in 2003, 2002 and 2001, respectively. As of December 31, 2003, we have no debt obligations. Absent any significant merger and acquisition activity, we do not expect to incur debt in 2004.

On October 4, 2001, our board of directors authorized a Stock Repurchase Plan, authorizing us to repurchase up to 2,000,000 shares of common stock at no more than $3.50 per share. In 2003, we purchased 115,000 shares under this Plan for $289,000 and in 2001, we purchased 35,000 shares for $119,250. We have the authority to purchase additional shares in the future.

We have entered into various agreements that obligate us to make future payments. The table below sets forth the contractual cash obligations that exist as of December 31, 2003:

	Payments Due by Period				
Contractual Obligations	**Total**	**Less than 1 Year**	**1-3 Years**	**4-5 Years**	**After 5 Years**
Minimum Royalty Payments(A)	$ 150,000	$ 30,000	$ 30,000	$ 30,000	$ 60,000
Firm Purchase Orders	136,336	136,336			
Operating Leases	10,513,602	2,478,144	4,868,472	3,166,986	
Total Contractual Cash Obligations	$ 10,799,938	$ 2,644,480	$ 4,898,472	$ 3,196,986	$ 60,000

(A) Total obligation reflected here assumes a 10-year term to the arrangement. The actual contract does not have a legal term and therefore could result in a more significant obligation.

We do not have any off-balance sheet arrangements.

Recent Accounting Pronouncements

In January 2003, the FASB issued FASB Interpretation No. 46, *Consolidation of Variable Interest Entities* (FIN 46). This interpretation provides guidance on the identification of variable interest entities (VIE) for which control is achieved through means other than through voting rights and how to determine when and which business enterprises should consolidate VIEs. The entity identified as the VIEs primary beneficiary is required to consolidate the VIE. Effective October 9, 2003, the FASB issued a Staff Position deferring the effective date for applying the provisions of FIN 46 for VIEs created before February 1, 2003. The new application date is the first interim or annual period ending after December 15, 2003. We have not identified any entity that would require consolidation. The maximum exposure to losses related to any entity that is determined to be a VIE is limited to the carrying amount of the investment in the entity.

In December 2002, the FASB issued SFAS No. 148, *Accounting for Stock-Based Compensation Transition and Disclosure*, an amendment of FASB Statement No. 123. This statement amends SFAS No. 123, *Accounting for Stock Based Compensation,* to provide alternative methods of voluntarily transitioning to the fair value based method of accounting for stock-based employee compensation. SFAS No. 148 also amends the disclosure requirements of SFAS No. 123 to require disclosure of the method used to account for stock-based employee compensation and the effect of the method on reported results in both annual and interim financial statements. The disclosure provisions became effective for the year ended December 31, 2002. We have currently chosen not to adopt the voluntary change to the fair value based method of accounting for stock-based employee compensation. If we should choose to adopt such a method, its implementation pursuant to SFAS No. 148 could have a material effect on our financial position and results of operations.

In April 2003, the FASB issued SFAS No. 149, *Amendment of Statement 133 on Derivative Instruments and Hedging Activities*. This statement amends and clarifies financial reporting for derivative instruments and for hedging activities accounted for under SFAS No. 133 and is effective for contracts entered into or modified, and for hedges designated, after June 30, 2003. Adoption of this standard is not expected to have a material impact on our financial position, results of operations or cash flows.

In May 2003, the FASB issued SFAS No. 150, *Accounting for Certain Instruments with Characteristics of Both Liabilities and Equity*. SFAS No. 150 requires that certain financial instruments issued in the form of shares that are mandatorily redeemable as well as certain other financial instruments be classified as liabilities in the financial statements. SFAS No. 150 is effective for financial instruments entered into or modified after May 31, 2003 and otherwise is effective at the beginning of the first interim period beginning after June 15, 2003. Adoption of this standard is not expected to have a material impact on our financial position, results of operations or cash flows.

In May 2003, the EITF clarified Issue 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables*. Issue 00-21 addresses a model to be used, in the context of a multiple-deliverable revenue arrangement, in determining (a) how the arrangement consideration should be measured, (b) whether the arrangement should be divided into separate units of accounting, and, if so, (c) how the arrangement consideration should be allocated to the separate units of accounting. Issue 00-21 is effective for revenue arrangements entered into in fiscal periods (annual or interim) beginning after June 15, 2003, with earlier adoption permitted. Adoption of this standard is not expected to have a material impact on our financial position, results of operations or cash flows.

BUSINESS

Overview

We collaborate with pharmaceutical and biopharmaceutical companies to advance their drug discovery process through our integrated and highly efficient collection of drug discovery technologies, products and services focused from the point immediately following identification of a drug target through when a drug candidate is ready for pre-clinical studies. Despite numerous technological advances in combinatorial chemistry, high throughput screening, genomics and proteomics, the process of drug discovery remains slow, expensive and often unsuccessful. In order to make the drug discovery process faster, less expensive and more likely to generate a drug candidate, we offer products and services such as assays, synthesis automation, design and synthesis of proprietary libraries of compounds, high-throughput screening, lead optimization, drug discovery informatics and toxicology. These products and services can be provided individually or as an integrated solution, depending on

our customers' requirements. We believe our depth of knowledge and experience, and our range of product offerings, across these areas of drug discovery differentiates us from our competitors. During 2003, we generated revenue from approximately 130 customers worldwide, including Pfizer, Merck, Novartis, Inspire Pharmaceuticals and GlaxoSmithKline.

Industry Background

The Genomics/Proteomics Revolution

The drug discovery process is undergoing fundamental changes as a result of advances in genomics and proteomics, the studies of genes and the proteins they encode. Prior to these advances, pharmaceutical and biopharmaceutical companies addressed less than 500 identified drug targets in the development of drugs. Industry experts predict that the application of genomics and proteomics will lead to the identification of thousands of new drug targets. Drug targets are biological molecules, such as enzymes, receptors, other proteins and nucleic acids that may play a role in the onset, maintenance and progression of a disease. The Pharmaceutical Research and Manufacturers of America reported that its members alone spent an estimated $32 billion worldwide in research and development in 2002, with approximately 25% of this total amount being spent on the stages of drug discovery in which we focus.

Genomics and proteomics have been the subject of intense scientific and commercial focus. Genomics has led to the identification of large numbers of genes encoding potential drug targets, increasing the demand for drug discovery products and services. Once a company has identified a potential drug target, it must still devote significant time and resources to validating the target's role in the disease process and screening libraries of compounds against the target to discover potential drug candidates, which must be optimized further before commencement of human testing.

The Drug Discovery Process

Despite numerous advances and technological breakthroughs in genomics, proteomics, high throughput screening and combinational chemistry, the process of discovering drug candidates from drug targets, as illustrated in the following figure and described below, remains slow, expensive and often unsuccessful.

Drug targets. According to the official website of the human genome project, the genomics revolution has identified over 30,000 human genes that encode the chemical information for cells to produce the proteins that determine human physiology and disease. Drug discovery organizations often advance these new drug targets into discovery with varying degrees of understanding about their role in disease processes and their susceptibility to modulation by chemical compounds. Modulation is defined as the process of selectively increasing or decreasing the biological activity of a particular drug target. Of the 30,000 human genes identified, it is estimated that between 5,000 and 10,000 are susceptible to modulation by chemical compounds.

Assays. Once a drug target has been identified and has been validated as having a role in a disease process, a corresponding set of biological assays, or tests, that relate to the activity of the drug target in the disease process must be developed. These assays are designed to show the effect of chemical compounds on the drug target and/or the disease process. Additionally, assays indicate the relative potency and specificity of interaction between the target and the compounds. The more potent and specific the interaction between the target and the compound, the more likely the compound is to become a drug.

Compound libraries. Typically, biologists or biochemists conduct assays in which they screen libraries consisting of thousands of compounds each to find those compounds that are active in modulating the behavior of the drug targets. Traditionally, chemists generated these compounds for testing by synthesizing them one at a time, or painstakingly isolating them from natural sources. During the last decade, the pharmaceutical industry has developed modular building block techniques, known as combinatorial chemistry, to generate many more diverse compounds far more quickly.

Screening. Screening is the process of testing compounds in assays to determine their potential therapeutic value. A typical screening campaign at a pharmaceutical company will entail screening hundreds of thousands of compounds from multiple compound sources. Today's automated high throughput screening, or HTS, systems can test hundreds of thousands of compounds per day and require only very small amounts of each compound and target material. To address the impact of

chemicals on complex systems, the drug discovery industry recently introduced the capability of High Content Screening, or HCS. HCS enables the analysis of multiple independent or interacting targets in intact cells, thereby providing a deeper understanding of drug action and target validity.

Hits-to-optimized-leads. A successful screening process will identify a number of compounds, or hits, that show activity against the drug target. One or more of the hits are then selected for optimization based on their potency and specificity against the drug target. The hits selected for the optimization process are generally referred to as leads.

Optimizing a lead compound involves repeatedly producing several slight chemical variants of the lead compound and screening them in assays to discover the relationship between the changes in the molecular structure of compounds and the positive or negative effect on biological activity of the target in the assay. These relationships are called structure-activity relationships, or SARs, and are used to identify the compounds that have the optimal effect on the biological activity of the target in the assay. Traditionally, defining SARs was painstakingly slow. Within the last several years, combinatorial chemistry methods have helped to speed this process by creating focused libraries that are comprised of dozens to hundreds of compounds, computationally designed to explore the SARs of leads.

ADME and toxicology. Once a lead compound with a well understood SAR is selected for further development, researchers undertake the process of establishing its absorption, distribution, metabolism and excretion, or ADME, and toxicology characteristics. Leads are studied in biochemical assays and pre-clinical animal studies to determine, among other things, whether they are likely to be safe in humans and stay in the body long enough to perform their intended function. Traditionally, these ADME and toxicology studies are performed at the end of the drug discovery process. There is a significant push in the industry, however, to attempt to provide ADME and toxicology information earlier in the process in order to avoid large expenditures on compounds that could ultimately fail due to their poor ADME and toxicology characteristics.

Drug candidates. If the results of the ADME and toxicology studies performed on a lead are favorable in pre-clinical studies, an investigational new drug application, or IND, may be filed with the Food and Drug Administration requesting permission to begin clinical trials of the drug candidate in humans.

Limitations of the Current Industry

To treat diseases and to meet growth expectations, pharmaceutical companies are under intense pressure to introduce new drugs, and they have increased research and development expenses approximately 300% from $8 billion in 1990 to $32 billion in 2002 according to the Pharmaceutical Research and Manufacturers of America. Nevertheless, the number of new chemical entities approved by the Food and Drug Administration per year has decreased. Despite major scientific and technological advances in areas such as genomics, HTS, HCS and combinatorial chemistry, the drug discovery process remains lengthy, expensive and often unsuccessful. We believe this is due to the following significant limitations to the current process of drug discovery.

Insufficient validation of targets. Drug discovery organizations are advancing many potential new drug targets into discovery without significantly understanding their role in disease processes and their susceptibility to modulation by compounds. Resources spent on pursuing these potential drug targets could be saved if there were better biological or chemical methods to eliminate early in the process those drug targets

exhibiting undesirable characteristics in these areas.

Inefficient production of compound libraries. The increase in the number of potential drug targets has increased the demand for high quality compounds for screening. Traditional methods produce either individual compounds in small numbers, or mixtures of compounds in large numbers whose components must be identified later using time-consuming tagging and screening techniques. Further,

the processes used to develop compound libraries have been labor intensive and have lacked the efficiencies created by automated instrumentation.

Low quality compound libraries. While combinatorial chemistry has vastly increased the number of compounds available for screening, many of the compounds generated have lacked the qualities necessary to become new drug candidates. Also, many libraries contain impure compounds that could lead to false positives or the inability to reproduce results. Inadequately validated chemistries generate compounds that are difficult or impossible to reproduce. In addition, libraries are often designed without paying adequate attention to diversity of chemical properties. These oversights result in libraries that have large numbers of redundant, or unproductively similar, compounds. Further, insufficient attention is devoted to analyzing the potential for the compounds to be used as drugs, leading to hits that could be toxic or have other fundamental ADME flaws.

Inadequate informatics and computational tools. Success of many drug discovery programs is predicated on screening large numbers of compounds, followed by the synthesis and testing of compounds for optimization and for their ADME and toxicology characteristics. This sequential approach is time-consuming and costly. Although many of the recent advances in drug discovery have been targeted at streamlining this process and have allowed large numbers of compounds to be generated and tested in higher throughput, these advances have been in small increments. In addition, the identification of thousands of new drug targets through the application of genomics and proteomics technologies has resulted in large amounts of data being generated. Pharmaceutical companies can save large expenditures of time and money by using informatics and computational tools to manage these data and develop increased and earlier knowledge about which targets are likely to be receptive to chemical modulation, the likely interaction of chemicals and biological targets and which compounds are likely to have unacceptable ADME and toxicological characteristics.

Lack of an integrated, noncompeting drug discovery solution. Many of the companies that provide drug discovery services to the pharmaceutical and biopharmaceutical industries provide only selected services. As a result, they are unable to provide the knowledge and efficiencies that can be gained by broad experience in all facets of drug discovery. Further, customers seeking a totally outsourced solution must use valuable resources to manage multiple vendors and integrate inconsistent or incompatible products. Many drug discovery service providers also compete with their potential customers by conducting internal, proprietary drug discovery activities.

Limited predictive value of model systems. Drug candidates are normally tested in animal models or in selected *in vitro* and *ex vivo* models to evaluate their efficacy. Many of these models only partially reflect the drug candidates' effects in humans. Proof for efficacy can often only be obtained in clinical studies. Methods and systems which allow a compound to continue through the pre-clinical phase in a cost effective manner and add to the understanding of the mechanisms of action of drug candidates in complex systems might significantly improve the discovery success rate.

Our Solution

We collaborate with pharmaceutical and biopharmaceutical companies to advance their drug discovery process through our integrated and highly efficient collection of drug discovery technologies focused from the point immediately following identification of a drug target through when a drug candidate is ready for pre-clinical studies. Our customers include many major pharmaceutical companies and numerous biopharmaceutical companies. We do not discover or develop drugs for our own account and we do not compete with our customers. We believe the broad range of products and services we offer or intend to offer will provide the following benefits:

Target validation. We have developed a large number of libraries of highly diverse compounds that are specifically designed to modulate many drug targets. We believe the use of these libraries, which

are not sold on a stand-alone basis but rather as part of an integrated suite of our products and services, may provide early information about whether a drug target is susceptible to chemical modulation and, if so, whether modulation of its activity has an important effect on the disease process or outcome. If these libraries are successful in providing this information early in the drug discovery process, our customers can save large amounts of time and resources by abandoning the pursuit of targets that exhibit undesirable characteristics. We believe our micro Arrayed Compound Screening, or μARCS, technology, a cost-effective HTS technology that we have licensed exclusively from Abbott Laboratories, has the potential to become an invaluable tool to use chemistry as an approach for target validation.

Efficient production of compound libraries. Our proprietary combinatorial system, referred to as directed sorting, combines the advantages of parallel synthesis and split-and-pool synthesis. In parallel synthesis, chemists perform multiple chemical reactions simultaneously, or "in parallel", to produce larger amounts of each individual compound. In split-and-pool synthesis, chemists take the product of one set of reactions and repeatedly split them for subsequent sets of reactions, allowing for very high productivity in generating compound libraries. Using our directed sorting technology chemists can synthesize compounds with high efficiency and speed and keep the compounds discrete in individually tagged reactors. Our directed sorting products have gained widespread acceptance throughout the pharmaceutical industry.

High quality compound libraries. Our chemistries are easily replicated and our compounds rapidly replenishable because we produce detailed synthesis protocols, or recipe books, for each compound library. We are able to rapidly create focused libraries containing slight variations of hits from our original discovery or targeted libraries to study SARs. Working with our customers, we design discovery libraries for maximum diversity using proprietary computer algorithms. Finally, after synthesis of a compound, we use multiple analytical methods to ensure a high degree of compound purity. As a consequence, our libraries contain highly diverse, drug-like compounds of high purity. Our Accelerated Retention Window, or ARW, method is used to purify large combinatorial libraries to the industry standard of 90% purity or greater.

Broad range of products and services for assay development, chemistry and screening. We currently offer a broad range of drug discovery products and services to pharmaceutical and biopharmaceutical companies targeted at assay development, chemistry and screening. We have performed almost 165 different assays for our customers and provide access to more than 800,000 discrete chemical compounds. Our approach for efficiently finding screening hits or drug leads combines proprietary computational methods for compound selection and data mining with our high throughput screening platform. In addition, our team of chemists and biologists has worked on several hit and lead optimization projects for our customers. We intend to employ our μARCS technology to improve the ease of access to screening and cost effectiveness of the screening process. In addition, we possess the capability to quantitatively study the effect of drugs on a sub-cellular level.

Development of an informatics and computational tools knowledge base. We apply sophisticated computational software tools to generate predictive information in the early stages of drug discovery. We use our tools to correlate information available on families of drug targets and compounds with screening data to predict which drug targets are likely to be receptive to chemical modulation, and which chemical structures are likely to react favorably with large families of drug targets or produce unacceptable ADME or toxicological results. We have also developed computer algorithms that reduce the number of compounds that must be screened to identify hits. We believe our computational tools complement the drug discovery process and reduce the time and resources involved.

Integrated drug discovery products and services. We offer a broad range of integrated drug discovery products and services that provide unique value to our customers and we intend to continue to expand our offerings to provide more complete drug discovery solutions. We believe our focus on

our customers' needs, rather than our own drug development efforts, makes our product and service offerings more attractive.

Our Strategy

Our strategy is to become the leading provider of a complete, integrated and highly efficient drug discovery platform designed to overcome many of the limitations associated with the slow and expensive traditional drug discovery process. Accordingly, we intend to implement our strategy by pursuing the following objectives:

Broaden and deepen our technology through internal invention and acquisition. We have assembled our current suite of advanced technologies, products and services both through internal invention and acquisition. We have developed our lead optimization capabilities and our directed sorting instrument systems and consumables internally. We have generated our assay development and screening capabilities, our ability to develop and synthesize large discovery libraries of compounds, our informatics technology and products, and our ADME and toxicology capabilities through acquisition. We intend to continue to invest in internal research and development and to acquire and integrate innovative products and services in order to stay at the forefront of drug discovery technology. For example, we have exclusively licensed μARCS, a next generation screening platform, from Abbott Laboratories, which is available to increase the efficiency of the high throughput

screening we perform for customers. We do not currently have any acquisitions pending.

Expand customer relationships through integration of products and services. We are using existing relationships with customers in individual areas of our business to sell products and services in multiple areas of drug discovery. We believe that our customers can best take advantage of the time and cost efficiencies of our products and services in integrated combinations. For example, we believe our lead optimization group will be in the best position to optimize hits generated using our compound libraries because our group will best understand the underlying synthesis chemistry. We have been successful in selling hit follow-up, chemistry and lead optimization services to customers that had previously purchased our other products and services.

Gain wider penetration of the biopharmaceutical industry. We will continue to focus on providing drug discovery products and services to the biopharmaceutical market. We have a skilled team of business development and marketing professionals targeting biopharmaceutical customers worldwide. During the period from 1999 to 2003, the top ten pharmaceutical companies' revenue and research and development expenditures increased by an estimated 7.1% and 6.3%, respectively, per year. During the same period, the top ten biopharmaceutical companies' revenue and research and development expenditures increased by an estimated 23.0% and 18.4%, respectively, per year. In addition, the number of new biotechnology drugs approved in the U.S. by the Food and Drug Administration has increased to approximately 180, approximately half of which were approved since 1999. We believe that, as the biopharmaceutical industry continues to mature and generate additional products, the resources dedicated to drug discovery and development will increase and we believe that this may provide an opportunity for us to sell additional products and services to biopharmaceutical companies.

Continue to generate multiple revenue streams and diversify our revenue base. We sell a variety of products and services and we believe that our multiple revenue streams reduce the potential negative consequences to us if any one of our product or service areas ceases to be productive. We expect to continue to sell to our customers primarily for current revenue, but when appropriate, we may structure financial terms to include milestone payments or royalties based on the success of the ultimate pharmaceutical product. We have more than 130 customers, however, during 2003, revenue from Pfizer represented 62% of total revenue. It is our intention to continue to grow our business and expand our customer base, which would reduce our dependency on Pfizer.

Continue to expand our knowledge base and streamline the drug discovery process. Because of the large number and diversity of our customers, we generate and are exposed to large amounts of highly useful information about the drug discovery process and about the general interaction between types of chemistries and types of drug targets. Much of this information is not specific to or proprietary to our customers and increases our understanding of the interaction of the drug targets we work on and the chemistries we apply to them as well as of the drug discovery process itself. We believe this knowledge will enable our customers and us to conduct drug discovery work faster, less expensively and with a greater likelihood of success. Our ultimate goal is to leverage our knowledge base to streamline the drug discovery process and to create new revenue opportunities for us.

Our Products and Services

We provide products and services designed to make the drug discovery process faster, less expensive and more likely to generate a high quality drug candidate. We currently offer products and services in many functional disciplines of the drug discovery process that can be purchased individually or as integrated solutions, depending on our customers' requirements. We intend to continue to add to our functional offerings in order to provide a comprehensive and integrated suite of drug discovery products and services to our pharmaceutical and biopharmaceutical customers.

Assays

We provide assay development services through our team of scientists who are experienced in working with major disease target classes such as protein kinases, G-protein-coupled receptors, nuclear receptors, phosphatases, and proteases. Biological systems about which we have expertise include enzymes, receptor-ligand interaction, protein-protein interaction, ion channel assays, reporter-gene assays in prokaryotic and eukaryotic cells, cellular proliferation, differentiation and physiologic response, and microbial growth. Most recently we established HCS technology in-house. This allows us to profile compounds for their effect on multiple intracellular events in one assay. We acquired the ability to provide assay development services through our acquisition of Discovery Technologies, Ltd. in 1999 and further internal development.

Through our acquisition of Xenometrix in 2001 and further internal development, we now offer unique cell-based assays with multiple gene response indicators, which give specific information on the biological activity of a pharmaceutical compound. Genetically engineered living cells allow us to determine the on and off state of gene promoters in the presence of compounds. Our portfolio of reporter cell lines may provide important efficacy and safety information to help optimize the selection of drug candidates before moving to the more costly stages of

pre-clinical and clinical testing.

Automation Products and Services

Through our IRORI line of products and services, we develop, manufacture and sell proprietary instruments and consumables for compound library synthesis. Our instruments are based on a patented core technology referred to as directed sorting, which enables our customers to generate large collections of compounds.

In the directed sorting process, we synthesize each unique compound in a library in a separate micro-reactor that contains a unique, electronically readable tagging device. A micro-reactor is a semi-porous container that allows the chemical reagents and solvents used in the synthesis process to pass in and out of it without allowing the compound being synthesized inside to escape. In this way, we can process tens, hundreds or even thousands of micro-reactors simultaneously through a synthesis step in the same reaction vessel, which can be a large flask or beaker. At the end of each chemical synthesis step, a computer that reads the electronic tags directs the sorting of the micro-reactors for the next synthesis step. The sharing of reaction vessels by many micro-reactors provides productivity gains. For

example, using only 30 reactions, directed sorting can complete a 1,000 compound library that results from a three-step synthesis procedure using ten reagents in each step. Using parallel synthesis, this same library would require between 1,110 and 3,000 reactions to complete.

Our current products that are based on the directed sorting technology include the NanoKan system, a high throughput chemistry system that can generate up to one million discrete compounds per year, the AutoSort system, an automated chemistry system and a manual chemistry system. All of these systems were developed internally by us, and include hardware and software platforms and use disposable micro-reactors that our customers purchase for every compound that is synthesized using these products. We also offer Crystal Farm, our proprietary self-contained crystallization and imaging system that provides automated high throughput incubation and imaging of thousands of protein crystallization experiments.

Proprietary Libraries of Compounds

As a result of internal development and our acquisitions of AAT in 2000 and SIDDCO in 2001, we are able to offer the following broad range of highly purified compound libraries for assay screening and rapid hit-to-lead activities:

Discovery libraries. We generate and sell discovery libraries, which are collections of diverse, drug-like compounds that are designed using computer programs to systematically explore specified areas of chemical space or types of chemistry. They are used in the initial stages of screening in which very little information is known about which compounds will alter the activity of the drug target in the assay.

Targeted libraries. We design and sell targeted libraries selected for a specified type of drug target. These libraries are a group of highly related compounds used much like discovery libraries, but they provide a more insightful medicinal chemistry starting point.

Focused libraries. We are able to rapidly generate focused libraries based on hits from our discovery or targeted libraries because we have previously invested significant resources to produce detailed synthesis protocols in the development of each library of compounds. Focused libraries explore subtle changes in the compound structure to quickly elicit SARs and evolve lead compounds. In addition, we develop focused libraries from hits generated by our customers.

Chemistry protocols. We may sell licenses to the detailed protocols, or chemical recipes, for generating our libraries to customers that purchase those libraries. This enables our customers to replenish compounds and to create additional compounds. We use a proprietary combinatorial chemistry technology platform to generate compound libraries that employs parallel synthesis and our directed sorting technology. Our approach provides the following advantages:

Purity: Maximum purity is important to minimize false positives during screening. We can deliver compounds that are greater than the current industry standard of 90% pure depending on customer specifications. Our quality control measures include high performance liquid chromatography, mass spectroscopy, nuclear magnetic resonance, evaporative light scattering detection and weight percent analysis. We achieve the required purity using several purification technologies including our proprietary ARW high throughput purification process;

Diversity: Each discovery library of approximately 1,000 to 5,000 drug-like compounds is designed to contain a set of highly diverse compounds using our chemical mapping and differentiation software;

Ease of optimization: The individual chemistries for each library are highly validated and characterized. This allows rapid generation of focused libraries around hits and rapid follow-up and modification by medicinal chemistry programs; and

Re-supply and reproducibility: Our synthesis approaches produce large quantities that allow rapid and cost effective restocking of customers' supplies. Our highly validated chemistries allow us or our customers to re-synthesize larger quantities on demand.

Screening

We offer high throughput screening services through an experienced staff of scientists located at our facility near Basel, Switzerland. We also offer our customers access to compounds from many of the world's leading compound suppliers as well as a significant collection of internally developed compounds. This allows our customers access to a large and diverse collection of compounds without the need to store and manage the compound collections in their own facilities.

Our HTS modules are equipped to quickly and efficiently process the particular assay being carried out. A module consists of the appropriate plate and liquid handling equipment, coupled with the best read out technology for the assay being run. We deliver a list of validated hits to our screening customers. We also provide hit follow-up and verification services and, when desired, actual physical samples of the hit compounds. We anticipate that our screening services will lead to additional revenue opportunities based on requests for hit characterization, data analysis and management as well as chemistry-based hit and lead optimization services. To improve the speed and cost effectiveness of the screening process, we have exclusively licensed from Abbott Laboratories and further developed µARCS, a next-generation high throughput screening technology. µARCS eliminates the need for microtiter plates by spotting compounds at a very high density directly onto microtiter plate size sheets, called ChemCards. Each ChemCard contains duplicates of 4,608 compounds. Savings may be realized in running the µARCS assays because the need for liquid handling automation is eliminated and very small amounts of reagent are required. This platform provides rapid and cost effective high performance high throughput screening while supporting a very broad range of biochemical and cellular assays.

We initially acquired our ability to offer these screening services in our acquisition of Discovery Technologies, Ltd. in 1999 and have added to our capabilities through further internal development.

Hits-to-Optimized-Leads

Through a combination of internal development and our acquisitions of SIDDCO in 2001, Structural Proteomics in 2000, Xenometrix in 2001 and AAT in 2000, we have developed products and services to advance early stage screening hits to optimized drug leads. These products and services include the following:

Custom focused libraries. In addition to our collection of proprietary libraries, we design and produce custom, focused libraries based upon hits identified from screening. These hits may be from our compound libraries, the customer's internal compound collection or even from another compound library supplier. Focused libraries consist of compounds that represent systematic variations of hits. Medicinal chemists use these focused libraries to begin refining hits to optimize the properties that have an effect on the drug target in the assay. Because we invest significant resources in the development of each of our compound libraries, we are able to generate focused libraries based on hits from our discovery libraries or targeted libraries more rapidly than when we begin from an isolated hit resulting from a customer's compound collection.

Medicinal chemistry. We also provide a wide range of medicinal chemistry and other lead optimization services. This includes the synthesis of compounds that modify the original hit or lead for improved potency, selectivity and other pharmaceutical characteristics. We have an experienced group of synthetic organic chemists and medicinal chemists with expertise in both solid phase chemistry and solution phase chemistry. In some cases we provide medicinal chemistry services in conjunction with our computational drug discovery efforts to design and construct small libraries of compounds to act on specific targets of known structure.

Biological profiling in the hit-to-optimized-lead phase. We also provide a broad range of biological profiling including the primary screening test, specificity assays, cellular assays, ADME and in vitro toxicology tests. Our multiparameter analysis tools allow efficient data analysis and selection of compounds, which fit the product profile.

Drug Discovery Informatics; ADME and Toxicology

In connection with our acquisitions in 2000 of AAT and Structural Proteomics, we acquired and are further developing computational tools that we believe will allow us to continue to increase our knowledge of the characteristics of targets, leads, and ligand-target interactions and which we believe can be applied throughout the drug discovery process to significantly reduce the time and cost of developing a drug. We currently have computer algorithms that allow us to design libraries of compounds with high diversity, thereby increasing the likelihood of finding hits during screening. When screened against large numbers of potential drug targets, we believe these large and highly diverse libraries will provide significant information about which drug targets are amenable to modulation by chemical means. We have developed novel algorithms to aid in the understanding and utilization of the data resulting from high throughput screening experiments. We have also developed a proprietary analysis tool which we believe will allow us to use screening data to correlate drug target families with the types of compounds which will likely bind to them. Using this tool, we will seek to design highly effective targeted libraries for whole drug target families. In addition, we will seek to use this tool to efficiently design potent compounds for a particular drug target and to efficiently search databases of compounds available from other vendors for likely leads.

We expect to further use our computational tools and screening data to help predict ADME and toxicological reactions to classes of compounds. This will allow our customers to avoid spending money and time on hits and leads that will ultimately fail due to their ADME and toxicological characteristics.

Integrated Drug Discovery Programs

We offer an integrated collaborative drug discovery program that provides our customers with many of the tools and capabilities needed to find and advance leads to pre-clinical candidates. In these collaborations we provide integrated access to our computational design and analysis, chemistry, and biology capabilities for the purpose of developing a pre-clinical lead for the client's target. As a result, we are able to provide our customers with the knowledge and efficiencies that we have gained from our broad experience in a number of areas of drug discovery. In addition, customers seeking a totally outsourced solution are not required to use valuable resources to manage multiple vendors and integrate inconsistent or incompatible products. Each integrated drug discovery program is customized to increase the likelihood of success. Milestone payments, which are due upon lead compounds demonstrating specified potency and selectivity requirements, may be included in addition to full-time equivalent fees. In 2003, milestone payments represented an immaterial portion of our total revenue and are not anticipated to be material to total revenue in the foreseeable future. We currently are conducting integrated drug discovery programs for Inspire Pharmaceuticals, Inc. and Theracos, Inc.

Customers

During 2003, we generated revenue from approximately 130 customers worldwide. The most significant by dollar volume and which we have previously disclosed are as follows:

Actelion Ltd.	Merck & Co., Inc.
Allergan Inc.	Novartis
Dupont Pharma, Inc.	Pfizer Inc
GlaxoSmithKline plc	Seikagaku America
Housey Pharmaceuticals, Inc.	The University of Georgia
Inspire Pharmaceuticals, Inc.	Theracos, Inc.
Kirin Brewery Company Ltd.	Xenon Genetics Inc.

In 2003, 2002 and 2001, 62%, 41% and 8%, respectively, of our revenue came from our chemistry contracts with Pfizer Inc. There were no other customers that represented over 10% of our revenue in 2003, 2002 or 2001.

Component Supply

Most of the raw materials used in the research, development and manufacture of our products and the offering of our services are available from more than one supplier. We depend on sole-source suppliers for the radio frequency, or RF, tags used in our combinatorial chemistry products and the two-dimensional bar code tags used in our NanoKan and X-Kan systems. These items are obtained from suppliers on standard commercial terms. We have no long-term supply agreements for these items. To date, we have not experienced difficulty in obtaining necessary raw materials. We believe that if our sole-source suppliers were unable to provide sufficient materials, we would have enough materials on hand

or could obtain the materials from other sources without significant additional cost or delay.

Sales and Marketing

We have a skilled team of eight full-time business development and marketing professionals targeting pharmaceutical and biopharmaceutical customers worldwide. Additionally, our senior executives coordinate global management of our key customers and manage our general sales and marketing efforts for our drug discovery offerings to major pharmaceutical customers and prospective customers worldwide. In addition to direct selling efforts we also use industry trade shows and industry journal advertising for sales and marketing.

Research and Development

Our research and development expenses totaled approximately $2.6 million in 2003, $6.2 million in 2002 and $13.0 million in 2001. None of these expenses were funded by outside parties. Our research and development expenses decreased due to the redeployment of development scientists and engineers to the direct revenue generating activities of customer funded research and development programs and collaborations as well as the decision to discontinue the development of chemical compounds to be sold out of inventory. We conduct research and development programs in three primary areas as follows:

Core instrumentation technology. These projects include the development of new instrumentation technologies that led to the development of our current IRORI products, including the NanoKan and X-Kan Systems. Core technology projects have also expanded beyond synthesis technology to include the development of other drug discovery instrumentation, including Crystal Farm, our proprietary self-contained crystallization and imaging system that provides automated high throughput incubation and imaging of thousands of protein crystallization experiments. We implement projects on our own behalf and in collaboration with customers to develop specific instruments we identify as product opportunities. In collaborative projects, we seek to retain the intellectual property and commercialization rights.

Drug discovery informatics. We have initiated drug discovery informatics projects that we believe will lead to a host of new products and services. We have begun to develop informatics tools that will aid in the design of new compound libraries that are optimized for potency toward a specific drug target and minimized for interactions with other undesired targets. Additionally, we are developing computational software and algorithms that may provide rapid advances in the areas of high throughput protein homology determination and cell-based and target-based virtual screening.

Assay development and high throughput screening. We continue to invest in new assay development and HTS technologies that we believe will allow us to broaden our product and service offerings. We are continually expanding our portfolio of assays and believe current research and development programs will allow us to address virtually every type of homogeneous or heterogeneous drug discovery assay. We are investing in the μARCS technology in order to improve the speed and cost effectiveness of the screening process as well as in ADME and safety profiling platforms.

The following table presents the geographic breakdown of our revenue for our last three fiscal years.

	Years Ended December 31,		
	2003	2002	2001
United States	80%	67%	62%
Foreign Countries	20%	33%	38%

The following table presents the geographic breakdown of our long-lived assets for our last three fiscal years.

	Years Ended December 31,		
	2003	2002	2001
United States	82%	78%	75%
Foreign Countries	18%	22%	25%

Our backlog as of February 27, 2004 was approximately $39 million, which compares to approximately $36 million on February 27, 2003.

Agreement with Pfizer

In February 2004, we entered into a broadened collaboration agreement with Pfizer that replaces our existing collaboration with Pfizer that we entered into in December 2001. Under this agreement, we collaborate with Pfizer to design and develop custom libraries of drug-like compounds that are owned by and exclusive to Pfizer. We manufacture and purify the compounds to high purity standards using, among other methods, our proprietary ARW purification technology. The agreement has a two-year term, however, Pfizer has a contractual right to terminate the contract, with or without cause, upon six months notice after January 5, 2005. In such event, Pfizer will retain exclusive rights to the libraries of compounds that we have delivered to Pfizer, and will be obligated to pay us for the minimum contracted compound libraries and manufacturing and purification services during the notice period. In addition, either party may terminate the agreement upon the material, uncured breach of the other party, and Pfizer may terminate the agreement if we are acquired by a third party or in the event of a change in control of our company. The estimated potential value of this 2-year collaboration may reach $46 million, making it material to our annual revenues for 2004 and 2005. Achieving the full amount is, in effect, subject to Pfizer not terminating the agreement. During 2003, revenue from Pfizer represented 62% of total revenue.

Intellectual Property

Our policy is to pursue patents, copyrights and trademarks and to otherwise endeavor to protect our technology, inventions and improvements that are commercially important to the development of our business. We also rely upon trade secrets and proprietary know-how that may be important to the development of our business.

Our success will depend in large part on our ability to:

- obtain and maintain patent and other proprietary protection for the technology, inventions and improvements we consider important to our business;
- defend our patents;
- preserve the confidentiality of our trade secrets; and
- operate without infringing the patents and proprietary rights of third parties.

We have implemented an aggressive patent strategy designed to maximize our intellectual property rights. We are pursuing patent coverage in the United States and those foreign countries that are home

to the majority of our anticipated customer base. We currently own 28 issued patents in the United States. In addition, our patent portfolio includes eight pending patent applications in the United States and corresponding international and foreign filings in major industrial nations.

United States patents issued from applications filed prior to June 8, 1995 have a term of the longer of 20 years from the earliest priority date or 17 years from issue. Eight of our applications were filed prior to June 8, 1995 and all of these applications have issued. United States patents issued from applications filed on or after June 8, 1995 have a term of 20 years from the application filing date or earlier claimed priority. Patents in most other countries have a term of 20 years from the date of filing of the patent application. Our remaining patent applications, including the applications from which 20 of our issued patents were derived, were filed after June 8, 1995. Because the time from filing to issuance of patent applications is often several years, this process may result in a shortened period of patent protection, which may adversely affect our ability to exclude competitors from our markets. Our issued United States patents have expiration dates ranging from April 2015 to April 2020. None of our licenses to use others' patents will expire within the next ten years. Our success will depend to a significant degree upon our ability to develop proprietary products and technologies and to obtain patents having claims that cover such products and technologies. We intend to continue to file patent applications covering any newly developed products and technologies.

Patents provide some degree of protection for our proprietary technology. However, the pursuit and assertion of patent rights, particularly in areas like pharmaceuticals and biopharmaceuticals, involve complex determinations and, therefore, are characterized by some uncertainty. In addition, the laws governing patentability and the scope of patent coverage continue to evolve, particularly in the area of biopharmaceuticals,

and due to the time between the filing and granting of a patent application, we may be infringing upon the patent rights of a third party without any knowledge of the patent. As a result, patents might not issue from any of our patent applications or from applications licensed to us. The scope of any of our issued patents may not be sufficiently broad to offer meaningful protection. In addition, our issued patents or patents licensed to us may be successfully challenged, invalidated, circumvented or rendered unenforceable so that our patent rights might not create an effective competitive barrier. Moreover, the laws of some foreign countries may not protect our proprietary rights to the same extent as do the laws of the United States. Any patents issued to us or our collaborators may not provide a legal basis for establishing an exclusive market for our products or services or provide us with any competitive advantages. In addition, patents issued to us or our collaborators may not ensure that the patents of others will not have an adverse effect on our ability to do business or to continue to use our technologies freely. In view of these factors, our intellectual property positions bear some degree of uncertainty.

Our European eukaryotic gene profiling patent was opposed by various companies. Oral proceedings were held before the Opposition Division of the European Patent Office in January 2003. At the conclusion of the hearing, the Opposition Division maintained our patent in amended form. The period during which an appeal of the Opposition Division decision could be made has expired. As amended, the patent claims kits and methods for identifying and characterizing the potential toxicity of a compound using expression profiles of four categories of stress.

We also rely in part on trade secret protection for certain of our technologies and proprietary know-how. The source code for our proprietary software is protected both as a trade secret and as copyrighted works. We attempt to protect our trade secrets by entering into confidentiality agreements with third parties, employees and consultants. Our employees also sign agreements requiring that they assign to us their interests in inventions and original expressions and any corresponding patents and copyrights arising from their work for us. However, it is possible that these agreements may be breached, invalidated or rendered unenforceable, and if so, there may not be an adequate corrective remedy available. Despite the measures we have taken to protect our intellectual property, parties to our agreements may breach the confidentiality provisions in our contracts or infringe or misappropriate

our patents, copyrights, trademarks, trade secrets and other proprietary rights. In addition, third parties may independently discover or invent competing technologies or reverse engineer our trade secrets or other technology.

Third parties may file claims asserting that our technologies or products infringe on their intellectual property. We cannot predict whether third parties will assert such claims against us or our licensees or against the licensors of technology licensed to us, or whether those claims will harm our business. If we are forced to defend against such claims, whether they are with or without merit, and whether they are resolved in our favor or against us, our licensees or our licensors, we will incur significant expenses and experience diversion of management's attention and resources. As a result of any disputes over intellectual property, we may have to develop at a substantial cost non-infringing technology or enter into costly licensing agreements. These agreements, if necessary, may be unavailable on terms acceptable to us, or at all, which could seriously harm our business or financial condition.

License Agreement with Abbott Laboratories. On January 2, 2001 we signed an agreement with Abbott Laboratories that provides us with the exclusive license to µARCS. We paid Abbott $2.0 million in prepaid royalties upon signing of the agreement and an additional $2.0 million in April 2002 and a final $2.0 million in March 2003. The Abbott µARCS technology provides high throughput screening of thousands of compounds per ChemCard against a very broad range of drug discovery targets, without the use of individual wells and the attendant liquid handling requirements. We believe this technology can enable virtually any laboratory to screen compounds against a wide range of targets faster and less expensively than other available screening methodologies. If any license disputes arise between us and Abbott relating to the µARCS technology and we are not able to resolve those disputes or if Abbott is unsuccessful in obtaining adequate patent coverage for the µARCS technology, our ability to screen compounds may be compromised and we may not be able to prevent competitors, including Abbott Laboratories, from using the µARCS technology, which could have a material adverse effect on our financial condition and results of operations.

Competition

We compete with companies in the United States and abroad that offer drug discovery products and services. These competitors include companies engaged in the following areas of drug discovery:

Assay development and screening, including Cerep, Evotec OAI AG, Argenta Discovery Ltd and Pharmacopeia Inc.;

Combinatorial chemistry instruments, including Argonaut Technologies and Mimotopes Proprietary Limited;

Compound libraries and lead optimization, including Albany Molecular Research Inc., Pharmacopeia Inc., Array Biopharma Inc., Evotec OAI AG, Biofocus plc and ArQule, Inc.;

Informatics, including Accelrys and Tripos, Inc.; and

Gene profiling, including Affymetrix and Gene Logic, Inc..

We face competition based on a number of factors, including size, relative expertise and sophistication, speed and costs of identifying and optimizing potential lead compounds and of developing and optimizing chemical processes. We compete with the research departments of pharmaceutical companies, biopharmaceutical companies, combinatorial chemistry companies, contract research companies, contract drug manufacturing companies and research and academic institutions. Many of these competitors have greater financial and other resources and more experience in research and development than we do. Smaller companies may also prove to be significant competitors, particularly through arrangements with large corporate collaborators.

Historically, pharmaceutical companies have maintained close control over their research and development activities, including the synthesis, screening and optimization of chemical compounds and the development of chemical processes. Many of these companies, which represent a significant potential market for our products and services, are developing or already possess in-house technologies and services offered by us. Academic institutions, governmental agencies and other research organizations are also conducting research in areas in which we provide services either on their own or through collaborative efforts.

We anticipate that we will face increased competition in the future as new companies enter the market and advanced technologies become available. Our services and expertise may be rendered obsolete or uneconomical by technological advances or entirely different approaches developed by one or more of our competitors. The existing approaches of our competitors or new approaches or technologies developed by our competitors may be more effective than those developed by us. We cannot assure you that our competitors will not develop more effective or more affordable technologies or services, thus rendering our technologies and/or services obsolete, uncompetitive or uneconomical. For example, advances in informatics and virtual screening may render some of our technologies, such as our large compound libraries, obsolete. We currently are investing in µARCS technology to improve screening processes. However, we may be unable to successfully sell this technology to customers and we may never recover the cost of our investment including the prepaid royalty to Abbott, which is carried on our balance sheet as prepaid royalty in an amount equal to approximately $6.0 million. We may not be able to compete successfully with existing or future competitors.

In addition, due to improvements in global communications, combined with the supply of lower cost PhD level scientific talent, we face the growing threat of competition for our chemistry and computational chemistry services from low-cost offshore locations such as China, India and Eastern Europe.

Government Regulation

We are subject to various federal, state and local laws and regulations relating to the protection of the environment. In the course of our business, we handle, store and dispose of chemicals. The laws and regulations applicable to our operations include provisions that regulate the discharge of materials into the environment. Usually these environmental laws and regulations impose strict liability, rendering a person liable without regard to negligence or fault on the part of such person. Such environmental laws and regulations may expose us to liability for the conduct of, or conditions caused by, others. We have not been required to expend material amounts in connection with our efforts to comply with environmental requirements, and we do not believe compliance with such requirements will have a material adverse effect upon our capital expenditures, results of operations or competitive position. Because the requirements imposed by these laws and regulations frequently change, we are unable to predict the cost of compliance with these requirements in the future, or the effect of these laws on our capital expenditures, results of operations or competitive position.

Employees

As of March 1, 2004, we had approximately 202 full-time employees worldwide. None of our employees are covered by a collective bargaining agreement. We believe our relationship with our employees is generally satisfactory.

Web Site Access to SEC Filings

We maintain an Internet website at *www.discoverypartners.com*. We make available free of charge on our Internet website our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

MANAGEMENT

The following table sets forth information regarding our current directors and executive officers as of March 10, 2004:

Name	Age	Position
Directors:		
Sir Colin T. Dollery	72	Director
Dieter Hoehn	63	Director
Harry F. Hixson, Jr., Ph.D.	65	Director
Alan J. Lewis, Ph.D.	58	Director
Riccardo Pigliucci	57	Chief Executive Officer and Chairman
Herm Rosenman	56	Director
Michael C. Venuti, Ph.D.	50	Director
John P. Walker	55	Director
Executive Officers:		
Riccardo Pigliucci	57	Chief Executive Officer and Chairman
Taylor Crouch	44	President and Chief Operating Officer
Craig Kussman	45	Chief Financial Officer, Senior Vice President Finance and Administration and Secretary
John Lillig	54	Chief Technology Officer, Vice President, Discovery Systems
Douglas Livingston, Ph.D	49	Senior Vice President and General Manager, Discovery Chemistry Services
Urs Regenass, Ph.D	53	Vice President, Integrated Drug Discovery
Richard Neale	40	Vice President, Business Operations

Directors:

Sir Colin T. Dollery has served as a member of our board of directors since March 2001. Since 1996, Sir Colin Dollery has served as Senior Consultant, Research & Development, to GlaxoSmithKline PLC (formerly SmithKline Beecham), a public pharmaceutical company. From 1991 to 1996, he was the dean of the Royal Post Graduate Medical School of the University of London. Sir Colin Dollery received a B.S. in physiology and a medical degree (M.B., Ch.B.) from the University of Birmingham in Birmingham, England.

Dieter Hoehn has served as a member of our board of directors since November 1996. Since May 1996, Mr. Hoehn has been a self-employed management consultant. From 1984 until 1996, he was a member of the senior corporate management of the Hewlett-Packard Company, a provider of computing and imaging products, measurement solutions and services, where he served as Vice President in charge of the Bioscience Program from May 1995 until his retirement in April 1996 and Vice President in charge of the Analytical Products Group from May 1987 to April 1995. Mr. Hoehn also served as Vice Chairman of the Board of Directors of Hewlett-Packard Shanghai Analytical Products Co., Ltd., China, an analytical instruments company, and as a director of Yokogawa Analytical Systems, Inc., Japan, an analytical instruments company, until April 1999. He is a member of the Advisory Board of the Barnett Institute at Northeastern University.

Harry F. Hixson, Jr., Ph.D. has served as a member of our board of directors since May 2001. Dr. Hixson currently serves as the Chairman of Elitra Pharmaceuticals, a biotechnology company, and from February 1998 to May 2003, he served as both the Chief Executive Officer and Chairman of Elitra Pharmaceuticals. From February 1991 to February 1998, Dr. Hixson was a self-employed individual investor. Dr. Hixson is also a director of SEQUENOM, a human genetics products and services company. Dr. Hixson holds a Ph.D. in physical biochemistry from Purdue University, a M.B.A. from The University of Chicago and a B.S. degree in chemical engineering from Purdue University.

Alan J. Lewis, Ph.D. has served as a member of our board of directors since April 2000. Since 2000, Dr. Lewis has been President of the Signal Research Division of Celgene Corporation, a biopharmaceutical company. From 1996 to 2000, Dr. Lewis was Chief Executive Officer and a director of Signal Pharmaceuticals, Inc., a drug discovery company. From 1994 to 1996, he was President of Signal. Prior to joining Signal, Dr. Lewis worked for 15 years at the Wyeth-Ayerst Research division of American Home Products Corporation, a pharmaceutical company, where he served as Vice President of Research from 1990 to 1994. Dr. Lewis received a B.S. in physiology and biochemistry from Southampton University and a Ph.D. in pharmacology from the University of Wales in Cardiff and completed his post-doctoral training at Yale University.

Riccardo Pigliucci has served as our Chief Executive Officer since May 1998 and chairman of our board of directors since May 1999. He previously served as Chief Executive Officer of Life Sciences International PLC, a supplier of scientific equipment and consumables to research, clinical and industrial markets, from 1996 to 1997. Prior to that, he held numerous management positions during his 23-year career at The Perkin-Elmer Corporation (now known as Applera Corporation), a life science and analytical instrument company, including President and Chief Operating Officer from 1993 to 1995. Mr. Pigliucci is also a director of Epoch Biosciences, Inc., a biotechnology company, Biosphere Medical, a medical device company, and Dionex Corporation, a provider of instrumentation and related accessories and chemicals.

Herm Rosenman has served as a member of our board of directors since December 2003. Since 2001, Mr. Rosenman has served as Vice President, Finance and CFO of Gen-Probe Incorporated. From 1997 to 2000, Mr. Rosenman was President and CEO of Ultra Acquisition Corp., a holding company with interests in consumer products. From 1994 to 1997, he was President and CEO of Radnet Management, Inc., the largest provider of diagnostic imaging services in California. Mr. Rosenman, CPA, received a BBA in Accounting and Finance from Pace College, and an MBA in Finance from The Wharton School of the University of Pennsylvania.

Michael C. Venuti, Ph.D. has served as a member of our board of directors since May 2003. Dr. Venuti has been designated by Axys Pharmaceuticals, pursuant to a standstill agreement between Axys Pharmaceuticals and us, for inclusion on our management slate of board of director nominees. The standstill agreement will terminate upon the closing of this offering. Since May 2003, Dr. Venuti has been Senior Vice President of Pharmacogenomics of the Celera Genomics Group of Applera Corporation, and previously was named Senior Vice President of Research of Celera Genomics and General Manager of Celera South San Francisco when Applera acquired Axys Pharmaceuticals in November 2001. From November 1994 through November 2001, Dr. Venuti held various research management positions within Axys Pharmaceuticals and a predecessor company, Arris Pharmaceutical Corporation, and was Senior Vice President of Research and Pre-clinical Development and Chief Technical Officer of Axys Pharmaceuticals at the time it was acquired by Applera. During his employment at Axys Pharmaceuticals and Arris Pharmaceutical Corporation, Dr. Venuti was actively involved with formation and management of the combinatorial chemistry business, which was later named Axys Advanced Technologies, and which we subsequently acquired in May 2000. Dr. Venuti received an A. B. degree in Chemistry from Dartmouth College and holds a Ph.D. in Organic Chemistry from The Massachusetts Institute of Technology. Dr. Venuti completed postdoctoral training at the Institute of Organic Chemistry at Syntex Research, Palo Alto, California.

John P. Walker has served as a member of our board of directors since April 2000. Since October 2002, Mr. Walker has been Chairman of Bayhill Therapeutics, a private pharmaceutical company. From April 2002 to December 2002, Mr. Walker served as Chairman and interim Chief Executive Officer of Centaur Pharmaceutical, a pharmaceutical company. From January 2001 to October 2002, Mr. Walker was a Venture Partner at Morgan Stanley Ventures, a venture capital firm. From February 1993 to May 2001, Mr. Walker served as Chairman of Axys Pharmaceuticals and as a member of the board of directors until Axys Pharmaceuticals was acquired by Applera in

November 2001. From 1993 to January 2001, he was also Chief Executive Officer of Axys Pharmaceuticals (including service from 1993 to 1997 as CEO of Arris Pharmaceutical Corporation, a predecessor corporation of Axys Pharmaceuticals). Mr. Walker also serves as a director of Geron Corporation, a biotechnology company, in addition to serving as director of Renovis, Inc., a biopharmaceutical company. He received a B.A. from the State University of New York, at Buffalo and completed the Advanced Management program at The Kellogg School of Management at Northwestern University.

Executive Officers:

Taylor Crouch has served as our President and Chief Operating Officer since July 2002. From March 1999 to April 2002, Mr. Crouch served as President and Chief Executive Officer at Variagenics, Inc., a biotechnology company specializing in pharmacogenomics. From January 1991 to March 1999, Mr. Crouch served as the Senior Vice President of Worldwide Marketing and Strategic Development for PAREXEL International Corporation, a contract research organization. Prior to that, he held various positions for over ten years with

Schering-Plough International and Pfizer. Mr. Crouch received his B.S. in chemical engineering, cum laude, from Princeton University and his M.B.A. in international finance and marketing from The University of Chicago. He is also a Director of Bruker-AXS, a manufacturer of X-ray instrumentation.

Craig Kussman has served as our Chief Financial Officer since November 2001. From August 2000 until joining us, he served as Executive Vice President and Chief Financial Officer of SYNAVANT, Inc., a provider of pharmaceutical relationship management solutions. From July 1998 to August 2000, Mr. Kussman served as Senior Vice President, Corporate Development at IMS HEALTH, a provider of information solutions to the pharmaceutical and healthcare industries. From November 1996 to June 1998, Mr. Kussman served as Vice President, Corporate Development and also Vice President Mergers and Acquisitions of Cognizant Corp., a provider of pharmaceutical, information technology, and media information and services. From May 1991 to October 1996, Mr. Kussman served as Assistant Vice President Financial Planning of The Dun and Bradstreet Corporation, a provider of business information and technology. Mr. Kussman holds a B.A. degree cum laude in economics and mathematics from Pomona College and an M.B.A. in finance from the Wharton School of Business of the University of Pennsylvania, where he graduated with distinction.

John Lillig has served as our Chief Technology Officer since August 1999, as Vice President of our Discovery Systems since June 2001, and has been a Vice President of the Company since August 1996. From 1991 until 1996, he served as Division Manager of the Analytical Systems Division of Bio-Rad Laboratories, a provider of analytical instrumentation and clinical diagnostics. Prior to that, Mr. Lillig served in positions of increasing responsibility, including Director of Engineering, for 18 years at Beckman Instruments, a provider of life science and clinical diagnostic systems. Mr. Lillig received a B.S. in electrical engineering from California Polytechnic University.

Douglas Livingston, Ph.D. has served as our Senior Vice President and General Manager of Discovery Chemistry Services since December 2002. From July 2000 until joining us, Dr. Livingston was Vice President of Chemistry and New Technologies at Structural Genomix. From August 1999 to June 2000, Dr. Livingston served as the Director of Chemistry at the Genomics Institute of the Novartis Research Foundation and as a consultant to Discovery Partners. From January 1998 to July 1999, he was Vice President of Combinatorial Chemistry in Axys Pharmaceuticals' Advanced Technologies Division, which we acquired in 2000. From May 1996 to January 1998, Dr. Livingston served as Director of Bioorganic Chemistry for Axys Pharmaceuticals. Dr. Livingston received his undergraduate education at the University of Washington, his Ph.D. in organic synthetic chemistry from Columbia University, and completed a postdoctoral fellowship in bioorganic chemistry at the ETH-Zurich.

Urs Regenass, Ph.D. has served as our Vice President of Integrated Drug Discovery since January 2003 and was Vice President of Biology from April 2001 until January 2003. From 1999 to April 2001, Dr. Regenass was Global Head for Knowledge/Information Management at Novartis, a pharmaceutical company, and from 1994 to 1999 he was Global Head of Core Technology Area in Research, first at Ciba-Geigy, Ltd. then at Novartis, a pharmaceutical company formed by the merger of Ciba-Geigy, Ltd. and Sandoz in 1996. Dr. Regenass joined Ciba-Geigy in 1981 in Oncology and served as a project and unit head until 1994. He obtained his Ph.D. in Cell Biology and Genetics from the Biocenter, University of Basel, Switzerland and completed his postdoctoral work at Jackson Laboratory, Bar Harbor, Maine.

Richard Neale has served as our Vice President, Business Operations since November 2002. Mr. Neale joined Discovery Partners International in January 2001 through its acquisition of Systems Integrated Drug Discovery Company (SIDDCO). At the time of the acquisition he was serving as the company's Vice President, Business Operations. Prior to joining SIDDCO, he served as the Vice President of Corporate Development and General Legal Counsel at Novopharm Biotech (now Viventia), a biotechnology company with multiple clinical products. Mr. Neale previously practiced in the corporate law group in a major Toronto law firm, Davies Ward Phillips & Vineberg where he focused on mergers, acquisitions and financings. Mr. Neale holds a B.Sc. in Chemistry and Microbiology from the University of Guelph, as well as an M.B.A. and a law degree from Dalhousie University.

PRINCIPAL AND SELLING STOCKHOLDERS

Offering Background

Under the terms of an investors' rights agreement entered into in April 2000 to which we and Axys Pharmaceuticals are parties, Axys Pharmaceuticals has the right to demand that we prepare and file with the SEC a registration statement covering the resale of any or all of the shares of our common stock issued to Axys Pharmaceuticals in April 2000 in connection with our acquisition of Axys Advanced Technologies,

along with shares issuable upon exercise of a warrant that we issued to Axys Pharmaceuticals at that time.

Axys Pharmaceuticals has exercised its demand registration rights under the investors' rights agreement and requested that we register for resale in a firmly underwritten offering 7,222,000 of the shares of our common stock that we issued to Axys Pharmaceuticals in connection with the Axys Advanced Technologies acquisition. We have filed the registration statement of which this prospectus is a part to meet our obligations under the investors' rights agreement. The 7,222,000 shares being registered do not include the 200,000 shares of our common stock issuable to Axys Pharmaceuticals upon exercise of the warrant referenced above, which has an exercise price of $8.00 per share and expires in May 2005. We have registered 1,083,300 shares of our common stock under the registration statement of which this prospectus is a part for sale by us only to cover over-allotments, if any, in connection with this offering. We will not receive any proceeds of the sale of shares by Axys Pharmaceuticals.

In November 2001, Axys Pharmaceuticals was acquired by the Celera Genomics Group of Applera Corporation and is now a wholly-owned subsidiary of Applera. Applera is a publicly-traded company with shares listed on the New York Stock Exchange. Axys Pharmaceuticals has informed us that, prior to its acquisition by Applera, it had granted options to purchase 337,500 of the shares of our common stock it held to seven of its employees, including two individuals who are now members of our board of directors, Mr. Walker and Dr. Venuti. In order to permit Axys Pharmaceuticals to deliver unencumbered shares to the underwriters in connection with this offering, Applera, on behalf of Axys Pharmaceuticals, has agreed to repurchase these options from the option holders, including Mr. Walker and Dr. Venuti, immediately prior to the closing of this offering, in exchange for cash equal to the number of shares covered by the applicable option multiplied by the difference between the per share proceeds to Axys Pharmaceuticals in this offering, net of underwriting discounts and commissions, and the per share exercise price of the option. Mr. Walker and Dr. Venuti are entering into these arrangements with Applera relating to these options solely to facilitate Axys Pharmaceuticals' sale of shares in this offering, and have not influenced or prompted Applera to offer these arrangements to them. Under these agreements, Mr. Walker's and Dr. Venuti's applicable options will only be bought out if the sale of shares by Axys Pharmaceuticals contemplated by this prospectus closes, and in that event, Mr. Walker and Dr. Venuti each will report a change in beneficial ownership of shares of our common stock in accordance with applicable SEC rules and regulations.

Stock Ownership of Principal and Selling Stockholders

The following table shows information known to us with respect to the beneficial ownership of our common stock as of March 4, 2004 by:

- each person or group of affiliated persons who is known by us to own beneficially more than 5% of our common stock;
- each of our directors and nominees for director;
- our Chief Executive Officer;

- our four most highly compensated executive officers other than our Chief Executive Officer, who are referred to in the table below as our named executive officers;
- all of our directors and executive officers as a group.

With respect to each such person, entity or group, the table sets forth:

- the number and percent of shares of our common stock that such person, entity or group beneficially owned prior to this offering;
- the number of shares of our common stock, if any, being offered for resale for the account of such person, entity or group under this prospectus; and

the number and percent of shares of our common stock to be held by such person, entity or group after the offering.

To our knowledge and except as indicated in the footnotes to this table and subject to community property laws where applicable, the persons named in the table have sole voting and investment power with respect to all shares of our common stock shown as beneficially owned by them. Beneficial ownership and percentage ownership are determined in accordance with the rules of the SEC. The columns titled "Shares Beneficially Owned Prior to Offering" and "Shares Beneficially Owned After Offering" include shares of common stock subject to stock options and/or warrants, which were exercisable or will become exercisable within 60 days after March 4, 2004. These shares underlying options and/or warrants are deemed outstanding for computing the percentage of the person or group holding such options and/or warrants, but are not deemed outstanding for computing the percentage of any other person or group. The address for those persons for which an address is not otherwise indicated is: 9640 Towne Centre Drive, San Diego, California 92121.

The information in this table is based upon information supplied by the listed stockholders and Schedules 13D and 13G filed with the SEC. The applicable percentages of ownership are based on an aggregate of 24,641,607 shares of our common stock issued and outstanding as of March 4, 2004.

	Shares Beneficially Owned Prior to Offering		Number of Shares Being Offered	Shares Beneficially Owned After Offering	
	Number	Percent		Number	Percent
Selling Stockholder					
Axys Pharmaceuticals, Inc.(1)(2)	7,422,000	29.7%	7,222,000	200,000	*
Directors and Named Executive Officers					
Riccardo Pigliucci(3)	941,507	3.8	0	941,507	3.8%
Taylor Crouch(4)	335,000	1.3	0	335,000	1.3
Craig Kussman(5)	285,000	1.1	0	285,000	1.1
John Lillig(6)	141,000	*	0	141,000	*
Douglas Livingston, Ph.D.(7)	46,874	*	0	46,874	*
Sir Colin T. Dollery(8)	40,000	*	0	40,000	*
Dieter Hoehn(9)	70,000	*	0	70,000	*
Harry F. Hixson, Jr., Ph.D.(10)	35,000	*	0	35,000	*
Alan J. Lewis, Ph.D.(11)	45,000	*	0	45,000	*
Herm Rosenman		0	0		0
Michael C. Venuti, Ph.D.(12)	5,000	*	0	5,000	*
John P. Walker(13)	45,000	*	0	45,000	*
All directors and executive officers as a group (14 persons)	2,160,799	8.2	0	2,160,799	8.2
Other Five Percent Stockholders					
Heartland Advisors, Inc.(14)	2,862,757	11.6	0	2,862,757	11.6
Strong Capital Management, Inc.(15)	2,123,911	8.6	0	2,123,911	8.6
Royce & Associates LLC(16)	2,720,800	11.0	0	2,720,800	11.0

* Represents less than 1%.

(1) Consists of the 7,222,000 shares offered under this prospectus and a warrant to purchase 200,000 shares held by Axys Pharmaceuticals having an exercise price of $8.00 per share. These shares are also deemed to be beneficially owned by Applera Corporation, the parent company of Ayxs Pharmaceuticals.

(2) We have entered into a standstill agreement with Axys Pharmaceuticals pursuant to which Axys Pharmaceuticals has agreed for itself and its affiliates not to acquire any of our additional voting securities or those of our subsidiaries, and not to undertake any proxy contest. The agreement gives Axys Pharmaceuticals the right to select designees to be included on, and requires Axys Pharmaceuticals to vote for, our management slate of directors each year. Upon the closing of this offering, the standstill agreement will terminate. Axys Pharmaceuticals' business address is 180 Kimball Way, South San Francisco, CA 94080.

(3) Includes 250,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of March 4, 2004.

(4) Includes 300,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of March 4, 2004.

(5) Includes 250,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of March 4, 2004.

(6) Includes 120,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of March 4, 2004.

(7) Consists of 46,874 shares of common stock issuable upon exercise of stock options exercisable within 60 days of March 4, 2004.

(8) Consists of 40,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of March 4, 2004.

(9) Includes 45,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of March 4, 2004.

(10) Consists of 35,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of March 4, 2004.

(11) Consists of 45,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of March 4, 2004.

(12) Does not include an option to purchase 75,000 shares of common stock granted by Axys Pharmaceuticals to Dr. Venuti as a result of a compensation plan implemented by Axys Pharmaceuticals, which option is being bought out by Applera in connection with this offering, as described above. Includes 5,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of March 4, 2004.

(13) Does not include an option to purchase 84,375 shares of common stock granted by Axys Pharmaceuticals to Mr. Walker as a result of a compensation plan implemented by Axys Pharmaceuticals, which option is being bought out by Applera in connection with this offering, as described above. Includes 45,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of March 4, 2004.

(14) Based on information reported in a Form 13G filed with the Securities and Exchange Commission on February 12, 2004. These 2,862,757 shares held by Heartland Advisors, Inc. may also be deemed beneficially owned by William J. Nasgovitz as a result of his ownership interest in Heartland Advisors, Inc. The stockholder's business address is 789 North Water Street, Milwaukee, WI 53202. Heartland Advisors, Inc and William J. Nasgovitz have shared voting power over 2,393,846 shares and shared dispositive power over 2,862,757 shares.

(15) Based on information reported in a Form 13G filed with the Securities and Exchange Commission on February 17, 2004. These 2,123,911 shares held by Strong Capital Management, Inc. also may be deemed beneficially owned by Richard S. Strong as a result of his position with and stock ownership of Strong Financial Corporation. The stockholder's business address is 100 Heritage Reserve, Menomonee Falls, WI 53051. Strong Capital Management, Inc. and Richard S. Strong have shared voting power over 2,123,911 shares and shared dispositive power over 2,123,911 shares.

(16) The stockholder's business address is 1414 Avenue of the Americas, New York, NY 10019. Royce & Associates LLC has sole voting power over the shares.

CERTAIN UNITED STATES FEDERAL INCOME TAX CONSIDERATIONS

The following discussion of certain United States federal income tax considerations is for general information only. Accordingly, all prospective holders of our common stock are urged to consult their own tax advisors with respect to the U.S. federal, state, local and foreign tax consequences of the acquisition, ownership and disposition of our common stock.

As used in this prospectus, the term "U.S. Holder" is a person who is a beneficial owner of our common stock and who is:

a citizen or resident of the United States;

a corporation or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state of the United States, or the District of Columbia;

an estate, the income of which is includible in gross income for United States federal income tax purposes regardless of its source; or

a trust subject to the primary supervision of a United States court and the control of one or more United States persons, or a trust, other than a wholly owned grantor trust, that was treated as a domestic trust despite not meeting the requirements described above.

The term "Non-U.S. Holder" means a beneficial owner of our common stock who is not a U.S. Holder.

This discussion does not consider:

state, local or foreign tax consequences;

the tax consequences for the stockholders, beneficiaries or holders of other beneficial interests in a Non-U.S. Holder;

special tax rules that may apply to selected holders, including without limitation, partnerships, holders of interests in domestic or foreign partnerships, banks or other financial institutions, insurance companies, dealers in securities, traders in securities, tax-exempt entities and United States expatriates; or

special tax rules that may apply to a holder that holds our common stock as part of a straddle, hedge, conversion, synthetic security, or constructive sale transaction for United States federal income tax purposes, or a holder that does not hold our common stock as a capital asset within the meaning of Section 1221 of the United States Internal Revenue Code of 1986, as amended, also known as the Code.

The following discussion is based on provisions of the Code, applicable Treasury regulations and administrative and judicial interpretations, all as of the date of this prospectus, and all of which are subject to change, retroactively or prospectively. We have neither requested a ruling from the United States Internal Revenue Service nor received an opinion of counsel concerning the tax consequences of holding or disposing of our common stock.

U.S. Holders

Dividends

We do not anticipate paying cash dividends on our common stock in the foreseeable future. In the event, however, that dividends are paid in cash or property on shares of our common stock, those payments will constitute dividends for United States tax purposes to the extent paid from our current and accumulated earnings and profits, as determined under United States federal income tax principles. To the extent those payments exceed our current and accumulated earnings and profits, the payments

will constitute a return of capital and will first reduce a holder's basis, but not below zero, and then will be treated as gain from the sale of stock. Any such dividend will be eligible for the dividends-received deduction, if received by a qualifying corporate U.S. Holder that meets the holding period and other requirements for the dividends-received deduction.

Recently enacted legislation reduces to 15%, the maximum U.S. federal income tax rate for certain dividends received by noncorporate taxpayers through taxable years beginning on or before December 31, 2008, so long as certain holding period requirements are met. Unless continuing legislation is enacted, dividends received by noncorporate taxpayers in taxable years beginning after December 31, 2008 will not benefit from this reduction in U.S. federal income tax rates and will thereafter be taxed as ordinary income subject to the U.S. Holder's applicable federal income tax rate.

Gain on Disposition of Common Stock

Upon a sale, exchange or other disposition of our common stock, a U.S. Holder will recognize capital gain or loss in an amount equal to the difference between the amount realized and such U.S. Holder's adjusted tax basis in the common stock. Recently enacted legislation generally reduces to 15% the maximum U.S. federal income tax rate on capital gains recognized by noncorporate taxpayers on the sale, exchange or other disposition of our common stock held for more than one year, through taxable years beginning on or before December 31, 2008. The deductibility of capital losses is subject to limitations. Unless continuing legislation is enacted, sales, exchanges or other dispositions of our common stock by noncorporate taxpayers in taxable years beginning after December 31, 2008 will not benefit from this reduction in U.S. federal income tax rates and will be taxed at a 20% maximum U.S. federal income tax rate.

Information Reporting and Backup Withholding Tax

In general, payments made to a U.S. Holder on or with respect to our common stock will be subject to information reporting. Certain U.S. Holders may be subject to backup withholding tax, at a rate of 28% for 2004, on payments made on or with respect to our common stock if such U.S. Holder fails to supply a correct taxpayer identification number or otherwise fails to comply with applicable U.S. information reporting or certification requirements. Certain persons are exempt from backup withholding, including, in certain circumstances, corporations and financial institutions. Any amounts withheld under the backup withholding rules from a payment to a U.S. Holder will be allowed as a refund or a credit against such U.S. Holder's U.S. federal income tax liability, provided that the required procedures are followed.

Non-U.S. Holders

Dividends

We do not anticipate paying cash dividends on our common stock in the foreseeable future. In the event, however, that dividends are paid in cash or property on shares of our common stock, those payments will constitute dividends for United States tax purposes to the extent paid from our current and accumulated earnings and profits, as determined under United States federal income tax principles. To the extent those payments exceed our current and accumulated earnings and profits, the payments will constitute a return of capital and will first reduce a holder's basis, but not below zero, and then will be treated as gain from the sale of stock. Dividends paid to a Non-U.S. Holder, out of earnings and profits, generally will be subject to withholding of United States federal tax at a 30% rate on the gross amount of the distribution or such lower rate as may be provided by an applicable income tax treaty.

Dividends that are effectively connected with a Non-U.S. Holder's conduct of a trade or business in the United States or attributable to a permanent establishment in the United States under an

applicable income tax treaty, known as "United States trade or business income," are generally not subject to the 30% withholding tax if the Non-U.S. Holder files the appropriate United States Internal Revenue Service form with the payor. However, such United States trade or business income, net of specified deductions and credits, is taxed at the same graduated rates applicable to United States persons. Any United States trade or business income received by a Non-U.S. Holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as specified by an applicable income tax treaty.

A Non-U.S. Holder of our common stock who claims the benefit of an applicable income tax treaty generally will be required to satisfy applicable certification and other requirements. Non-U.S. Holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A Non-U.S. Holder that is eligible for a reduced rate of United States withholding tax or other exclusion from withholding under an income tax treaty may obtain a refund or credit of any excess amounts withheld by filing an appropriate claim for a refund with the United States Internal Revenue Service.

Gain on Disposition of Common Stock

A Non-U.S. Holder generally will not be subject to United States federal income tax in respect of gain recognized on a disposition of our common stock unless:

- the gain is United States trade or business income, in which case the regular income tax and, in the case of a corporate Non-U.S. Holder, the branch profits tax described above may apply;
- the Non-U.S. Holder is an individual who is present in the United States for more than 182 days in the taxable year of the disposition and meets other requirements; or
- we are, or have been, a "United States real property holding corporation" for United States federal income tax purposes at any time during the shorter of the five-year period ending on the date of disposition or the period that the Non-U.S. Holder held our common stock.

Generally, a corporation is a "United States real property holding corporation" if the fair market value of its "United States real property interests" equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. We believe we have never been, are not currently, and are not likely to become a United States real property holding corporation for United States federal income tax purposes.

Information Reporting and Backup Withholding Tax

We must report annually to the United States Internal Revenue Service and to each Non-U.S. Holder, the amount of dividends paid to such holder and the tax withheld with respect to such dividends. Copies of the information returns reporting dividends and withholding may also be made available to the tax authorities in the country in which the Non-U.S. Holder is a resident under the provisions of an applicable income tax treaty or agreement.

Under certain circumstances, United States Treasury Regulations require information reporting and backup withholding tax on specified payments on our common stock. A Non-U.S. Holder of our common stock that fails to certify, under penalties of perjury, its Non-U.S. Holder status in accordance with applicable United States Treasury Regulations may be subject to backup withholding tax.

The payment of the proceeds of the disposition of our common stock by a holder to or through a United States office of a broker, or through a foreign office of a broker who is a United States person or a "United States related person", as defined below, generally will be subject to information reporting and backup withholding tax unless the holder provides the requisite certification of status as a

Non-U.S. Holder, the broker has documentary evidence in its files that the holder is a Non-U.S. Holder and the broker has no actual knowledge, or reason to know, to the contrary or another exemption is established. For this purpose, a "United States related person" is:

- a "controlled foreign corporation" for United States federal income tax purposes;
- a foreign partnership if, at any time during its taxable year, (A) United States persons own more than 50% of the income or capital interests in the partnership, or (B) the partnership is engaged in a United States trade or business;
- a foreign person, 50% or more of whose gross income from all sources for the three-year period ending with the close of its taxable year preceding the payment, (or for such part of the period that the person has been in existence), effectively connected with the conduct of a United States trade or business; or
- some U.S. branches of foreign banks or insurance companies.

Any amounts withheld under the backup withholding rules from a payment to a Non-U.S. Holder that result in an overpayment of taxes will be refunded, or credited against the holder's United States federal income tax liability, if any, provided that the required information is furnished to the United States Internal Revenue Service.

UNDERWRITING

We, Axys Pharmaceuticals and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to the terms and conditions of the underwriting agreement, the underwriters named below have severally agreed to purchase from Axys Pharmaceuticals the number of shares of our common stock set forth opposite their names on the table below at the public offering price, less the underwriting discounts and commissions set forth on the cover page of this prospectus, as follows:

Name	Number of Shares
SG Cowen Securities Corporation	
Merriman Curhan Ford & Co.	
Roth Capital Partners, LLC	
Total	7,222,000

The underwriting agreement provides that the obligations of the underwriters to purchase the shares of common stock offered hereby are conditional and may be terminated upon the occurrence of certain events specified in the underwriting agreement. The underwriters are severally committed to purchase all of the shares of common stock being offered by Axys Pharmaceuticals if any shares are purchased.

The underwriters propose to offer the shares of common stock to the public at the public offering price set forth on the cover of this prospectus. The underwriters may offer the common stock to securities dealers at the price to the public less a concession not in excess of $ per share. Securities dealers may reallow a concession not in excess of $ per share to other dealers. After the shares of common stock are released for sale to the public, the underwriters may vary the offering price and other selling terms from time to time.

We have granted to the underwriters an option, exercisable not later than 30 days after the date of this prospectus, to purchase up to an aggregate of 1,083,300 additional shares of common stock at the public offering price set forth on the cover page of this prospectus less the underwriting discounts and commissions. The underwriters may exercise this option only to cover over-allotments, if any, made in connection with the sale of common stock offered hereby. If the over-allotment option is exercised in full, the underwriters will purchase additional common shares from us in approximately the same proportion as shown in the table above.

The following table summarizes the compensation to be paid to the underwriters by Axys Pharmaceuticals and us, and the proceeds, before expenses, payable to Axys Pharmaceuticals and us. We will not pay any such compensation to the underwriters or receive any such proceeds unless the

over-allotment option is exercised by the underwriters. We will not receive any proceeds from the offering of shares by Axys Pharmaceuticals under this prospectus.

	Total

	Per Share	Total Without Over-Allotment	Total With Over-Allotment
Public offering price			
Underwriting discount			
Proceeds, before expenses, to selling stockholder			
Proceeds, before expenses, to us			

We estimate that the total expenses of this offering, excluding underwriting discounts and commissions, will be approximately $450,000. Pursuant to the terms of an investors' rights agreement entered into in April 2000 to which we and Axys Pharmaceuticals are parties, all of these expenses are payable by Axys Pharmaceuticals.

We and Axys Pharmaceuticals have agreed to indemnify the underwriters against certain civil liabilities, including liabilities under the Securities Act of 1933, and to contribute to payments the underwriters may be required to make in respect of any such liabilities.

Our directors and executive officers and Axys Pharmaceuticals have agreed with the underwriters that, for a period of 90 days beginning on the date of this prospectus, they will not offer, sell, assign, transfer, pledge, contract to sell or otherwise dispose of or hedge any shares of our common stock or any securities convertible into or exchangeable for shares of our common stock, other than the shares being sold pursuant to this offering. Such shares may be transferred, however, by gift or for estate planning purposes if the transferee agrees to be bound by those restrictions. The underwriters may, in their sole discretion, at any time without prior notice, release all or any portion of the shares from the restrictions in any such agreement. We have entered into a similar agreement with the underwriters provided we may, without the consent of the underwriters, (i) grant options and sell shares pursuant to our employee benefit plans as currently in existence and (ii) issue shares pursuant to currently outstanding options, warrants or rights. There are no agreements between the underwriters and any of our directors and executive officers or Axys Pharmaceuticals releasing them from these lock-up agreements prior to the expiration of the 90-day period.

The underwriters may engage in over-allotment, stabilizing transactions, syndicate covering transactions, penalty bids and passive market making in accordance with Regulation M under the Securities Exchange Act of 1934, as amended. Over-allotment involves syndicate sales in excess of the offering size, which creates a syndicate short position. Covered short sales are sales made in an amount not greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters may close out a covered short sale by exercising its over-allotment option or purchasing shares in the open market. Naked short sales are sales made in an amount in excess of the number of shares available under the over-allotment option. The underwriters must close out any naked short sale by purchasing shares in the open market. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Syndicate covering transactions involve purchases of the shares of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. Penalty bids permit the representatives of the underwriters to reclaim a selling concession from a syndicate member when the shares of common stock originally sold by such syndicate member are purchased in a syndicate covering transaction to cover syndicate short positions. Penalty bids may have the effect of deterring syndicate members from selling to people who have a history of quickly selling their shares. In passive market making, market makers in the shares of our common stock who are underwriters or prospective underwriters may, subject to certain limitations, make bids for or purchases of the shares of

common stock until the time, if any, at which a stabilizing bid is made. These stabilizing transactions, syndicate covering transactions and penalty bids may cause the price of the shares of our common stock to be higher than it would otherwise be in the absence of these transactions. These transactions may be commenced and discontinued at any time.

A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering. The representatives of the underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us, Axys Pharmaceuticals or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

SG Cowen Securities Corporation provides financial advisory services to us from time to time in the ordinary course of its business, for which we pay customary compensation.

LEGAL MATTERS

Cooley Godward LLP, San Diego, California will pass upon the validity of the common stock offered by this prospectus. Certain legal matters will be passed upon for the selling stockholder by Paul, Hastings, Janofsky & Walker LLP. Certain legal matters will be passed upon for the underwriters by Morrison & Foerster LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent auditors, have audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2003 as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's web site at http://www.sec.gov. You may also read and copy any document we file with the SEC at the SEC's public reference room at 450 Fifth Street, N.W., Washington, D.C. 20549. You may obtain information on the operation of the SEC's public reference room by calling the SEC at 1-800-SEC-0330. Our file number under the Securities Exchange Act of 1934, as amended, is 000-31141.

The SEC allows us to incorporate by reference into this prospectus the information in documents we file with it, which means that we can disclose important information to you by referring you to those documents. Any statement contained herein or in any document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded, for purposes of this prospectus, to the extent that a statement contained in or omitted from this prospectus, or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein, modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus. We incorporate by reference all documents that we file with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, after the date of this prospectus and before the termination of the offering of the common stock offered in this prospectus, which documents shall be deemed incorporated by reference into this prospectus and to be a part of this prospectus from the respective date of filing such documents, and the documents listed below:

- Our Form 10-K for the fiscal year ended December 31, 2003, which was filed on March 10, 2004; and
- the description of our common stock, including related rights to purchase shares of our Series A Junior Participating preferred stock, contained in our registration statements on Form 8-A dated July 25, 2000 and February 24, 2003.

You may request a copy of these filings at no cost, by writing or telephoning us at the following address:

Discovery Partners International, Inc.
9640 Towne Centre Drive
San Diego, CA 92121
(858) 455-8600
Attention: Craig Kussman, Chief Financial Officer

We have filed with the SEC a registration statement on Form S-3 under the Securities Act covering the common stock described in this prospectus. This prospectus does not contain all of the information included in the registration statement, some of which is contained in exhibits

included with or incorporated by reference into the registration statement. The registration statement, including the exhibits contained or incorporated by reference therein, can be read at the SEC web site or at the SEC office referred to above. Any statement made in this prospectus concerning the contents of any contract, agreement or other document is only a summary of the actual contract, agreement or other document. If we have filed or incorporated by reference any contract, agreement or other document as an exhibit to the registration statement, you should read the exhibit for a more complete understanding of the document or matter involved. Each statement regarding a contract, agreement or other document is qualified in its entirety by reference to the actual document.

7,222,000 Shares

Common Stock

PROSPECTUS

SG Cowen

Merriman Curhan Ford & Co.

Roth Capital Partners

, 2004

QuickLinks

TABLE OF CONTENTS
PROSPECTUS SUMMARY
RISK FACTORS
FORWARD-LOOKING INFORMATION
USE OF PROCEEDS
PRICE RANGE OF COMMON STOCK
SELECTED CONSOLIDATED FINANCIAL DATA
MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS
BUSINESS
MANAGEMENT

PRINCIPAL AND SELLING STOCKHOLDERS
CERTAIN UNITED STATES FEDERAL INCOME TAX CONSIDERATIONS
UNDERWRITING
LEGAL MATTERS
EXPERTS
WHERE YOU CAN FIND ADDITIONAL INFORMATION